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Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Chemical Review Committee
Seventeenth meeting
Rome (online), 20–24 September 2021
Item 4 (b) (vi) of the provisional agenda*

Technical work: review of notifications of final regulatory action: terbufos

Terbufos: supporting documentation provided by Mozambique

Note by the Secretariat

As is mentioned in the note by the Secretariat on terbufos: notifications of final regulatory action (UNEP/FAO/RC/CRC.17/8/Rev.1), the annex to the present note sets out documentation provided by Mozambique to support its notification of final regulatory action for terbufos in the pesticide category. The present note, including its annex, has not been formally edited.

* UNEP/FAO/RC/CRC.17/1.

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Annex

Terbufos: supporting documentation provided by Mozambique

List of documents:

1. Deliberacao Nr. 001/DNSA/2014 - National Directorate of Agriculture and Agrarian Services (The Pesticide Register Authority) in Portuguese and English.

2. Come A.M. & van der Valk H., 2014. Reducing Risks of Highly Hazardous Pesticides in Mozambique: Step 1 – Shortlisting highly hazardous pesticides Consultancy report undertaken under the Project EP/MOZ/101/UEP.

3. Come A.M.; Dona L.L.; Mancini F. & van der Valk H., 2014. Reducing Risks of Highly Hazardous Pesticides in Mozambique: Step 2 – Survey of pesticide use practices in selected cropping systems.

4. FAO/WHO (2008) Report of the 2nd Joint Meeting on Pesticide Management and the 4th Session of the FAO Panel of Experts on Pesticide Management. 6-8 October 2008, Geneva. Food and Agriculture Organization of the United Nations, Rome & World Health Organization, Geneva. http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/Code/Report.pdf (p.14 – 18).

5. Lahr J., R. Kruijne & J. Groenwold, 2014. Hazards of pesticides imported into Mozambique, 2002-2011. Wageningen, Alterra Wageningen UR (University & Research centre).

6. Pesticides Properties Database (PPDB): https://sitem.herts.ac.uk/aeru/ppdb/en/Reports/621.htm (abstract).

7. JMPR evaluation on Terbufos, 2005 - http://www.fao.org/fileadmin/templates/agphome/documents/Pests_Pesticides/JMPR/Evaluation05/2005_Terbufos1.pdf.

8. IPCS-INCHEM International Programme on Chemical Safety -Pesticide residues in food - 2003 - Joint FAO/WHO Meeting on Pesticide Residues TERBUFOS – Toxicological studies,http://www.inchem.org/documents/jmpr/jmpmono/v2003pr13.htm#tox (abstract).

República de Moçambique

MINISTÉRIO DA AGRICULTURA
DIRECÇÃO NACIONAL DE SERVIÇOS AGRÁRIOS

Deliberação Nº 001/DNSA/2014

OS pesticidas são produtos usados para a preservação das culturas e seus produtos contra diferentes pragas. Estes produtos, são por sua natureza tóxica e o uso indevido do mesmo pode perigar a saúde Humana, Animal e danificar o meio ambiente. Deste grupo de químicos, existem alguns que são considerados Altamente Perigoso. O Projecto de Redução dos de Riscos de Pesticidas Altamente Perigosos identificou os Pesticidas Altamente Perigosos que estão registados em Moçambique e depois de auscultar diferentes intervenientes (sector público, sector privado, sociedade civil e outros) conclui-se que para alguns deles dever-se-ia fazer o cancelamento imediato do registo e consequente não aprovação do seu uso em Moçambique e para outros o registo deveria ser cancelado no final do ano. Existe um outro grupo que carece de maior análise antes da tomada de decisão.

Desta forma e usando das competências atribuídas no artigo 3, coadjuvado com o artigo 1 e 4 de Decreto 6/2009 de 31 de Março a DNSA determina:

1. O Cancelamento imediato de todos os pesticidas que contenham as seguintes substâncias activas:

    a. Alachlor
    b. Aldicarb
    c. Carbendazim
    d. Carbofuran
    e. Diafenthiuron
    f. Diazinon (> 300 g/L)
    g. Diclofop–methyl
    h. Difenacoum
    i. Ethion
    j. Fenamiphos
    k. Iprodione
    l. Furfural
    m. Methidathion
    n. Methiocarb
    o. Monocrotophos
    p. Terbufos

DNSA-Rua da Resistência,Nr. 1746, Segundo Andar E-mail- dnsa.minag@gmail.com
Endereço Postal: DNSA, Caixa Postal 2272, Maputo-Moçambique;
Fax: (258)21 415103, Telefone: (258) 21415110

q. Thiodicarb
r. Zinc phosphide
s. Brodifacoum (formulações líquidas – 0.75 & 2.5 g/L)
t. Difethialone
u. Methamidophos
v. Benomyl
w. Methomyl 900 g/kg
x. Chlorfenvinphos
y. Carbaryl
z. Oxyfluorfen

2. Cancelamento à 31 de Dezembro de 2014 de todos os produtos que contenham as substâncias activas:

   a. 2,4-D dimethylamine
   b. Paraquat
   c. Endosulfão
   d. Diuron

3. Os produtos que contenham as substâncias activas listadas nos números 1 e 2 importados antes do cancelamento dos mesmos podem continuar a ser usados estando dentro do prazo de validade.

Maputo aos 15 de Julho de 2014

O Director Nacional

Mahomed Rafik Valá
(Tecnico Superior Agro-Pec de N1)

KC/19/10/2014

DNSA-Rua da Resistência,Nr. 1746, Segundo Andar E-mail- dnsa.minag@gmail.com
Endereço Postal: DNSA, Caixa Postal 2272, Maputo-Moçambique;
Fax: (258)21 415103, Telefone: (258) 21415110

Republic de Mozambique

MINISTRY OF AGRICULTURE

N N. 00I / DNSA / 2014

National Directorate of Agrarian Services

Deliberation N. 00I / DNSA / 2014

Pesticides are products used for the protection of crops and their products against different pests.

These products are by their nature toxic and their improper use can damage human health, animal health and damage the environment. among this group of chemicals, there are some that are considered Highly Hazardous. The project of Risk Reduction of Highly Hazardous Pesticides identified Highly Hazardous Pesticides that are registered in Mozambique and after consulting with different actors (public sector, private sector, civil society and others) it has been concluded that: for some of them the immediate cancellation of registration and consequent non-approval of their use in Mozambique should be done while for others the registration should be cancelled at the end of the year. There is another group for which further analysis is needed before taking the decision

In this way and using the competences assigned by article 3, in conjunction with article I and 4 of Decree 6/2009 of March 31, DNSA determines:

l. The immediate cancellation of all pesticides containing the following active substances:

Alachlor
Aldicarb
Carbendazim
Carbofuran
Diafenthiuron
Diazinon 300 g / L)
Diclofop-methyl
Difenacoum
Ethion
Fenamiphos
Iprodione
Furfural
Methidathion
Methiocarb
Monocrotophos
Terbufos
Thiodicarb
Zinc phosphide
Brodifacoum (liquid formulations -0.75 & 2.5 g/L)
Difethialone
Methamidophos
Benomyl
Methomyl 900 g/kg
Chlorfenvinphos
Carbaryl
Oxyfluorfen

II. Cancellation as of 31 December 2014 of all the products containing the active substances:

2,4-D dimethylamine
Paraquat
Endosulfan
Diuron

III. Products containing the active substances listed in N. 1 and 2 imported before theircancellation can continue to be used as long as they are within the validity period.

Maputo on July 15, 2014

The National Director

Dahomgd Rafikö

Reducing Risks of Highly Hazardous Pesticides in Mozambique

Step 1 – Shortlisting highly hazardous pesticides

Armando Marcos W. Come
Harold van der Valk

[final – 5 May 2014]

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With financial support from the SAICM Quick Start Programme

Acknowledgements

This study was conducted within the framework of Project EP/MOZ/101/UEP – *Reducing Risks of Highly Hazardous Pesticides in Mozambique*. The project is funded by the Quick Start Program of the Strategic Approach to International Chemicals Management (SAICM), the Food and Agriculture Organization of the United Nations and the Government of Mozambique.

The authors would like to gratefully acknowledge the information provided and the contributions made to this study by Ida Chongo and Marcelina Xavier (Ministry of Agriculture), Khalid Cassam and Francesca Mancini (FAO), Kimberly Nesci and Cathleen Barnes (US Environmental Protection Agency),

FAO Disclaimer

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1. Introduction

1.1 Project background

Pesticides are widely used in most areas of crop production in Mozambique to minimize infestations by pests and thus protect crops from potential yield losses and reduction of product quality. They are also widely applied for public health purposes, e.g. in malaria control.

The average annual volume of pesticide imports into Mozambique is approximately 1800 tonnes of formulated products (Figure 1). The import value of these pesticides is estimated, over the last three years, to be at least 495 million Meticais, or 16.6 million $US. An almost five-fold increase in pesticide imports has occurred in Mozambique since the 2003, well above world averages.

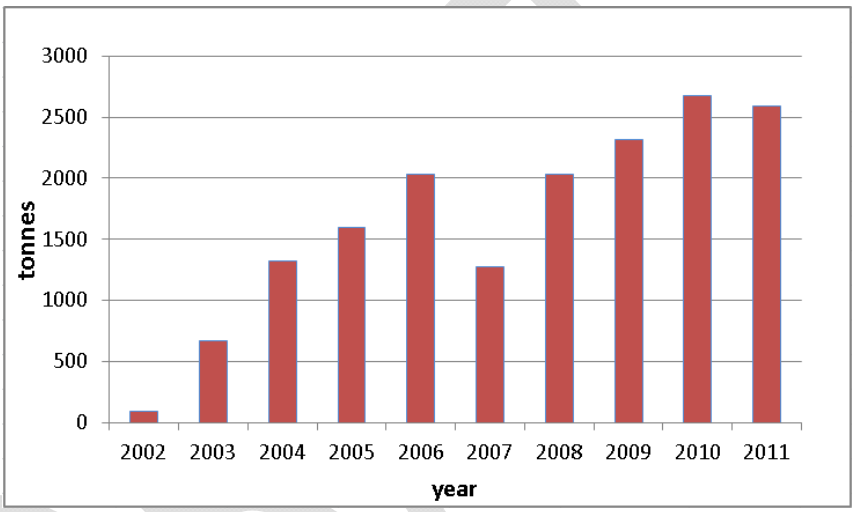

Figure 1. Annual imports of formulated pesticides into Mozambique between 2002 and 2011 (metric tons). Note that the data for 2002 are incomplete. (source: Lahr et al., 2014 based on Ministry of Agriculture statistics)

The large majority of pesticides, about 85%, are imported into Mozambique by private sector distributors and retailers, reflecting major change since the 1980s when pesticides were imported by a single state-run company. The remaining 15% of pesticides are imported directly by commercial farms, by commodity companies, and by various smaller importers. Direct pesticide imports by the state are now virtually non-existent, and state-funded imports are mainly limited to pesticides bought by the Ministry of Health for vector control and by INCAJU for cashew production.

A large part of pesticide distribution to end-users is conducted by private sector distributors and retailers, although exact figures are not available. Furthermore, private distributors deliver the pesticides they import to commodity companies which in turn will distribute the products to end-user farmers. This occurs mostly in cotton and to a smaller extent in tobacco. The private sector may also deliver pesticides to government structures who then distribute them to end-users. This is the case for INCAJU, which distributes pesticides to cashew farmers, and for the Ministry of Health, which distributes a part of the pesticides it orders to community groups to carry out mosquito control. In total, distribution by government structures represented less than 8% of the total pesticides imports.

Pesticide use may have benefits for different stakeholders, not only of farmers or consumers, but also of the society as a whole. At the same time, there is evidence of both direct and indirect risks involved in the use of these chemical substances both for humans and the environment. These risks will vary in importance (i.e. size, duration, extent, acceptability) depending on the type of pesticide and the specific use situation. Risk mitigation measures should be developed for all risks that are considered by the national regulatory authority to be unacceptable. However, given limited human and financial resources in many countries, and also in Mozambique, it may be more cost-effective to focus first on those pesticides and use situations that pose the highest risks and which are considered unacceptable by all relevant stakeholders.

Therefore, with the goal of reducing the greatest risks associated with pesticide use in Mozambique, a project entitled *Reducing Risks of Highly Hazardous Pesticides (HHPs) in Mozambique* was initiated by the Government of Mozambique, with the technical support of FAO's Pesticides Management Unit, and funded by SAICM Quick Start Programme Trust Fund. Its ultimate goal is to develop and implement an "HHP Risk Reduction Action Plan" in Mozambique for the most dangerous pesticides and use situations, resulting over time in the implementation of a variety of risk reduction measures based on a review of use conditions. These could include the cancellation of specific registrations of HHPs, implementation of risk mitigation measures, appropriate use restrictions, development of alternative pest management strategies, promotion of good agricultural practices, and possible phase-out of specific pesticides.

1.2 National and international policy framework

1.2.1 National framework

The major national legislative basis for pesticide distribution use in Mozambique is the Pesticide Management Regulation published under Decree 6/2009 of 31 March 2009 (RepMoz, 2009). The main objective of this Regulation, as laid out in its Article 2.1, is "*to ensure that all processes that involve working with or handling pesticides are executed without prejudice to public, animal and environmental health*". The Regulation further stipulates, in its Article 14, that pesticides will not be approved for use in Mozambique if, among others:

- the pesticide has unacceptable effects on organisms that are intended to be protected;
- the normal and recommended use of the pesticide has the potential to affect negatively human and/or animal health;
- the pesticide causes an unacceptable negative impact on the environment, particularly soil and water contamination, or affects organisms that are not targeted.

This clearly sets the boundaries within which the regulatory authorities in Mozambique can authorize a pesticide for use in the country.

In addition to the Pesticides Management Regulation, environmental, public health and labour legislation further defines the acceptability of risks of chemicals in general, and pesticides in particular, in Mozambique.

1.2.2 International framework

The International Code of Conduct on the Distribution and Use of Pesticides (FAO, 2002) describes the shared responsibility of many sectors of society to work together so that the

benefits to be derived from the necessary and acceptable use of pesticides are achieved without significant adverse effects on human health or the environment.

With respect to the availability and use of pesticides in a country, the Code stipulates in its Article 7, among others, that:

- Responsible authorities should give special attention to drafting rules and regulations on the availability of pesticides. These should be compatible with existing levels of user training and expertise. The parameters on which such decisions on availability are based vary widely and must be left to the discretion of each government.
- Two methods of restricting availability can be exercised by the responsible authority: not registering a product or, as a condition of registration, restricting the availability to certain groups of users in accordance with a national assessment of the hazards involved in the use of the product.
- Prohibition of the importation, sale and purchase of highly toxic and hazardous products, such as those included in WHO classes Ia and Ib, may be desirable if other control measures or good marketing practices are insufficient to ensure that the product can be handled with acceptable risk to the user.

For these reasons, pesticide risk reduction is one of the priority areas of FAO's pesticide management program.

At the request of the Committee on Agriculture (COAG), one of the governing bodies of FAO, the FAO/WHO Joint Meeting on Pesticide Management (JMPM) was asked in 2007 to provide guidance to FAO on the options to define highly hazardous pesticides (HHPs), beyond the definition provided in Article 7 of the Code, as well as on activities that could be initiated to reduce their risks. The JMPM defined on which basis HHPs could be identified (see Chapter 2.1 and FAO/WHO, 2008). The JMPM also recommended, as a general principle, that HHPs should not be registered for use unless:

i. governments establish a clear need;

ii. no alternatives, based on a risk–benefit analysis, are available; and

iii. control measures as well as good marketing practices are sufficient to ensure that the product can be handled with acceptable risk to human health and the environment.

In conjunction with these considerations, the Rotterdam Convention on the Prior Informed Consent (PIC) Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (Rotterdam, 2009) demonstrates the commitment of FAO and UNEP to address challenges associate with highly hazardous and other pesticide use in Mozambique and other developing countries. Information available on banned or severely restricted pesticides under PIC helps strengthen national decision making on pesticides. The PIC procedure assists countries like Mozambique in avoiding imports of hazardous chemicals that they cannot manage safely under national conditions of use. As such, the Convention helps to prevent incidents before they occur, serving as an early warning system or first line of defence, internationally, that helps keep countries apprised of actions that are being taken by other countries in dealing with problematic chemicals.

These and other efforts, internationally, provide a framework for strengthened pesticide management actions on the ground, in countries such as Mozambique. And in return, as projects such as this one go forward, they contribute to achieving the overall objective of the Strategic Approach to International Chemicals Management (SAICM), which is the sound management of chemicals throughout their life cycle so that, by 2020, chemicals are used and produced in ways that lead to the minimization of significant adverse effects on human health and the environment.

1.3 The project

1.3.1 Objectives

The main objectives of the project are to:

- Identify pesticides and pesticide use situations which can be considered highly hazardous under Mozambican conditions.
- Elaborate a plan of action to reduce the risks posed by these highly hazardous pesticides.
- Initiate implementation of priority risk reduction activities.
- Review the results of priority risk reduction activities.
- Develop mid- and longer-term policies, programmes and projects to reduce the risk of highly hazardous pesticides.

1.3.2 Approach

The project is organized in five key steps, which are:

- **Step 1** will develop a database of pesticide products presently registered and legally imported to the country in the last 3 years, review Mozambique's registered pesticides against the JMPM criteria for HHPs, identify a list of HHPs being used within the country and development of survey methodology to be used in step 2.
- **Step 2** will conduct field surveys for the identified HHPs, to assess actual use and exposure under local conditions in Mozambique, as well as additional hazard and risk assessments as appropriate.

  On the basis of Steps 1 and 2, HHPs and cropping systems (or use situations) that require risk reduction measures will be identified.
- **Step 3** will develop Risk Reduction Action Plans, with the government and other relevant stakeholders, for HHPs and cropping systems or use situations where risks to human health and/or the environment are likely to be unacceptable.
- **Step 4** will focus on initial implementation of the Action Plans, with the national government, local communities, private/corporate sector, farmers, NGOs/CSOs, academia, scientific and technical community, and other relevant stakeholders carrying out a variety of risk activities both within the scope of this project, as well as in the longer term; and
- **Step 5** will review the Action Plan results achieved, make recommendations going forward, and evaluate the project.

This report specifically covers Step 1 of the project. Its main objective is to provide a short-list of HHPs on which to focus field surveys and hazard/risk assessments in Step 2.

The different activities in Steps 1 and 2 are outlined in Figure 2. They include:

i. Evaluation of all pesticides registered in Mozambique against the JMPM criteria.

ii. Elaboration of a list of HHPs and of pesticides "coming close" to HHPs (see Chapter 2 for more information).

iii. Evaluation of pesticide import statistics for Mozambique to assess which HHPs are presently being used in the country.

iv. Elaboration of a short-list of HHPs which will be further assessed through field surveys and hazard/risk assessments

The ultimate goal of Steps 1 and 2 is to define a list of HHPs, cropping systems and pesticide use situations which would require risk reduction, and for which Risk Reduction Action Plans will be developed under Step 3 of the project.

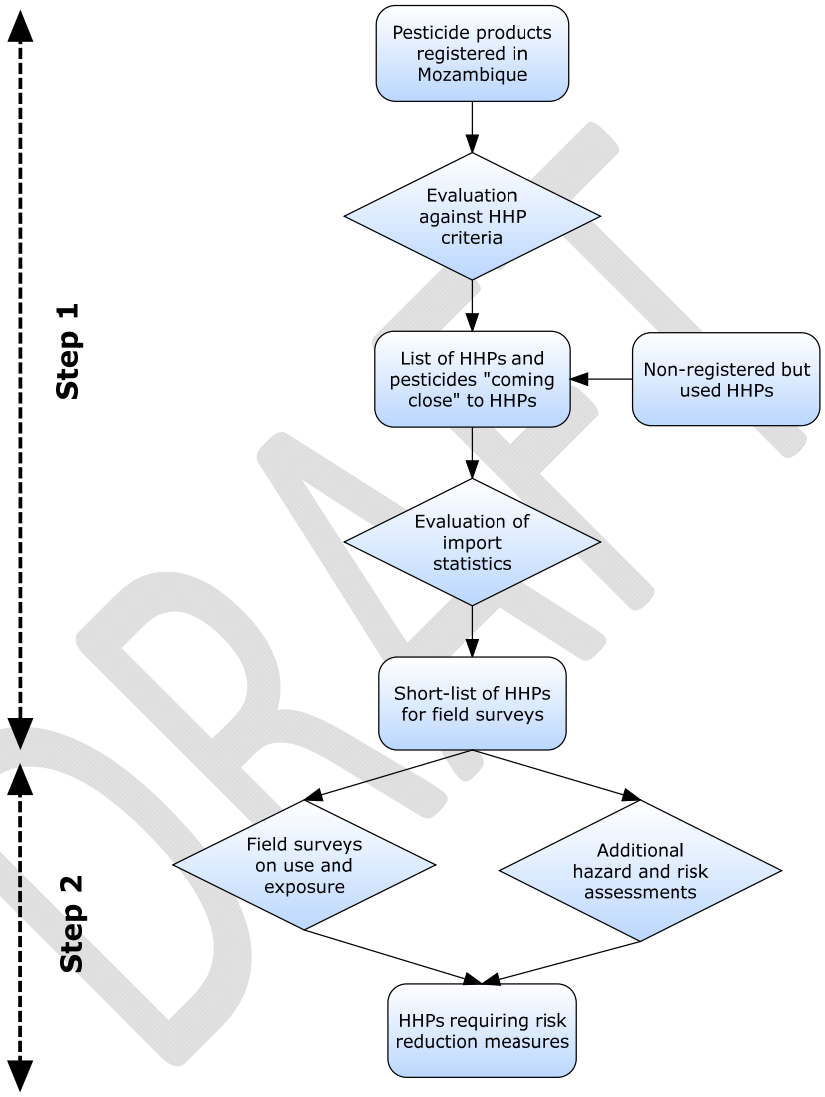

Figure 2. Schematic outline of the various activities in Steps 1 and 2 of the project. This report primarily covers Step 1.

2. Methodology

2.1 Criteria to define HHPs

The criteria that were used in this study to identify highly hazardous pesticides (HHPs) were those established by the FAO/WHO Joint Meeting on Pesticide Management (JMPM) (FAO/WHO, 2008). The JMPM recommended that HHPs should be defined as having one or more of the following characteristics:

- pesticide formulations that meet the criteria of classes Ia or Ib of the *WHO Recommended Classification of Pesticides by Hazard*;

  or

- pesticide active ingredients and their formulations that meet the criteria of carcinogenicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

  or

- pesticide active ingredients and their formulations that meet the criteria of mutagenicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

  or

- pesticide active ingredients and their formulations that meet the criteria of reproductive toxicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

  or

- pesticide active ingredients listed by the *Stockholm Convention* in its Annexes A and B, and those meeting all the criteria in paragraph 1 of annex D of the Convention;

  or

- pesticide active ingredients and formulations listed by the *Rotterdam Convention* in its Annex III;

  or

- pesticides listed under the *Montreal Protocol*;

  or

- pesticide active ingredients and formulations that have shown a high incidence of severe or irreversible adverse effects on human health or the environment.

The JMPM criteria above were used to establish a list of HHPs registered in Mozambique.

Added to this list were:

- Pesticides that are not registered in Mozambique anymore, but for which limited (left-over) quantities are still used in the country.
- Pesticides with characteristics which "come close" to the HHP criteria. A number of pesticides did not meet the WHO class criteria defined by the JMPM, but their acute or chronic toxicity "comes close" to the criteria limits, or they have been marked in the WHO classification as of particular concern with respect to their toxicity.

The following criteria were applied to identify such pesticides "coming close" to HHPs:

- For liquid formulations: pesticide products with an acute oral LD_{50}< 200 mg/kg or an acute dermal LD_{50}< 400 mg/kg (note that these are the Class Ib limits in the previous version of the WHO Classification (WHO, 2005)).
- For solid formulations: pesticide products with an acute oral LD_{50}< 100 mg/kg or an acute dermal LD_{50}< 200 mg/kg.
- Pesticides marked in the WHO classification as of particular concern with respect to chronic toxicity other than the CMR-criteria (*carcinogenicity-mutagenicity-reproductive toxicity*) listed in sections 2.2.4 to 2.2.6 below.
- Pesticides for which carcinogenicity evaluations by different registration/assessment authorities did not lead to consistent classification as GHS Category 1A or 1B, but which were, based on the evidence of one of these authorities, considered of particular concern for use in Mozambique.

2.2 Data collection

2.2.1 Introduction

In principle, the pesticide registration dossier should contain the information that is required for a responsible authority to identify whether a pesticide may be considered an HHP. However, in many developing countries, registration dossiers do not contain sufficient information for such an evaluation. And even if the information is provided in the dossier, the registration authority will often not have the technical capacity to assess the accuracy of the information or to evaluate submitted studies against all the JMPM criteria.

No international or national databases exist which list highly hazardous pesticides (HHPs) based on all the criteria listed by the JMPM. However, various databases are available for individual criteria. These include international databases, e.g. for the criteria linked to the Rotterdam and Stockholm Conventions, or for the *WHO Classification of pesticides by hazard*; others are national or regional, such as the classification and labelling of chemicals databases of the European Union.

In this study, registration dossiers submitted to the registration authority of Mozambique were used to assess pesticides against some of the HHP criteria. International databases or assessments, as well as national or regional databases of various reputable pesticide registration authorities, we accessed to review pesticides against other HHP criteria. The exact procedures for each of the HHP criteria are further described in the chapters below.

2.2.2 Starting data set

The initial dataset used for this study was the list of pesticides registered for use in Mozambique in June 2012, as provided by the Ministry of Agriculture of Mozambique (Minag, 2012). At that date, 646 formulated pesticide products were registered in the country

The 646 registered products contained 192 active substances, of which six were synergists or other additives, and nine others were microbial pesticides.

2.2.3 WHO hazard class

HHPs

The JMPM considers as HHP all *"Pesticide formulations that meet the criteria of classes Ia or Ib of the WHO Recommended Classification of Pesticides by Hazard"*. The latest version of the WHO Classification (WHO, 2010) is shown in Table 1.

Table 1. WHO classification of pesticides by hazard (WHO, 2010)

WHO Class		**LD_{50} for the rat** *(mg/kg body weight)*	
		Oral	**Dermal**
Ia	Extremely hazardous	< 5	< 50
Ib	Highly hazardous	5–50	50–200
II	Moderately hazardous	50–2000	200–2000
III	Slightly hazardous	> 2000	> 2000
U	Unlikely to present acute hazard	≥5000	

To evaluate this criterion, all pesticide formulations registered in Mozambique were classified against the WHO Classification. The oral and dermal LD_{50} value of the formulation, as provided in the registration dossier, was used as the basis for the classification.

In addition, for all formulations a theoretical LD_{50} was calculated, based on the LD_{50} value of the active ingredient(s) and its concentration(s) in the formulated product. LD_{50} values for the active ingredient were obtained from the WHO Classification or, if not listed, from the FootPrint Pesticides Properties Database (PPDB, 2012). This theoretical LD_{50} of the formulation was used in case there were no values in the registration dossier, or to check whether the LD_{50} values provided in the dossier appeared reasonable given the active ingredient content. LD_{50} values from the registration dossier which deviated greatly from the theoretical values were omitted from the analysis.

Whenever there were more products registered for the same active ingredient and concentration, and different LD_{50} values were reported for these pesticide formulations, the lowest LD_{50} value was used for final classification. If oral and dermal LD_{50} values resulted in different classifications, the more hazardous classification was retained for the pesticide product.

2.2.4 GHS carcinogenic hazard

The JMPM considers as HHP all *"Pesticide active ingredients and their formulations that meet the criteria of carcinogenicity Categories 1A and 1B of the Globally Harmonized System on Classification and Labelling of Chemicals (GHS)"*.

The carcinogenicity categories 1A and 1B are defined as by the GHS(2011) as shown in Table 2.

Table 2. Hazard categories for carcinogens, according to the GHS. See GHS (2011) for further details.

Category	Description
1	Known or presumed human carcinogen.
1A	Known to have carcinogenic potential for humans; the placing of a substance is large based on human evidence.
1B	Presumed to have carcinogenic potential for humans; the placing of a substance is largely based on animal evidence.
2	Suspected human carcinogen.

The GHS itself does not provide lists of pesticides and their classifications. Therefore, the following data sources were used to check whether a pesticide would meet GHS Class 1A or 1B for carcinogenicity:

i. The ***WHO Classification of Pesticides by Hazard*** (WHO, 2010)

The footnotes to the various tables were checked for references to carcinogenicity. If a pesticide was listed as carcinogenic in the WHO Classification, it was considered, for this assessment, to meet GHS carcinogenicity Category 1A or 1B.

ii. The ***IARC Monographs on the evaluation of carcinogenic risks to humans*** (IARC, 2012).

Pesticides classified as IARC Group 1 (*carcinogenic to humans*) and Group 2A (*probably carcinogenic to humans*) were considered, for this assessment, to meet GHS carcinogenicity Category 1A or 1B.

iii. The ***European Union Pesticides Database*** (EU, 2012)

This database provides information on plant protection products, but not on other pesticides (biocides). EU hazard classifications follow the GHS. Therefore, pesticides listed in this database as "*carc. 1A*" are GHS Category 1A, and those listed as "*carc. 1B*" are GHS Category 1B.

iv. The ***European Chemical Substances Information System (ESIS)***– *Database of Harmonized Classification and Labelling Elements (CLP/GHS)* (ESIS, 2012)

In addition to plant protection products, this database provides hazard classification informationon biocides. EU hazard classifications follow the GHS. Therefore, pesticides listed in this database as "*carc. 1A*" are GHS Category 1A, and those listed as "*carc. 1B*" are GHS Category 1B.

v. The US EPA evaluations of carcinogenic potential, as provided in the ***Integrated Risk Information System (IRIS)*** (IRIS, 2012).

For this assessment, the following correlations were assumed between the various EPA carcinogenicity classifications and the GHS carcinogenicity categories:

– 1986 guidelines: *"EPA class A (human carcinogen)"* were assumed to be GHS Category 1A, and *"EPA class B1 or B2 (probable human carcinogen)"*to be GHS Category 1B.

– 1996 guidelines: "*EPA known/likely carcinogen"* was assumed to be GHS Category 1A or 1B.

– 1999 guidelines: "*EPA carcinogenic"* was assumed to be GHS Category 1A and *EPA "likely carcinogenic* " was assumed to be GHS Category 1B.

– 2005 guidelines: *"EPA carcinogenic"* was assumed for this assessment to be GHS Category 1A and *"EPA likely carcinogenic"* was assumed to be GHS Category 1B.

vi. The list of **Chemicals Evaluated for Carcinogenic Potential,** compiled by the Office of Pesticide Programs of the US EPA (US-EPA, 2012a).

The same correlations were assumed as listed above (section v.) between the various EPA carcinogenicity classifications and the GHS carcinogenicity categories.

If pesticides were not covered by one or more of the previous sources, the data reviews mentioned below were verified:

vii. Pesticides evaluated by the FAO/WHO ***Joint Meeting on Pesticide Residues*** (JMPR, 2012).

The JMPR toxicology reviews were accessed for selected pesticides to check whether the pesticide is considered to be carcinogenic. Since no standardised carcinogenicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

viii. US EPA ***Pesticide Chemical Search*** (US-EPA, 2012b)

This database was accessed to obtain reviews for selected pesticides, generally *Pesticide Fact Sheets* or *Re-registration Eligibility Documents* (REDs). Since no standardised carcinogenicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

ix. WHO ***Specifications for pesticides used in public health*** (WHO, 2012)

For a limited number of pesticides, the *WHO Specifications for pesticides used in public health*(new procedure) were accessed. Since no standardised carcinogenicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

In principle, if one of these data sources classified a pesticide as (equivalent to) GHS Categories 1À or 1B, the pesticide was considered a HHP. Only if the positive classification appeared outdated, and more recent comprehensive reviews or classifications were available showing that the pesticide was not carcinogenic, the pesticide was not considered a HHP based on this criterion.

2.2.5 GHS mutagenic hazard

The JMPM considers as HHP all *"Pesticide active ingredients and their formulations that meet the criteria of mutagenicity Categories 1A and 1B of the Globally Harmonized System on Classification and Labelling of Chemicals (GHS)"*

The mutagenicity categories 1A and 1B are defined as by the GHS (2011) as shown in Table 3.

Table 3. Hazard categories for mutagens, according to the GHS. See GHS (2011) for further details.

Category	Description
1	Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans.
1A	Substances known to induce heritable mutations in germ cells of humans.
1B	Substances which should be regarded as if they induce heritable mutations in the germ cells of humans.
2	Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans.

The GHS itself does not provide lists of pesticides and their classifications. Therefore, the following data sources were used to check whether a pesticide would meet GHS Class 1A or 1B for germ cell mutagenicity.

i. The ***WHO Classification of Pesticides by Hazard*** (WHO, 2010)

The footnotes to the various tables were checked for references to mutagenicity. If a pesticide was listed as mutagenic in the WHO Classification, it was considered, for this assessment, to meet GHS mutagenicity Category 1A or 1B.

ii. The ***European Union Pesticides Database*** (EU, 2012)

This database provides information on plant protection products, but not on other pesticides (biocides). EU hazard classifications follow the GHS. Therefore, pesticides listed in this database as "*muta. 1A*" are GHS Category 1A, and those listed as "*muta. 1B*" are GHS Category 1B.

iii. The ***European Chemical Substances Information System (ESIS)*** – *Database of Harmonized Classification and Labelling Elements (CLP/GHS)* (ESIS, 2012)

In addition to plant protection products, this database provides hazard classification information on biocides. EU hazard classifications follow the GHS. Therefore, pesticides listed in this database as "*muta. 1A*" are GHS Category 1A, and those listed as "*muta. 1B*" are GHS Category 1B.

If pesticides were not covered by one or more of the previous sources, the data reviews mentioned below were verified:

iv. Pesticides evaluated by the FAO/WHO ***Joint Meeting on Pesticide Residues*** (JMPR, 2012).

The JMPR toxicology reviews were accessed for selected pesticides to check whether the pesticide is considered to be germ cell mutagens. Since no standardised mutagenicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

v. US EPA ***Pesticide Chemical Search*** (US-EPA, 2012b)

This database was accessed to obtain reviews for selected pesticides, generally *Pesticide Fact Sheets* or *Re-registration Eligibility Documents* (REDs). Since no standardised mutagenicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

vi.. WHO ***Specifications for pesticides used in public health*** (WHO, 2012)

For a limited number of pesticides, the *WHO Specifications for pesticides used in public health*(new procedure) were accessed. Since no standardised mutagenicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

In principle, if one of these data sources classified a pesticide as (equivalent to) GHS Categories 1À or 1B, the pesticide was considered a HHP. Only if the positive classification appeared outdated, and more recent comprehensive reviews or classifications were available showing that the pesticide was not a germ cell mutagen, the pesticide was not considered a HHP based on this criterion.

2.2.6 GHS reproductive toxicity hazard

The JMPM considers as HHP all *"Pesticide active ingredients and their formulations that meet the criteria of reproductive toxicity Categories 1A and 1B of the Globally Harmonized System on Classification and Labelling of Chemicals (GHS)"*

The reproductive toxicity categories 1A and 1B are defined as by the GHS (2011) as shown in Table 4.

Table 4. Hazard categories for reproductive toxicants, according to the GHS. See GHS (2011) for further details.

Category	Description
1	Known or presumed human reproductive toxicant
1A	Known human reproductive toxicant
1B	Presumed human reproductive toxicant
2	Suspected human reproductive toxicant

The GHS itself does not provide lists of pesticides and their classifications. Therefore, the following data sources were used to check whether a pesticide would meet GHS Class 1A or 1B for reproductive toxicity.

i. The ***WHO Classification of Pesticides by Hazard*** (WHO, 2010)

The footnotes to the various tables were checked for references to reproductive toxicity. If a pesticide was listed as a reproductive toxicant in the WHO Classification, it was considered, for this assessment, to meet GHS reproductive toxicity Category 1A or 1B.

ii. The ***European Union Pesticides Database*** (EU, 2012)

This database provides information on plant protection products, but not on other pesticides (biocides). EU hazard classifications follow the GHS. Therefore, pesticides listed in this database as "*repro. 1A*" are GHS Category 1A, and those listed as "*repro. 1B*" are GHS Category 1B.

iii. The ***European Chemical Substances Information System (ESIS)*** – *Database of Harmonized Classification and Labelling Elements (CLP/GHS)* (ESIS, 2012)

In addition to plant protection products, this database provides hazard classification information on biocides. EU hazard classifications follow the GHS. Therefore, pesticides listed in this database as "*repro. 1A*" are GHS Category 1A, and those listed as "*repro. 1B*" are GHS Category 1B.

If pesticides were not covered by one or more of the previous sources, the data reviews mentioned below were verified:

iv. Pesticides evaluated by the FAO/WHO ***Joint Meeting on Pesticide Residues*** (JMPR, 2012).

The JMPR toxicology reviews were accessed for selected pesticides to check whether the pesticide is considered to be a reproductive toxicant. Since no standardised reproduction toxicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

v. US EPA ***Pesticide Chemical Search*** (US-EPA, 2012b)

This database was accessed to obtain reviews for selected pesticides, generally *Pesticide Fact Sheets* or *Re-registration Eligibility Documents* (REDs). Since no standardised reproduction toxicity classification is used in these reviews, pesticides were assessed on a case-by-case basis.

vi. WHO ***Specifications for pesticides used in public health*** (WHO, 2012)
For a limited number of pesticides, the *WHO Specifications for pesticides used in public health* (new procedure) were accessed. Since no standardised classification for reproductive toxicants is used in these reviews, pesticides were assessed on a case-by-case basis.

In principle, if one of these data sources classified a pesticide as (equivalent to) GHS Categories 1À or 1B, the pesticide was considered a HHP. Only if the positive classification appeared outdated, and more recent comprehensive reviews or classifications were available showing that the pesticide was not a reproductive toxicant, the pesticide was not considered a HHP based on this criterion.

2.2.7 Stockholm Convention

The JMPM considers as HHP all *"Pesticide active ingredients listed by the Stockholm Convention in its Annexes A and B, and those meeting all the criteria in paragraph 1 of Annex D of the Convention"*

Pesticides listed in Annex A and B were obtained directly from the Convention web site (Stockholm, 2012).

Annex D of the Stockholm Convention lists the screening criteria for inclusion of a pesticide in Annex A, B and/or C of the Convention (Stockholm, 2009). With respect to Annex D, the Stockholm Convention stipulates in its Article 3, that :

> **3.** *Each Party that has one or more regulatory and assessment schemes for new pesticides or new industrial chemicals shall take measures to regulate with the aim of preventing the production and use of new pesticides or new industrial chemicals which, taking into consideration the criteria in paragraph 1 of Annex D, exhibit the characteristics of persistent organic pollutants.*
>
> **4.** *Each Party that has one or more regulatory and assessment schemes for pesticides or industrial chemicals shall, where appropriate, take into consideration within these schemes the criteria in paragraph 1 of Annex D when conducting assessments of pesticides or industrial chemicals currently in use.*

Therefore, and in particular to meet Article 3.4 above, all pesticides registered in Mozambique were reviewed against the criteria listed in Annex D. The screening criteria that identify a POP, as defined in paragraph1 of Annex D are listed in Table 5.

For each of the registered pesticides, the data were compiled using the FootPrint Pesticide Properties Database (PPDB, 2012), as follows:

Persistence

- Half-life (DT_{50}) in water: aqueous photolysis DT_{50}; aqueous hydrolysis DT_{50}, and water phase only DT_{50} of the water-sediment study. The latter parameter, or any listed field data, had preference in the assessment of persistence in water. The range of relevant values was noted in the evaluation spreadsheet.
- Half-life (DT_{50}) in soil: DT_{50} (typical), DT_{50} (lab), DT_{50} (field), any DT_{50} values (lab or field) given in the "note" to this section in FootPrint. Any listed field data had preference in the assessment of persistence in soil. The range of relevant values was noted in the evaluation spreadsheet.
- Half-life (DT_{50}) in sediment: Water-Sediment DT_{50}

Table 5. Screening criteria to identify a Persistent Organic Pollutant (POP) according to the Stockholm Convention (Annex D) (Stockholm, 2009)

Characteristic	Criteria	
b. Persistence	(i)	Evidence that the half-life of the chemical in water is greater than two months, or that its half-life in soil is greater than six months, or that its half-life in sediment is greater than six months; or
	(ii)	Evidence that the chemical is otherwise sufficiently persistent to justify its consideration within the scope of this Convention;
c. Bio-accumulation	(i)	Evidence that the bio-concentration factor or bio-accumulation factor in aquatic species for the chemical is greater than 5,000 or, in the absence of such data, that the log K_{ow} is greater than 5;
	(ii)	Evidence that a chemical presents other reasons for concern, such as high bio-accumulation in other species, high toxicity or ecotoxicity; or
	(iii)	Monitoring data in biota indicating that the bio-accumulation potential of the chemical is sufficient to justify its consideration within the scope of this Convention;
d. Potential for long-range environmental transport	(i)	Measured levels of the chemical in locations distant from the sources of its release that are of potential concern;
	(ii)	Monitoring data showing that long-range environmental transport of the chemical, with the potential for transfer to a receiving environment, may have occurred via air, water or migratory species; or
	(iii)	Environmental fate properties and/or model results that demonstrate that the chemical has a potential for long-range environmental transport through air, water or migratory species, with the potential for transfer to a receiving environment in locations distant from the sources of its release. For a chemical that migrates significantly through the air, its half-life in air should be greater than two days; and
e. Adverse effects	(i)	Evidence of adverse effects to human health or to the environment that justifies consideration of the chemical within the scope of this Convention; or
	(ii)	Toxicity or ecotoxicity data that indicate the potential for damage to human health or to the environment.

Bioaccumulation

- Octanol–water partition coefficient – log K_{ow} (= log P in FootPrint).
- Bioconcentration factor in aquatic species (BCF).
- Bioacummulation factor in aquatic species (BAF) (if listed).
- Bioacummulation factor in other species (BAF) (if listed).

Potential for long-range transport

- This characteristic was not assessed, as it was not considered relevant for the identification of HHPs in Mozambique itself.

Adverse effects

- This characteristic was only assessed for pesticides which were both persistent and bioaccumulative according to the criteria listed above. For this study, such pesticides were considered HHPs if they fell in WHO hazard class II or higher.
- No other toxicity or ecotoxicity assessments were conducted to assess whether there was "potential for damage to human health or to the environment".

2.2.8 Rotterdam Convention

The JMPM considers as HHP all *"Pesticide active ingredients and formulations listed by the Rotterdam Convention in its Annex III"*.

Pesticides listed in Annex III were obtained directly from the Convention web site (Rotterdam, 2012)

2.2.9 Montreal Protocol

The JMPM considers as HHP all *"Pesticides listed under the Montreal Protocol"*.

The only pesticide presently listed under the Montreal Protocol is methyl bromide (Montreal, 2012)

2.2.10 High incidence of severe or irreversible adverse effects

The JMPM considers as HHP all *"Pesticide active ingredients and formulations that have shown a high incidence of severe or irreversible adverse effects on human health or the environment"*.

This parameter was not assessed in Step 1 of the project, as it requires information from actual use in Mozambique, or from similar use situations. Pesticide use surveys have been programmed for Step 2 of the project, however.

2.2.11 Import statistics

Import statistics were obtained from the Pesticide Registration Section of the Ministry of Agriculture. Mozambique applies an import permit system and all official pesticide imports are registration by the Ministry of Agriculture. While such a system does not allow for records of illegal imports, the import register in Mozambique is generally considered to represent a large fraction of pesticides entering the country. No local pesticide manufacturing or formulation takes place in Mozambique.

For this study, the import statistics of 2010, 2011 and the first half of 2012 were reviewed. Total quantities imported during that period for all products with the same active ingredient(s) were considered a proxy for the present use of that active ingredient in the country. Implicitly, it was assumed that pesticides imported before 2010 would have been used up by the time of the study and not be used anymore.

2.3 Data compilation

All assessments made and data compiled as described in the sections above were compiled in a spreadsheet. This was done to allow full transparency with respect to the identification process of the HHPs, but also to allow updating of the list of HHPs would new information become available. The latest version of the spreadsheet is available on request. This version does not contain the detailed import statistics, however, as these are considered confidential.

3. Results

3.1 Data availability

Using the data sources laid out in Chapter 2, it was possible to review all HHP criteria defined by the JMPM for most of the pesticides registered in Mozambique, except for the last criterion, which refers to pesticides that have shown a high incidence of severe or irreversible adverse effects – see Section 2.2.10).

Acute toxicity

LD_{50} values for the pesticide formulations were provided in the registration dossier for 97% (oral LD_{50}) and 93% (dermal LD_{50}) of the registered products. However, in some cases the LD_{50} values of the formulation appeared erroneous when compare to the theoretical values calculated on the basis of the a.i.; in others, the LD_{50} of the formulation provided by the registrar was identical to the a.i. In total, 12% of the oral LD_{50} values for the formulations were either not reported in the dossier or were considered erroneous; this was the case for 10% of the dermal LD_{50} values. However, in many cases, LD_{50} values of the formulation could be estimated based on the LD_{50} values of the a.i.

As a result, LD_{50} values for the formulation were available or could be estimated for all registered pesticide products except for three microbial pesticides and one citronella oil (i.e. > 99% of the total).

Overall, data availability for acute toxicity, which is at the basis of the WHO Class criterion of the JMPM, can be considered satisfactory.

Carcinogenicity, mutagenicity, reproductive toxicity (CMR)

Evaluations on carcinogenic potential were available for 93% of the active ingredients registered in Mozambique, representing 96% of the number of registered formulated products. Of the 11 a.i.'s lacking carcinogenicity evaluations, four were adjuvants/synergists, one a repellent, one a microbial pesticide and one a pheromone; the remaining four were "regular" chemical pesticides.

Evaluations on germ cell mutagenicity were available for 90% of the active ingredients registered in Mozambique, representing 95% of the number of registered formulated products. Of the 20 a.i.'s lacking carcinogenicity evaluations, four were adjuvants/synergists, three repellents, one a microbial pesticide and one a pheromone; the remaining 11 were "regular" chemical pesticides.

Evaluations on reproductive toxicity were available also for 90% of the active ingredients registered in Mozambique, representing 94% of the number of registered formulated products. Of the 20 a.i.'s lacking reproductive toxicity evaluations, four were adjuvants/synergists, two repellents, one a microbial pesticide and one a pheromone; the remaining 12 were "regular" chemical pesticides.

Overall, data to evaluate the CMR criteria of the JMPM were available for >90% of the a.i. and >94% of registered formulations. Eight to twelve active ingredients of "regular" chemical pesticide a.i.'s had not been evaluated and/or classified for CMR criteria by any of the used sources. It can certainly not be excluded that evaluation of other data sources would result in proper classification of these a.i.'s, but that was not further attempted in this study.

Rotterdam and Stockholm Conventions, and Montreal Protocol

Inclusion in the lists of regulated chemicals of these three international instruments was obviously complete and did not show any data gaps.

On the other hand, there were data gaps in the parameters needed to classify a pesticide as a POP according to Annex D of the Stockholm Convention. Only one data source was used to obtain this information, the FootPrint Pesticide Properties Database. However, since the FootPrint database compiles its data from various reputable reviews and databases, it is generally considered to be rather complete.

In spite of the extensiveness of the FootPrint database, for 36 a.i.'s (19% of the total) half-lives in water were not available. In many cases this absence was understandable (e.g. for microbial pesticides, repellents, pheromones), but for 17 a.i.'s of "regular" chemical pesticides registered in Mozambique, this information was not present either.

Half-lives in soil were available for more pesticides in the FootPrint database. Data were lacking for 27 a.i.'s (15% of the total), of which eight were "regular" chemical pesticides registered in Mozambique.

In contrast, half-life data for sediments (water-sediment studies) were not available for 42% of the a.i.'s. This included 58 "regular" chemical pesticide a.i.'s for which data were lacking. This is not entirely surprising, as water-sediment studies are fairly recent requirements in pesticide registration in Europe and the U.S.

Bioaccumulation potential is assessed using the bioconcentration factor (BCF) for aquatic organisms, or the bioaccumulation factor (BAF) for aquatic or terrestrial organisms. BAFs were not available in FootPrint for any of the registered a.i.'s. BCFs were not available for 76 a.i.'s (40% of the total).

In the absence of BCFs, the octanol-water partition coefficient (K_{ow} or P) of the pesticide is used to evaluate bioaccumulation potential. K_{ow}-values were available for most pesticides, with data absent for only 21 a.i.'s (10% of the total), most of which were microbial pesticides, synergists or adjuvants, and pheromones.

Based on the above, it may be concluded that for the majority of pesticides registered in Mozambique it was possible to assess whether a pesticide is persistent or bioaccumulative according to the Stockholm Convention, but that there were still considerable data gaps.

3.2 Identification of HHPs

Taking into account the limitations due to data gaps described above, in total 57 registered pesticide formulations, containing 24 active ingredients, were identified as HHPs. In addition, two pesticides were also listed as HHP: DDT and methyl-bromide (Figure 3). The latter two pesticides are not registered in Mozambique anymore, but remaining stocks are still being used (for DDT) or their use is still temporarily being allowed (for methyl bromide). Further details for all identified HHPs are provided in Table 6.

The majority of HHPs were identified on the basis of their acute toxicity. Thirty-seven out of 59 formulated products were WHO class Ia or Ib (based on acute toxicity; not on chronic), or highly toxic by inhalation (Figure 4).

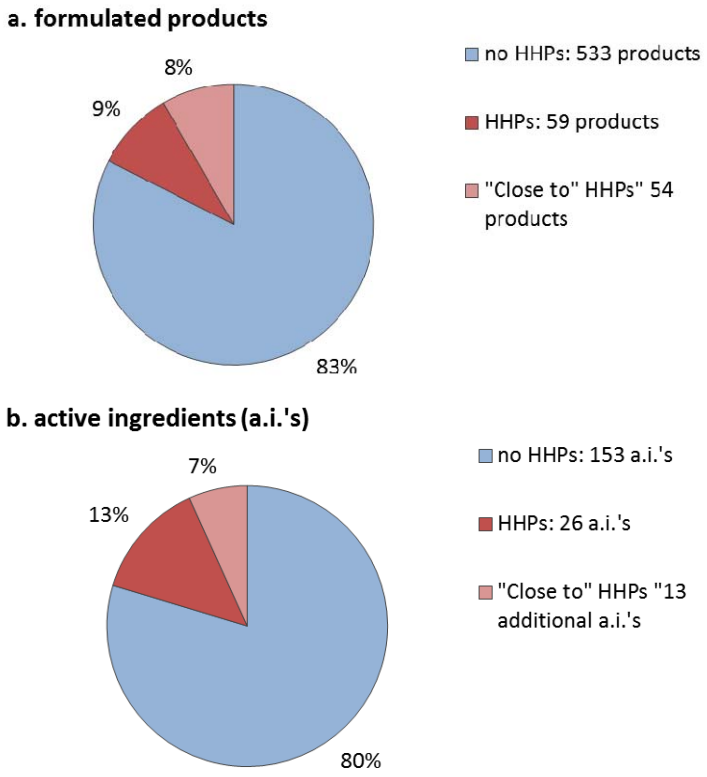

Figure 3. The number and percentage of identified highly hazardous pesticides (HHPs), pesticides "close to HHPs" in Mozambique. a. formulated products (total = 646), and b. active ingredients (a.i.'s) (total = 192).

The second most important criterion was listing in Annex III of the Rotterdam Convention (Figure 4). This was the case for 17 out of 59 formulated products, or 6 out of 26 active ingredients identified as HHP.

Two active ingredients, representing 5 pesticide products, were listed in Annex A or B of the Stockholm Convention. Three other pesticide active ingredients were both persistent and bioaccumulative according to Annex D criteria (diafenthiuron, difenacoum and difethialone), but only diafenthiuron is moderately toxic to humans. Furthermore, the insecticide diafenthiuron is considered hazardous to aquatic organisms while difenacoum and difethialone, both rodenticides, are considered hazardous to aquatic organisms as well as to birds and mammals. While this does not mean that these organisms will be unacceptably affected when the pesticides are applied, the "potential for damage to the environment" exists (as indicated in Annex D of the Stockholm Convention), and these pesticides were therefore identified as HHPs in Table 6.

One pesticide was listed under the Montreal Protocol.

Two active ingredients were classified as GHS Category 1A & 1B carcinogen, three a.i.'s as mutagen and three a.i.'s as reproductive toxicant. For 14 active ingredients, carcinogenicity evaluations by the EU and the US-EPA did not lead to the same conclusion with respect to classification; these were further evaluated under Section 3.3.

In total, seven active ingredients met more than one JMPM HHP criterion (Table 6).

Table 6. Highly hazardous pesticides (HHPs) identified among the pesticide products registered in Mozambique, and pesticide products "coming close" to being considered HHPs. For the selection criteria and the applied methodology see Chapter 2 of this report.

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
Pesticides meeting the HHP criteria							
455	Controler 48% SE	Alachlor 336 g/l (+ Atrazine 144 g/l)	Rott. Annex III	Maize, sunflower, soybean, groundnut, vegetables	0		EU: No (H[2]& E[3]) USA: Yes
666	Volcano alachlor 48% EC	Alachlor 480 g/l	Rott. Annex III				
509	Seter 48% EC	Alachlor 480 g/l	Rott. Annex III				
644	Volcano Aldicarb 15% GR	Aldicarb 150 g/kg	WHO Ib; Rott. Annex III	Citrus (nurseries)	0		EU: No (E) USA: Yes, but being phased out (H & E)
1172	Fumate 56% FT	Aluminium Phosphide 560 g/kg	Highly toxic by inhalation	Storage insect pests of: tobacco, cereals, groundnut, oilseeds	29844 kg (2010) 14690 kg (2011) 1311 kg (2012) 705 (2013)		EU: Yes USA: Yes
1054	Moz Aluminium Phosphide Pellets	Aluminium Phosphide 560 g/kg	Highly toxic by inhalation				
581	Phosgard 56% FT	Aluminium phosphide 560 g/kg	Highly toxic by inhalation				
773	Falfume 57% FT	Aluminium Phosphide 570 g/kg	Highly toxic by inhalation				
1071	Moz Aluminium Phosphide Tablets	Aluminium Phosphide 570 g/kg	Highly toxic by inhalation				
1129	Quickphos 57% FT	Aluminium Phosphide 570 g/kg	Highly toxic by inhalation				
1080	Biophos 57% FW	Aluminium phosphide 570 g/kg	Highly toxic by inhalation				
1028	Celphos 57% FT	Aluminium phosphide 570 g/kg	Highly toxic by inhalation				
664	Volcano Aluminium Phosphide 57% FT	Aluminium phosphide 570 g/kg	Highly toxic by inhalation				
467	Benopec 50% WP	Benomyl 500 g/kg	Mutagen; reproductive toxicant	Apple, pineapple	5600 kg (2010)		EU: No (H & E) USA: No; voluntary

[1] EU (2012) and US-EPA (2012b), checked on 26 October 2012

[2] H = not registered due to unacceptable risk to human health

[3] E = not registered due to unacceptable risk to the environment

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
772	Volcano Demeter 50% WP	Benomyl 500 g/kg	Mutagen; reproductive toxicant		2000 kg (2012)		cancellation (H)
793	Supa-Kill Líquid Rat and Mouse Bait	Brodifacoum 0,75 g/L	WHO class Ib	Rodents	40 L (2011) 28 L (2012)	Also formulation with lower concentration registered	EU: No (NS[4]) USA:Yes
952	Brokir 0,075% CB	Brodifacoum 0,75 g/L	WHO class Ib				
837	Rodex Profissional Líquid Concentrate	Brodifacoum 2,5 g/kg	WHO class Ib				
681	Duett 25% SC	Carbendazim 125 g/l (+ Epoxiconazole 125 g/l)	Mutagen; reproductive toxicant	Cereals, groundnut	5 L (2011)		EU: Yes USA:Yes
126	Curaterr 10% GR	Carbofuran 100 g/kg	WHO class Ib	Maize, sugarcane	0		EU: No (H & E) USA:No; cancellation in progress (H & E)
504	Carbofurão 5% GR	Carbofuran 50 g/kg	WHO class Ib				
254	Polo 50% SC	Diafenthiuron 500 g/l	Stockh. Annex D (persistent, bioaccumulative and potential for damage to the humans or the environment)	Beans, cucumber, pepper, tomato, potato	0		EU: No (NS) USA: No
1202	Divos 100% EC	Dichlorvos 1000 g/l	WHO class Ib	Flowers, vegetables, stored cereals, domestic uses, veterinary uses	448 L (2010) 3000 L (2011) 2400 L (2012) 2584 (2013)		EU: No (H) USA:Yes
984	Nuvan 100% EC	Dichlorvos 1000 g/l	WHO class Ib				
774	Falcovos 100% EC	Dichlorvos 1000 g/l	WHO class Ib				
984	Nuvam 100% EC	Dichlorvos 1000 g/l	WHO class Ib				
1220	Diclofop–methyl 37,8% EC	Diclofop–methyl 378 g/l	carcinogen	Wheat, barley, triticale, peas	0		EU: Yes USA:Yes
1055	Moz Tornado 0,01% BB	Difenacoum 0,1 g/kg	Stockh. Annex D (persistent, bioaccumulative and potential for damage to the environment)	Rodents	48 (2013)		EU: Yes USA: Yes

[4] NS = not registered because no (complete) dossier was submitted

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
944	Finale Rat And Mouse Grain Bait	Difethialone 0,025 g/kg	Stockh. Annex D (persistent, bioaccumulative and potential for damage to the environment)	Rodents	0		EU: No (NS) USA: Yes
969	Finale Rat And Mouse Pellets	Difethialone 0,025 g/kg	Stockh. Annex D (persistent, bioaccumulative and potential for damage to the environment)				
943	Finale Rat And Mouse Wax Bait	Difethialone 0,025 g/kg	Stockh. Annex D (persistent, bioaccumulative and potential for damage to the environment)				
719	Ratex Pellts	Difethialone 0,025 g/kg	Stockh. Annex D (persistent, bioaccumulative and potential for damage to the environment)				
1027	Endocel 35% EC	Endosulfan 350 g/l	Stockh. Annex A; Rott. Annex III	Cotton, cocoa, cereals, vegetables, flowers,	2585 L (2010) 7280 L (2011) 9150 L (2012)		EU: No (H & E) USA:Yes,but phase out in progress
447	Endopec 35% EC	Endosulfan 350 g/l	Stockh. Annex A; Rott. Annex III				
825	Enticer 35% EC	Endosulfan 350 g/l	Stockh. Annex A; Rott. Annex III				
605	Volcano Endosulfão 35% EC	Endosulfan 350 g/l	Stockh. Annex A; Rott. Annex III				
518	Eticide 101% EC	Ethion 1010 g/l	WHO class Ib	Veterinary use	0		EU: No (NS) USA:No; voluntary cancellation (H)
483	Nemacur 40% EC	Fenamiphos 400 g/l	WHO class Ib	Tobacco, citrus, vegetables, potato, groundnut, grape, peach, pineapple	30 L (2013)	Also a granular formulation with lower hazard registered	EU: Yes USA: Voluntary cancellation (H & E)
715	Volamiphos 40% EC	Fenamiphos 400 g/l	WHO class Ib				
1056	Moz Fenamiphos 400 SC	Fenamiphos 400 g/l	WHO class Ib				

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
1115	Vet Fume B	Formaldehyde 370 g/l	Carcinogen	Disinfectant	1660 (2010) 4060 (2011) 1910 (2012) 3525 (2013)		EU: No (NS) USA:Yes
746	Crop Guard 90% EC	Furfural 900 g/l	WHO class Ib	Vegetables, tobacco, flowers, maize, groundnut	200 (2013)		EU: No (NS) USA: Yes
1163	Chemaron 58% SL	Methamidophos 585 g/l	WHO Ib; Rott. Annex III	Cotton, tobacco, vegetables	34760 L (2010) 13050 L (2011) 37832 L (2012) 28556 L (2013)		EU: No (RE)[5] USA:No; voluntary cancellation
1163	Chemeron 58% SL	Methamidophos 585 g/l	WHO Ib; Rott. Annex III				
1199	Sniper 58.5% SL	Methamidophos 585 g/l	WHO Ib; Rott. Annex III				
639	Volmet 58,5% SL	Methamidophos 585 g/l	WHO Ib; Rott. Annex III				
361	Mesurol 80 WP	Methiocarb 800 g/kg	WHO class Ib	Maize, groundnut, potato, vegetables, citrus	0	Also formulation with lower concentration registered	EU: Yes USA: Yes
1198	Methomex 90% SP	Methomyl 900 g/kg	WHO class Ib	Vegetables, tobacco, cereals, flowers	500 kg (2012) 1000 kg (2013)	Also formulation with lower concentration registered	EU: Yes USA: Yes
480	Delta Super 25,75% EC	Monocrotophos 250 g/l (+ Deltamethrin 7,5 g/l)	Rott. Annex III	Cotton, maize, tobacco	0		EU: No (NS) USA: No (cancelled in 1991)
478	Zipper Super 28% EC	Monocrotophos 250 g/l (+ Cypermethrin 30 g/l)	Rott. Annex III				
454	Monopec 40% SL	Monocrotophos 400 g/l	WHO Ib; Rott. Annex III				
1151	Monocrotophos 40% EC	Monocrotophos 400 g/l	WHO Ib; Rott. Annex III				
1185	Oxadate 31% SL	Oxamyl 310 g/l	WHO class Ib	Tobacco, sugarcane,	500 kg (2010)		EU: Yes

[5] RE = not registered because registration expired and was not renewed

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
810	Vydate 31% SL	Oxamyl 310 g/l	WHO class Ib	fruits, vegetables, groundnut	300 kg (2011) 400 kg (2012)		USA: Yes
1065	Moz Terbufos 15% GR	Terbufos 150 g/kg	WHO class Ia	Maize, sorghum, potato, beans	0		EU: No (NS) USA:Yes
1167 822	Ratikill 80% AB Ratil 80% AB	Zinc phosphide 800 g/kg Zinc phosphide 800 g/kg	WHO class Ib WHO class Ib	Rodents	0		EU: Yes USA:Yes
Total	***[57**/646]*	***[24**/225]*					
Pesticides not registered, but used in Mozambique and complying with the HHP criteria							
--	DDT 50% WP	DDT	Stockh. Annex B; Rott. Annex III	Malaria mosquito control	0 (but use of existing stocks)		EU: No (P)[6] USA: No
--	Brometo de metilo	Methyl bromide	Montreal Protocol	Quarantine treatments (stored products)	0 (but use of existing stocks)		EU: No (H) USA: Yes
Total		***[2]***					
Registered pesticides not complying with the JMPM criteria, but "coming close"							
570	Volcano 2,4 D 72% SL	2,4-D dimethylamine 720 g/l	WHO class II, but dermal hazard close to Ib	Sugar cane, coffee, cocoa, rice, palm trees.	47000 L (2010) 32600 L (2011) 52000 L (2012) 19600 L (2013)		EU: No USA: Yes
1063	Moz Paraquat 20% SL	Paraquat 200 g/l	WHO Class II but chronic toxicity alert; dermal hazard close to Class Ib; very low AOEL[7]	Forestry, fruits, vegetables, cotton, coffee, tea, flowers, banana, sugar cane,	22700 L (2010) 35100 L (2011) 17952 L (2012)		EU: No (A)[8] USA: Yes

[6] P = not registered because all use is prohibited in the EU

[7] AOEL = Acceptable Operator Exposure Level

[8] A= not registered because registration annulled by the Court

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
1303	Paracot 20% SL	Paraquat 200 g/l	WHO Class II but chronic toxicity alert; dermal hazard close to Class Ib; very low AOEL	pasture, potato	18440 L (2013)		
1262	Para-Cure 20% SL	Paraquat 200 g/l	WHO Class II but chronic toxicity alert; dermal hazard close to Class Ib; very low AOEL				
458	Paraxone 20% SL	Paraquat 200 g/l	WHO Class II but chronic toxicity alert; dermal hazard close to Class Ib; very low AOEL				
764	Volquato 20% SL	Paraquat 200 g/l	WHO Class II but chronic toxicity alert; dermal hazard close to Class Ib; very low AOEL				
1181	Gramozat 20% SL	Paraquat 200 g/l	WHO Class II but chronic toxicity alert; dermal hazard close to Class Ib; very low AOEL				
544	Ficam 80% WP	Bendiocarb 800 g/kg	WHO class II, but oral hazard close to Class Ib	Malaria mosquito control	5810 kg (2010) 14560 kg (2011) 30000 kg (2013)		EU: No (NS) USA: No; voluntary cancellation
735	Tocaia 80% WP	Bendiocarb 800 g/kg	WHO class II, but oral hazard close to Class Ib				
884	Avisnail 5% RB	Carbaryl 20 g/kg (+metaldehyde 30 g/kg	Carcinogen (see Annex I)	Cotton, potato, maize, sorghum, tobacco, groundnut, vegetables	400 kg (2010) 4200 kg (2011) 2200 kg (2012) 2600 kg (2013)		EU: No (H & E) USA: Yes
811	Supona 30% EC	Chlorfenvinphos 300 g/l	WHO class II, but oral hazard close to Class Ib	Veterinary uses	600 L (2012) 812 L (2013)		EU: No (NS) USA: No

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
816	Dazzel N.F 30% EC	Diazinon 300 g/l	WHO class II, but dermal hazard close to Class Ib	Veterinary uses	18 L (2010) 24 L (2011) 30 L (2012) 64 L (2013)		EU: No (H) USA: Yes
1155	Dichlorvos 10% EC	Dichlorvos (DDVP)100 g/l	WHO class II, but dermal and oral hazard close to Class Ib	Stored grains, vegetables, domestic use, veterinary use	1411 L (2010) 1462 L (2011) 2400 L (2012) 4000 L (2013)	More concentrated formulations in HHP shortlist above.	EU: No (H) USA: Yes
985	Nuvan Profi 12,4% AE	Dichlorvos 124 g/l	WHO class II, but dermal and oral hazard close to Class Ib				
986	Metrad 75% WG	Diuron 400 g/kg (+metribuzin 360 g/kg)	Carcinogen (see Annex I)	Sugarcane, cotton, macadamia nuts, coffee, banana, pineapple, wheat, tea, coconut, fruits trees, cocoa, rubber tree, industrials areas	47368 L (2010) 54140 L (2011) 58900 L (2012) 44660 L (2013)		EU: Yes USA: Yes
461	Dipec 80% WP	Diuron 800 g/kg	Carcinogen (see Annex I)				
849	Volcano Diuron 80% WG	Diuron 800 g/kg	Carcinogen (see Annex I)				
532	Volcano Diurão 800 SC	Diuron 800 g/l	Carcinogen (see Annex I)				
1061	Moz Diuron 80% SC	Diuron 800 g/l	Carcinogen (see Annex I)				
1211	Iprodione 25,5% SC	Iprodione 255 g/l	Carcinogen (see Annex I)	Vines, fruit trees, vegetables	12 L (2013)		EU: Yes USA: Yes
1101	Milthane Super 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)	Tobacco, vegetables, pineapple, ornamentals, fruit trees, potato, groundnut, vines , cereals, nuts, olive, coffee, soybean	68890 kg (2010) 77740 kg (2011) 30500 kg (2012) 59570 kg (2013)		EU: Yes USA: Yes
663	Volcano Crater MX 70% WP	Mancozeb 100 g/kg (+metalaxyl 600 g/kg)	Carcinogen (see Annex I)				
508	Etylit MZ 70% WP	Mancozeb 350 g/kg (+fosetyl-aluminium 350 g/kg)	Carcinogen (see Annex I)				
1236	Crater 455 SC	Mancozeb 455 g/l	Carcinogen (see Annex I)				
477	Megatop 50,5% WP	Mancozeb 465 g/kg (+cymoxanil 40 g/kg)	Carcinogen (see Annex I)				
1075	Dithane NT 60% OS	Mancozeb 600 g/kg	Carcinogen (see Annex I)				

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
875	Volcano Crater MX 72% WP	Mancozeb 640 g/kg (+ Metalaxyl 80 g/kg)	Carcinogen (see Annex I)				
546	Ridomil Gold 68% WP	Mancozeb 640 g/kg (+metalaxyl 40 g/kg)	Carcinogen (see Annex I)				
472	Ekyp MZ 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)	Carcinogen (see Annex I)				
823	Mascot 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)	Carcinogen (see Annex I)				
1136	Metaman FAE PM 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)	Carcinogen (see Annex I)				
1087	Neltylxyl 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)	Carcinogen (see Annex I)				
844	Ridomil Gold MZ 68 WG	Mancozeb 640 g/kg (+metalaxyl-M 40 g/kg)	Carcinogen (see Annex I)				
1045	Moz Controller	Mancozeb 700 g/kg (+cymoxanil 60 g/kg)	Carcinogen (see Annex I)				
1307	Cotzeb 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
1162	Curethane 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
1078	Dithane NT 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
1143	Mazole 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
1133	Policar MZ 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
1221	Ventum 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
534	Volcano mancozeb 800 WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				
457	Mancopec 80% WP	Mancozeb 800 g/kg	Carcinogen (see Annex I)				

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
466	Metacidine 40% WP	Methidathion 400 g/kg	WHO class II, but oral hazard close to Class Ib	Cotton, tobacco, sugar cane, vegetables, maize	0		EU: No (NS) USA: No; voluntary cancellation in progress
646	Mesurol Super Snail Pellets 1.5% RB	Methiocarb 5 g/kg+	WHO class II, but oral hazard close to Class Ib	Maize, groundnut, potato, vegetables, citrus	0	More concentrated formulations in HHP shortlist above.	EU: Yes USA: Yes
887	Volomyl 20% SL	Methomyl 200 g/l	WHO class II, but oral hazard close to Class Ib	Maize, groundnut, potato, vegetables, citrus, cotton, tobacco, flowers,	550 L (2012)	More concentrated formulations in HHP shortlist above.	EU: Yes USA: Yes
463	Rikki 20% SL	Methomyl 200 g/l	WHO class II, but oral hazard close to Class Ib				
1105	Volxyl 24% EC	Oxyfluorfen 240 g/l	Carcinogen (see Annex I)	Cotton, soybean, groundnut, vegetables, citrus, pine trees, eucalyptus trees	900 L (2010) 1200 L (2012)		EU: Yes USA: Yes
1131	King Insectos Voadores	Permethrin 0,4 g/kg (+d-Allethrin 0,82 g/kg +piperonyl butoxide 3,3 g/kg)	Carcinogen (see Annex I)	Stored grain, public health and domestic use	4958 L (2010) 27820 L (2011) 5000 L (2013)		EU: No (E) USA: Yes
974	Majestic Ultra 50% EC	Permethrin 100 g/l (+pirimiphos methyl 400 g/l)	Carcinogen (see Annex I)				
967	Cooper Aerosol Fly and Mosquito Killer	Permethrin 15 g/kg (+piperonyl butoxide 15 g/kg)	Carcinogen (see Annex I)				
1132	King Insectos Rastejantes	Permethrin 2,5 g/kg (+pyrethrins 1 g/kg)	Carcinogen (see Annex I)				
1123	Majestic super 2% DP	Permethrin 3 g/kg (+pirimiphos methyl 16 g/k)	Carcinogen (see Annex I)				
629	Super Guard Dust 2% DP	Permethrin 4 g/kg (+pirimiphos methyl 16 g/kg)	Carcinogen (see Annex I)				

Reg. no.	Trade name	Active ingredient (a.i.)	Reason for identification as potential HHP	Registered uses in Mozambique (summary)	Import volumes (2010 – 2013)	Notes	Registration status of a.i. elsewhere[1]
163	Larvin 37,5% SC	Thiodicarb 375 g/l	WHO class II, but very close to Class Ib	Cotton	0		EU: No (H & E) USA: Yes
Total	***[54]***	***[16]*** *(of which 3 a.i.'s already listed in HHP shortlist above)*					

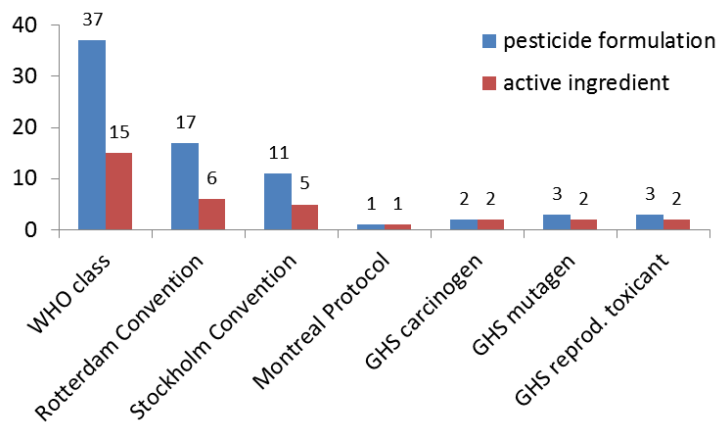

Figure 4. The number of identified highly hazardous pesticides (HHPs) in Mozambique according to the various JMPM criteria. Note that a pesticide may be identified as HHP based on more than one criterion.

3.3 Identification of pesticides "coming close" to HHPs

Using the criteria listed in Section 2.1, 54 formulated pesticide products containing 16 different active ingredients were identified as "coming close" to being an HHP (Figure 3 and Table 6). Of the 16 active ingredients, 13 were not listed under the HHPs.

Pesticide products were most often classified as being "close to" HHPs based on the acute oral or dermal toxicity of the formulations. In addition, the carcinogenicity evaluations of 16 active ingredients did not result in similar conclusions between the EU and the US-EPA. Generally, these pesticides which were evaluated as likely or probable carcinogens by the US-EPA, but not by the EU. Seven of the 16 active ingredients were considered a sufficiently great concern for Mozambique to include them under the group of pesticides "coming close" to HHPs (see Annex 1 for the justification).

In the case of paraquat, the WHO Classification notes in addition that it "*has serious delayed effects if absorbed. It is of relatively low hazard in normal use but may be fatal if the concentrated product is taken by mouth or spread on the skin*" (WHO, 2010). The occupational hazard of paraquat is confirmed by the very low Acceptable Operator Exposure Level defined in the EU (PPDB, 2012).

3.4 Registrations elsewhere

In national decision making on the continuation or modification of the registration of a HHP, it may be useful to review how other, reputable, registration authorities have evaluated the pesticide and what final registration decision they have taken.

In this step of the project, a quick search was conducted of the registration status in the EU and the USA of all pesticides listed in Table 6. This shows that some pesticides listed as HHP in Mozambique are not registered, or are being phased out, in both the EU and the USA (i.e. 9 active ingredients of HHPs and 3 additional ones for the "close to" HHPs). In some cases, this was for health and/or environmental reasons, but in others because the registration dossier was incomplete or because the pesticide was never submitted for registration in the first place. The

majority of the pesticides listed in Table 6, however, is still registered in either the EU or the USA, or in both.

When deciding on risk reduction measures for HHPs in Mozambique, including possible phase-out of certain products, it is therefore important to evaluate why exactly other registration authorities have decided not to register a pesticide; or if they have registered the pesticide, under which conditions it is allowed. These justifications and conditions should then be compared to the – actual or expected – use situation in Mozambique to evaluate whether the pesticide can continue to be used in the country, and with what possible restrictions.

3.5 Import statistics

The volumes of pesticides identified as HHPs and "coming close" to HHPs that were imported into Mozambique in the period 2010 – mid-2012 are listed in Table 6. The main objective of reviewing the import statistics is to identify which pesticides are likely not used (anymore) in the country, and for which no use surveys or additional hazard/risk assessments (Project Step 2) need to be conducted.

For 21 out of the listed 38 HHP-and "close to" HHPs active ingredients, no pesticide products were imported at all. For another seven active ingredients, less than 250 kg or litres were imported annually, and these would have a relatively low priority for further use surveys.

The most imported HHPs are products containing aluminium phosphide, benomyl, dichlorvos, difethialone, endosulfan, formaldehyde and metamidophos, with average annual imports greater than 2000 kg or litres; the most imported pesticides "coming close" to HHPs are 2,4-D dimethylamine, bendiocarb, diuron, mancozeb, paraquat and permethrin.

4 Conclusion

4.1 Methodology

The approach used for this first step of the project was entirely desk-based. It consisted of comparing all pesticide products registered in Mozambique against the criteria for highly hazardous pesticides (HHPs) as defined by the FAO/WHO Joint Meeting on Pesticide Management (JMPM). Since no international databases exist of HHPs, various reputable data sources were used to verify the criteria for each registered pesticide.

Overall, this approach allowed the assessment of the large majority of pesticide products registered in Mozambique. Some data gaps were identified, however, mainly for microbial pesticides, adjuvants/synergists and repellents. These pesticides could not be evaluated against all HHP criteria. But because these groups are generally of low hazard, it is not very likely that HHPs would have been missed.

On the other hand, a limited number of "regular" chemical pesticides could not be evaluated either for some criteria, using the data sources chosen for this study. Data were lacking mainly with respect to chronic toxicity (carcinogenicity, mutagenicity and reproductive toxicity) and for characteristics to identify persistent organic pollutants (POPs). Therefore, it cannot be excluded that the list of HHPs would be slightly longer if data would have been available for all pesticides.

The assessment of import volumes is very useful to distinguish between pesticides which have been registered but are not used in Mozambique, and those that are. This greatly helps to reduce the short-list of HHPs which require further use and exposure surveys and/or hazard/risk assessments.

4.2 Short-list of HHPs

The main objective of this first step of the project was to identify highly hazardous pesticides (HHPs) that are registered and used in Mozambique, and prepare a short-list of products that require further surveys on use and exposure and/or risk assessments. It is on the basis of the combined information from theoretical hazard assessments, more realistic risk assessments and actual use and exposure information that the Ministry of Agriculture can make informed decisions on further authorization of use of these HHPs.

This first step therefore results in a short-list on which to focus activities under Step 2 of the project. Based on the evaluation of HHP criteria discussed above, and the import statistics, it is recommended to focus the use and exposure surveys in the field, and further hazard and risk assessments, on the pesticide products listed in Table 7. These are all pesticides which average annual imports of more than approximately 250 kg or L. Identified HHPs that are imported in lower volumes are not given priority for Step 2 activities.

In total, Table 7 consists of 76 pesticide products containing 18 different active ingredients. These represent 10% of registered pesticide products and 8% of registered active ingredients in Mozambique.

Table 7. Short-list of highly hazardous pesticides (HHPs) and pesticides "coming close" to HHPs, prioritized for further study in Step 2 of the project.

Reg. no.	Trade name	Active ingredient
HHPs		
1172	Fumate 56% FT	Aluminium Phosphide 560 g/kg
1054	Moz Aluminium Phosphide Pellets	Aluminium Phosphide 560 g/kg
581	Phosgard 56% FT	Aluminium phosphide 560 g/kg
773	Falfume 57% FT	Aluminium Phosphide 570 g/kg
1071	Moz Aluminium Phosphide Tablets	Aluminium Phosphide 570 g/kg
1129	Quickphos 57% FT	Aluminium Phosphide 570 g/kg
1080	Biophos 57% FW	Aluminium phosphide 570 g/kg
1028	Celphos 57% FT	Aluminium phosphide 570 g/kg
664	Volcano Aluminium Phosphide 57% FT	Aluminium phosphide 570 g/kg
467	Benopec 50% WP	Benomyl 500 g/kg
772	Volcano Demeter 50% WP	Benomyl 500 g/kg
1202	Divos 100% EC	Dichlorvos 1000 g/l
774	Falcovos 100% EC	Dichlorvos 1000 g/l
984	Nuvam 100% EC	Dichlorvos 1000 g/l
944	Finale Rat And Mouse Grain Bait	Difethialone 0,025 g/kg
969	Finale Rat And Mouse Pellets	Difethialone 0,025 g/kg
943	Finale Rat And Mouse Wax Bait	Difethialone 0,025 g/kg
719	Ratex Pellts	Difethialone 0,025 g/kg
1027	Endocel 35% EC	Endosulfan 350 g/l
447	Endopec 35% EC	Endosulfan 350 g/l
825	Enticer 35% EC	Endosulfan 350 g/l
605	Volcano Endosulfão 35% EC	Endosulfan 350 g/l
1115	Vet Fume B	Formaldehyde 370 g/l
1163	Chemaron 58% SL	Methamidophos 585 g/l
1199	Sniper 58.5% SL	Methamidophos 585 g/l
639	Volmet 58,5% SL	Methamidophos 585 g/l
1198	Methomex 90% SP	Methomyl 900 g/kg
1185	Oxadate 31% SL	Oxamyl 310 g/l
810	Vydate 31% SL	Oxamyl 310 g/l
"close to" HHPs		
570	Volcano 2,4 D 72% SL	2,4-D dimethylamine 720 g/l
1063	Moz Paraquat 20% SL	Paraquat 200 g/l
1303	Paracot 20% SL	Paraquat 200 g/l
1262	Para-Cure 20% SL	Paraquat 200 g/l
458	Paraxone 20% SL	Paraquat 200 g/l
764	Volquato 20% SL	Paraquat 200 g/l
1181	Gramozat 20% SL	Paraquat 200 g7l

Reg. no.	Trade name	Active ingredient
544	Ficam 80% WP	Bendiocarb 800 g/kg
735	Tocaia 80% WP	Bendiocarb 800 g/kg
884	Avisnail 5% RB	Carbaryl 20 g/kg (+metaldehyde 30 g/kg
811	Supona 30% EC	Chlorfenvinphos 300 g/l
1155	Dichlorvos 10% EC	Dichlorvos (DDVP)100 g/l
985	Nuvan Profi 12,4% AE	Dichlorvos 124 g/l
986	Metrad 75% WG	Diuron 400 g/kg (+metribuzin 360 g/kg)
461	Dipec 80% WP	Diuron 800 g/kg
849	Volcano Diuron 80% WG	Diuron 800 g/kg
532	Volcano Diurão 800 SC	Diuron 800 g/l
1061	Moz Diuron 80% SC	Diuron 800 g/l
1101	Milthane Super 80% WP	Mancozeb 800 g/kg
663	Volcano Crater MX 70% WP	Mancozeb 100 g/kg (+metalaxyl 600 g/kg)
508	Etylit MZ 70% WP	Mancozeb 350 g/kg (+fosetyl-aluminium 350 g/kg)
1236	Crater 455 SC	Mancozeb 455 g/l
477	Megatop 50,5% WP	Mancozeb 465 g/kg (+cymoxanil 40 g/kg)
1075	Dithane NT 60% OS	Mancozeb 600 g/kg
875	Volcano Crater MX 72% WP	Mancozeb 640 g/kg (+ Metalaxyl 80 g/kg)
546	Ridomil Gold 68% WP	Mancozeb 640 g/kg (+metalaxyl 40 g/kg)
472	Ekyp MZ 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)
823	Mascot 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)
1136	Metaman FAE PM 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)
1087	Neltylxyl 72% WP	Mancozeb 640 g/kg (+metalaxyl 80 g/kg)
844	Ridomil Gold MZ 68 WG	Mancozeb 640 g/kg (+metalaxyl-M 40 g/kg)
1045	Moz Controller	Mancozeb 700 g/kg (+cymoxanil 60 g/kg)
1307	Cotzeb 80% WP	Mancozeb 800 g/kg
1162	Curethane 80% WP	Mancozeb 800 g/kg
1078	Dithane NT 80% WP	Mancozeb 800 g/kg
1143	Mazole 80% WP	Mancozeb 800 g/kg
1133	Policar MZ 80% WP	Mancozeb 800 g/kg
1221	Ventum 80% WP	Mancozeb 800 g/kg
887	Volomyl 20% SL	Methomyl 200 g/l
463	Rikki 20% SL	Methomyl 200 g/l
1105	Volxyl 24% EC	Oxyfluorfen 240 g/l
1131	King Insectos Voadores	Permethrin 0,4 g/kg (+d-Allethrin 0,82 g/kg +piperonyl butoxide 3,3 g/kg)
974	Majestic Ultra 50% EC	Permethrin 100 g/l (+pirimiphos methyl 400 g/l)
967	Cooper Aerosol Fly and Mosquito Killer	Permethrin 15 g/kg (+piperonyl butoxide 15 g/kg)

Reg. no.	Trade name	Active ingredient
1132	King Insectos Rastejantes	Permethrin 2,5 g/kg (+pyrethrins 1 g/kg)
1123	Majestic super 2% DP	Permethrin 3 g/kg (+pirimiphos methyl 16 g/k)
629	Super Guard Dust 2% DP	Permethrin 4 g/kg (+pirimiphos methyl 16 g/kg)

References

ESIS (2012) European Chemical Substances Information System (ESIS) – Database of Harmonized Classification and Labelling Elements (CLP/GHS). Institute for Health and Consumer Protection, Joint Research Centre, Ispra. (Accessed at various instances between July and October 2012)[http://esis.jrc.ec.europa.eu/index.php?PGM=cla]

EU (2012) European Union Pesticides Database. Health and Consumer Department (SANCO), European Commission, Brussels. (Accessed at various instances between July and October 2012) [http://ec.europa.eu/food/plant/pesticides/pesticides_database/index_en.htm]

FAO (2002) International Code of Conduct on the Distribution and Use of Pesticides. Revised version. Food and Agriculture Organization of the United Nations, Rome.

FAO/WHO (2008) Report of the 2nd Joint Meeting on Pesticide Management and the 4th Session of the FAO Panel of Experts on Pesticide Management. 6-8 October 2008, Geneva. Food and Agriculture Organization of the United Nations, Rome & World Health Organization, Geneva. [http://www.fao.org/agriculture/crops/core-themes/theme/pests/code/panelcode/en/]

GHS (2011) Globally Harmonized System of Classification and Labelling of Chemicals (GHS). 4th Revised edition. Part 3 – Health hazards. United Nations, New York and Geneva. [http://www.unece.org/trans/danger/publi/ghs/ghs_rev04/04files_e.html]

IARC (2012) Agents Classified by the *IARC Monographs*, Volumes 1–104. International Agency for Research on Cancer (IARC), Lyon. [http://monographs.iarc.fr/ENG/Classification/index.php]

IRIS (2012) Integrated Risk Information System (IRIS). United States Environmental Protection Agency, Washington D.C. (Accessed at various instances between July and October 2012) (http://www.epa.gov/IRIS/)

JMPR (2012) Pesticides evaluated by the FAO/WHO Joint Meeting on Pesticide Residues (JMPR). Food and Agriculture Organization of the United Nations, Rome. (Accessed at various instances between August and October 2012) [http://www.fao.org/agriculture/crops/core-themes/theme/pests/lpe/en/]

Lahr J, Kruijne R & Groenwold J (2014) Hazards of pesticides imported intoMozambique,2002-2011. January 2014. Alterra, Wageningen University and Research, Wageningen.

Minag (2012) Lista dos pesticidas registados em Moçambique – junho de 2012. Ministério da Agricultura, Maputo

Montreal (2012) The Montreal Protocol on Substances that deplete the Ozone Layer. List of controlled substances (Accessed in July 2012). **[**http://ozone.unep.org/new_site/en/Treaties/treaties_decisions-hb.php?art_id=59,60,61,62,63]

PPDB (2012) FootPrint Pesticide Properties Database. University of Hertfordshire, Hatfield. [http://sitem.herts.ac.uk/aeru/footprint/en/index.htm]

RepMoz (2009) Regulamento sobre a Gestão de Pesticides / Pesticides Management Regulation. Decree 6/2009 of 31 March 2009. Council of Ministers of the Republic of Mozambique, Maputo.

Rotterdam (2012) Rotterdam Convention on the Prior Informed Consent Procedure for certain hazardous Chemicals and Pesticides in international trade. Annex III (Accessed in July 2012).

[http://www.pic.int/TheConvention/Chemicals/AnnexIIIChemicals/tabid/1132/language/en-US/Default.aspx]

Stockholm (2009) Stockholm Convention on Persistent Organic Pollutants (POPS). Text and Annexes as amended in 2009. [http://chm.pops.int/Convention/ConventionText/tabid/2232/Default.aspx]

Stockholm (2012) Stockholm Convention on Persistent Organic Pollutants (POPS). Annexes A and B. (Accessed in July 2012). [http://chm.pops.int/Convention/ThePOPs/ListingofPOPs/tabid/2509/Default.aspx]

US-EPA (2012a) Chemicals evaluated for carcinogenic potential. November 2012. Office of Pesticide Programs, United States Environmental Protection Agency, Washington D.C.

US-EPA (2012b). US EPA *Pesticide Chemical Search* database. Office of Pesticide Programs, United States Environmental Protection Agency, Washington D.C. (Accessed at various instances between August and October 2012) [http://iaspub.epa.gov/apex/pesticides/f?p=chemicalsearch:1]

WHO (2005) WHO classification of pesticides by hazard and Guidelines to classification 2004. World Health Organization, Geneva.

WHO (2010) WHO classification of pesticides by hazard and Guidelines to classification 2009. World Health Organization, Geneva. [http://www.who.int/ipcs/publications/pesticides_hazard/en/index.html].

WHO (2012) WHO specifications for pesticides used in public health. (Accessed at various instances between August and October 2012). World Health Organization, Geneva. [http://www.who.int/whopes/quality/newspecif/en/]

Annex 1: Carcinogenicity – ambiguous cases

This annex lists the pesticides for which the carcinogenicity evaluations by WHO/IARC, EPA and the EU did not result in the same outcome. The final conclusion for the HHP assessment in Mozambique is in the last column of the table. Those considered a carcinogen equivalent to GHS class 1A and 1B are listed as "Yes" and included under the section *Registered pesticides not complying with the JMPM criteria, but "coming close"* of Table 6 of this report.

Active ingredient	**Reviews: carcinogenic** (similar to GHS 1A&1B) **yes/no?** [date of publication of review]				**Conclusion for HHP identification.** **Carcinogenic** (similar to GHS 1A&1B) **yes/no?**
	IARC	**EPA carcinogenicity list**	**EU**	**WHO Classification**	
Alachlor	Not evaluated	Yes: likely at high doses; not likely at low doses; [June 1997] Note: US registered	No; unlikely at doses attained in use (Carc[9]. = Cat. 2) [Jan 2007] Note: EU not registered	No – carcinogenicity mechanism not relevant to humans [2010]	No. US registered, and EU not registered. Most recent reviews conclude pesticide is not carcinogenic at relevant rates
Carbaryl	No [1987]	Yes: likely to be carcinogenic [Feb 2002] Note: US registered, but basic or extensive PPE required for handling and use ; wettable powders only packaged in water-soluble bags, to reduce cancer risk (amended RED[10], 2008)	No (Carc. = Cat. 2) [Sep 2006] Note: EU not registered; potential carcinogenic properties of the active substance is noted as a concern (Review report[11], 2006)	Not evaluated	Yes. EU not registered. US registered, but with PPE other risk mitigations

[9] Carc.: Carcinogenicity classification (EU)

[10] RED: Reregistration Eligibility Document (US – Environmental Protection Agency)

[11] Review report: Review report on active substances (EU - Standing Committee on the Food Chain and Animal Health)

Active ingredient	Reviews: carcinogenic (similar to GHS 1A&1B) yes/no? [date of publication of review]				Conclusion for HHP identification. Carcinogenic (similar to GHS 1A&1B) yes/no?
	IARC	EPA carcinogenicity list	EU	WHO Classification	
Chlorothalonil	Not evaluated	Yes: likely to be carcinogenic [Oct 1997] Note: US registered. Dietary cancer risk due to HCB impurities in chlorothalonil; limit < 40 ppm is acceptable. (RED Factsheet[12] 1999)	No (Carc. = Cat. 2) [Sep 2006] Note: EU registered	Not evaluated	No; unless products in Mozambique contain high levels of HCB impurities Registered in both US and EU.
Diuron	Not evaluated	Yes: known/likely to be carcinogenic [July 1997] Note: US registered. However, occupational cancer risk of concern; i.e. use of backpack sprayers prohibited (RED, 2003)	No (Carc. = Cat. 2) [Jul. 2008] Note: EU registered	Not evaluated	Yes Explicit prohibition of use with backpack sprayers in US; so a concern for Mozambique
Epoxicionazol	Not evaluated	Yes: likely to be carcinogenic [Jan 2001] Note: US only an import tolerance; dietary risk acceptable; occupational risk not evaluated	No (Carc. = Cat. 2) [sep 2010] Note: EU registered	Not evaluated	No Registered in EU and tolerance in US.

[12] Factsheet: US – EPA pesticide registration factsheets

Active ingredient	**Reviews: carcinogenic** (similar to GHS 1A&1B) **yes/no?** [date of publication of review]				**Conclusion for HHP identification.** **Carcinogenic** (similar to GHS 1A&1B) **yes/no?**
	IARC	**EPA carcinogenicity list**	**EU**	**WHO Classification**	
Iprodione	Not evaluated	Yes: likely to be carcinogenic [Feb 1998] Note: US registered. However, all residential uses cancelled due to cancer risk concerns. Also, backpack sprayers, mixers should wear double layer PPE, masks and gloves. (RED, 1998)	No (Carc. = Cat. 2) [sep 2004] Note: EU registered	Not evaluated	Yes Registered in both EU and US. However, US proposed risk mitigation measures (PPE for sprayers/handlers and cancellation of residential uses) poses significant concern for Mozambican use situation.
Isoxaflutole	Not evaluated	Yes: likely to be carcinogenic [Sep 1997] Note: US registered.	No (Carc. not classified) [oct 2003] Note: EU registered	Not evaluated	No. Registered in both EU and US.
Kresoxim-methyl	Not evaluated	Yes: likely to be carcinogenic [Aug 1999] Note: US registered. But only on ornamental crops (Factsheet 1998)	No (Carc. = Cat. 2) [jan 2012] Note: EU registered	Not evaluated	No. Registered in both EU and US.
Mancozeb (cancer risk due to ETU metabolite)	Not evaluated	Yes: probable human carcinogen [Jul 1999] Note: US registered. Cancer risk below EPA thresholds; but (at least) layer PPE required; WP formulations only as water-soluble bags (RED 2005)	No (Carc. not classified) [july 2006] Note: EU registered	Not evaluated	Yes. Registered in both EU and US. However, US proposed risk mitigation measures (full PPE for sprayers/handlers and requirement for water-soluble bags for WPs) poses significant concern for Mozambican use situation.

Active ingredient	**Reviews: carcinogenic** (similar to GHS 1A&1B) **yes/no?** [date of publication of review]				**Conclusion for HHP identification.** **Carcinogenic** (similar to GHS 1A&1B) **yes/no?**
	IARC	**EPA carcinogenicity list**	**EU**	**WHO Classification**	
Metiram	Not evaluated	Yes: probable human carcinogen [Jul 1999] Note: US registered. (RED, 2005)	No (Carc. not classified) [july 2006] Note: EU registered (review report 2005: "no evidence of carcinogenic potential")	Not evaluated	No. Registered in both EU and US. Most recent EU review concludes pesticide is not carcinogenic
Oxadiazon	Not evaluated	Yes: likely to be carcinogenic [May 2001] Note: US registered. Cancer risks for occupational handlers of wettable-powder formulations of oxadiazon are of concern. Exposure scenarios of concern include mixing/ loading/ applying wettable powder formulations. To reduce these risks, the wettable powder formulations will be packaged in water-soluble packaging (WSP) only (RED Factsheet 2008)	No Carc. not classified. [jan 2010] Note: EU registered EFSA Conclusion (2010): "humans are not responsive to this class of non-genotoxic carcinogens and therefore, oxadiazon is unlikely to present a carcinogenic risk to humans"	Not evaluated	No. Registered in both EU and US. Most recent review indicates low cancer risk.
Oxyfluorfen	Not evaluated	Yes: likely to be carcinogenic [Mar 2010] Note: US registered. Cancer risk of handlers applicators / workers: Double layer Personal Protective Equipment (PPE) for all other mixers, loaders, and applicators; closed mixing/loading/ application systems required for use in several major crops.	No (Carc. not classified) [jan 2012] Note: EU registered EFSA Conclusion (2010): … classification as Carc Cat 3 – *limited evidence of a carcinogenic effect* – was proposed by EFSA.	Not evaluated	Yes. Registered in both EU and US. However, US proposed risk mitigation measures (double PPE and closed systems) poses significant concern for Mozambican use situation.

Active ingredient	**Reviews: carcinogenic** (similar to GHS 1A&1B) **yes/no?** [date of publication of review]				**Conclusion for HHP identification.** **Carcinogenic** (similar to GHS 1A&1B) **yes/no?**
	IARC	**EPA carcinogenicity list**	**EU**	**WHO Classification**	
Permethrin	No [1991]	Yes: likely to be carcinogenic [Oct 2002] Note: US registered. In some application scenarios, cancer risk exceeds the threshold. WP and DP formulations require double layer PPE. (Factsheet, 2009).	No (Carc. not classified) Note: EU not registered. (due to incomplete dossiers, mainly for ecotox topics).	Not evaluated	Yes. Registered in US, but not in EU. Certain uses in US require extensive PPE – to be compared with Mozambique uses of permethrin.
Tetrachlorvinphos	No	Yes: likely to be carcinogenic [Mar 2002] No: Group C: possible human carcinogen [July 2006] Note: US registered.	No (no classification because no toxicological information) Note: EU not registered.	Not evaluated	No. Latest US evaluation does not place this pesticide in the HHP category
Thiabendazole	Not evaluated	Yes: Likely human carcinogen at high doses; not likely at low doses [Mar 2002] Note: US registered. "Carcinogenic risks at expected doses not pose a concern" (Factsheet, 2002)	No (Carc. not classified) Note: EU registered.	Not evaluated	No. Registered in both EU and US.
Thiodicarb (Note: rapid degradation to methomyl)	Not evaluated	Yes: Probable human carcinogen. [Jun 1996] Note: US registered. Relatively standard PPE requirements; no specific PPE to reduce carcinogenicity risk (RED, 1998)	No (Carc. not classified) Note: EU not registered. Overall, thiodicarb does not show genotoxic or carcinogenic potential (EFSA Opinion, 2005)	Not evaluated	No. Most recent EU review concludes pesticide is not carcinogenic

Reducing Risks of Highly Hazardous Pesticides in Mozambique

Step 2 – Survey of pesticide use practices in selected cropping systems

Armando Marcos W. Come

Khalid Cassam

Livia Loy Dona

Francesca Mancini

Harold van der Valk

[9 July 2014]

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Acknowledgements

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FAO Disclaimer

Contents

1. Introduction

A project entitled *Reducing Risks of Highly Hazardous Pesticides (HHPs) in Mozambique* was initiated by the Government of Mozambique with the objective to reduce the greatest risks associated with pesticide use in the country. This project is implemented with technical support of FAO's Pesticides Management Unit and is funded by SAICM Quick Start Programme Trust Fund.

The ultimate goal is to develop and implement an "HHP Risk Reduction Action Plan" for the most dangerous pesticides and use situations, resulting over time in the implementation of a variety of risk reduction measures based on a review of use conditions. These may include the cancellation of specific registrations of HHPs, implementation of risk mitigation measures, appropriate use restrictions, development of alternative pest management strategies, promotion of good agricultural practices, or phase-out of specific pesticides.

In the first step of the project, a review of all pesticides registered in Mozambique was carried out and a shortlist of highly hazardous pesticides was established. This shortlist was based on an assessment of the hazards of the pesticides, based on criteria established by the FAO/WHO Joint Meeting on Pesticide Management (Come & Van der Valk, 2014).

During the second step of the project, a use survey was carried out in selected regions and cropping systems in Mozambique. The main goal of the survey was to identify the conditions under which pesticides are being used in the country and their contribution to potential risks for human health and the environment.

The third step of the project consisted of a stakeholder consultation to further discuss the use and risks of highly hazardous pesticides in Mozambique and fine-tune the shortlist based on the survey results and the expertise and experience of stakeholders.

2. Methodology

2.1 Cropping systems

Cropping systems were selected for the study in which pesticides are used on a regular basis and/or HHPs were known to be applied. These are vegetables, cotton and tobacco, generally managed by smaller subsistence farmers. Farmers were surveyed in eight different regions of Mozambique, which was expected to provide a broad sample of pesticide use practices in the country (Table xx). In the regions where the commodity crops cotton and tobacco are grown, limited information was also collected for other crops grown by the same farmers.

In addition, pesticide use practices were also assessed in bananas and sugar cane, both plantation crops run by larger commercial farms.

Table 1 Geographical distribution and cropping systems covered by the pesticide use survey

Region	Number of districts concerned	Crops included in the survey	Number of farmers interviewed	Survey period (2013)
Maputo Ciudade	2	Vegetables	40	1–14 February
Maputo Provincia	3	Vegetables	28	31 Jan. – 8 Feb.
Gaza	2	Vegetables	30	1–19 February
Zambésia	5	Cotton Tobacco (Other crops)	15 19 (34)	29 Jan. – 14 Feb.
Tete	8	Cotton Tobacco (Other crops)	23 50 (73)	16–25 January
Nampula	4	Cotton (Other crops)	20 (20)	16 Jan. – 2 Feb.
Niassa	5	Tobacco Cotton (other crops)	25 11 (36)	17 Jan. – 1 Feb.
Cabo Delgado	4	Cotton (Other crops)	64 (64)	n.a.
Total	**33**		**325**	

Surveys were conducted in January and February 2013, during the rainy season. During this period, vegetables are grown and harvested, cotton has been sown and the plant is in early stages of development, and tobacco approaches the harvest.

2.2 Survey questionnaires

The surveys were conducted using a standard questionnaire, specific for each cropping system. The questionnaires were elaborated to obtain maximum information on pesticide use which could subsequently be used to assess the local risks of HHPs in Mozambique and evaluate the possibilities to introduce alternatives posing a lower risk. Various existing pesticide use or exposure surveys were reviewed (e.g. WHO, 2001; Amera & Abate, 2008; Rotterdam Convention, undated), as well as general guidance on development of this type of questionnaires (e.g. FAO, 1997). The first version of the questionnaire was tested among a

limited number of vegetable farmers around Maputo and various modifications were made to the final version.

The questionnaires followed a structure that was similar, though not identical, for all cropping systems:

1. Demographical socio-economic information
   - e.g.: location, sex, age, education, contact details
2. Crop information for the season 2012/2013 (vegetables, cotton, tobacco, plantation crops) and/or 2011/2012 (cotton, tobacco)
   - e.g.: type of crop, area cultivated, duration of cropping cycle
3. Pesticide application for the season 2012/2013 (vegetables, cotton, tobacco, plantation crops) and/or 2011/2012 (cotton, tobacco)
   - e.g.: name of applied pesticide(s), when applied, against which pest, application rate, number of applications per cropping cycle.
4. Pesticide product information
   - e.g.: type of formulation, type of packaging, label, where and how much purchased, costs
5. Pesticide application conditions
   - e.g.: who prepares the mixture and who applies the pesticide; source of advice on use; personal protective equipment, knowledge of label instructions; type of application equipment; management of empty containers
6. Alternative pest control methods
   - e.g.: awareness of alternative control methods; monitoring and spraying regime (for cotton)
7. Health effects
   - e.g.: if/when exposed to pesticides; decontamination; signs and symptoms of poisoning

The complete questionnaires are provided in Annex xx.

2.3 Interviewers

Interviews of farmers and pesticide distributors were performed by the plant protection officers of the Provincial Directorates of Agriculture. The interviewers were trained in a three-day session in which survey techniques and the data collection form were discussed in detail and subsequently tested in the field. Two training sessions were conducted in January 2013, in Nampula and Maputo, for five and three interviewers respectively.

2.4. Data entry and analysis

Data entry of questionnaire information was produced in Mozambique entered in excel datasets per province. The data was subsequently integrated and harmonised at FAO HQ and analysed using excel 2014.

3. Results

3.1 Socio-demographic coverage

Of the total of 325 farmer that were interviewed, 82% were male and 18% female. Most female farmers were encountered in vegetable production in Gaza and Maputo provinces (Figure xx). Only male farmers were interviewed in cotton in Tete and Zambesia provinces.

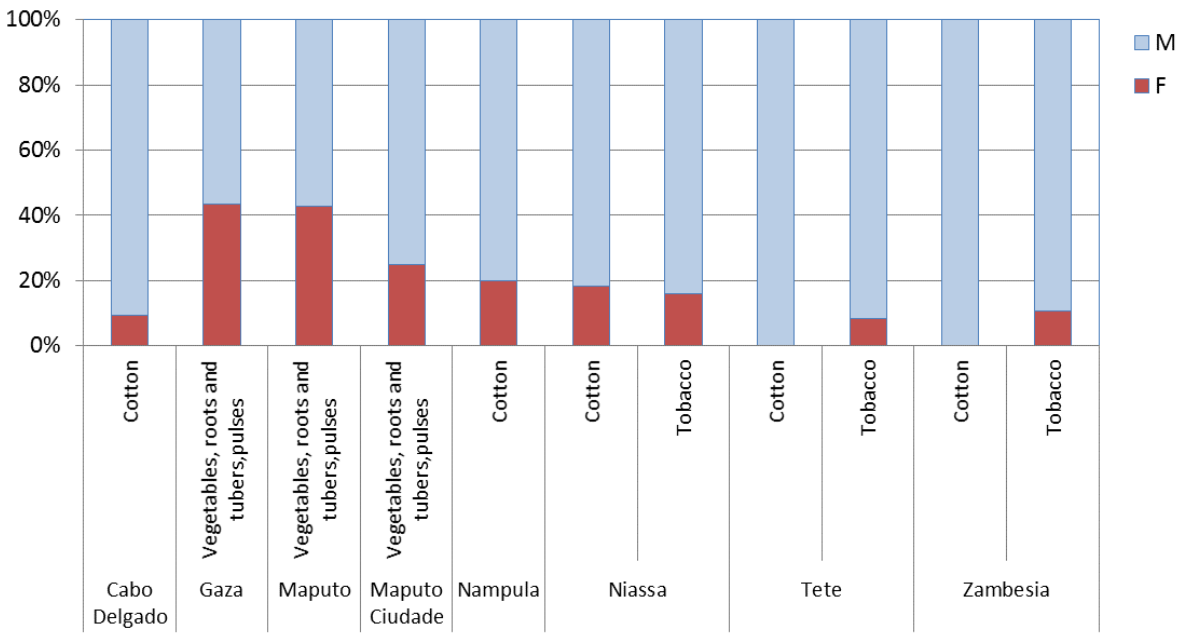


Figure 1 Gender distribution of interviewed farmers, per region and cropping system. F=female, M=male.

Overall, 68% of the interviewed farmers were between the age of 26 and 55. However, age distributions among cropping systems differed (Figure xx). Vegetable farmers were relatively older, with 60% of respondents being over 45 years of age. In contrast, cotton farmers were younger, with 35% under 35 years.

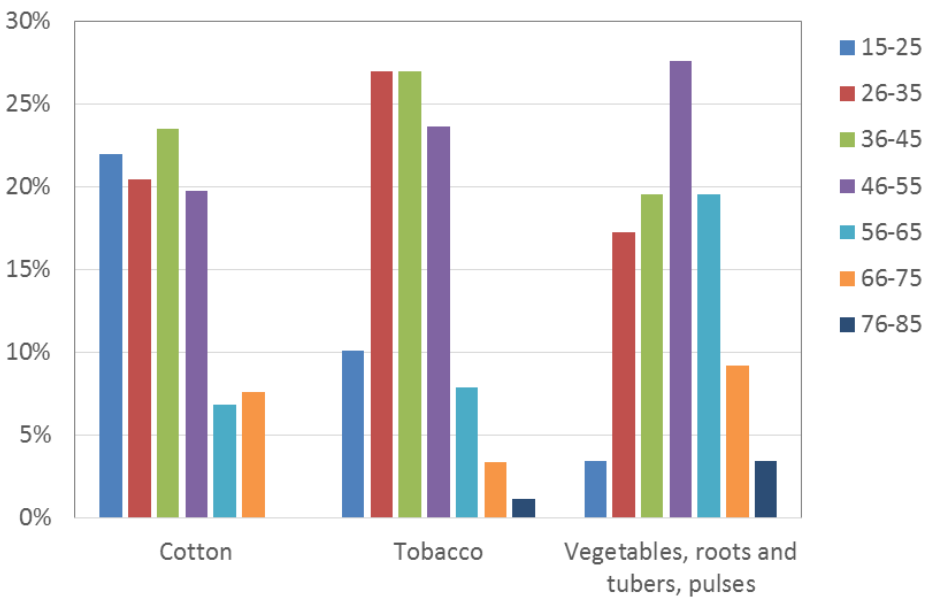


Figure 2 Gender distribution of interviewed farmers, per cropping system.

- The majority of farmers had either elementary education (33% of respondents) or had done level 5-10 (33%); 24% had no education at all. Education levels of respondents were fairly similar in Maputo, Gaza and Niassa. In Tete, Cabo Delgado and Nampula, education levels were on average slightly higher, while in Zambésia they were on average lower.

Table 2 ***Number of farmers interviewed***

Region	Number	Gender		Education[2]						
		Male	Female	None	Elementary	Level 5-10	Level 11-12	Basic agrarian level	Medium agrarian level	Higher level
Maputo Ciudade	40	30	10	4	21	10	2	0	0	0
Maputo Provincia	28	16	12	7	12	7	0	0	0	0
Gaza	30	17	13	4	14	9	0	0	1	1
Zambésia	34	31[1]	2	19	11	3	0	0	0	0
Tete	73	69	4	15	22	34	2	0	0	0
Nampula	20	16	4	3	5	12	0	0	0	0
Niassa	36	30	6	13	16	7	0	0	0	0
Cabo Delgado	64	58	6	14	24	24	1	1	0	0
Total	***325***	***267***	***57***	***79***	***125***	***106***	***5***	***1***	***1***	***1***

[1] One interview with a production company; gender not indicated.
2 For 7 persons education level not indicated.

3.2. Crop distribution

Table 3 crop distribution per province in database

provinces	Cotton	Tobacco	Vegetables, roots and tubers,pulses
Cabo Delgado	100.00%	0.00%	0.00%
Gaza	0.00%	0.00%	100.00%
Maputo	0.00%	0.00%	100.00%
Maputo Ciudade	0.00%	0.00%	100.00%
Nampula	100.00%	0.00%	0.00%
Niassa	30.56%	69.44%	0.00%
Tete	34.25%	65.75%	0.00%
Zambesia	44.12%	55.88%	0.00%
Grand Total	**41.54%**	**28.31%**	**30.15%**

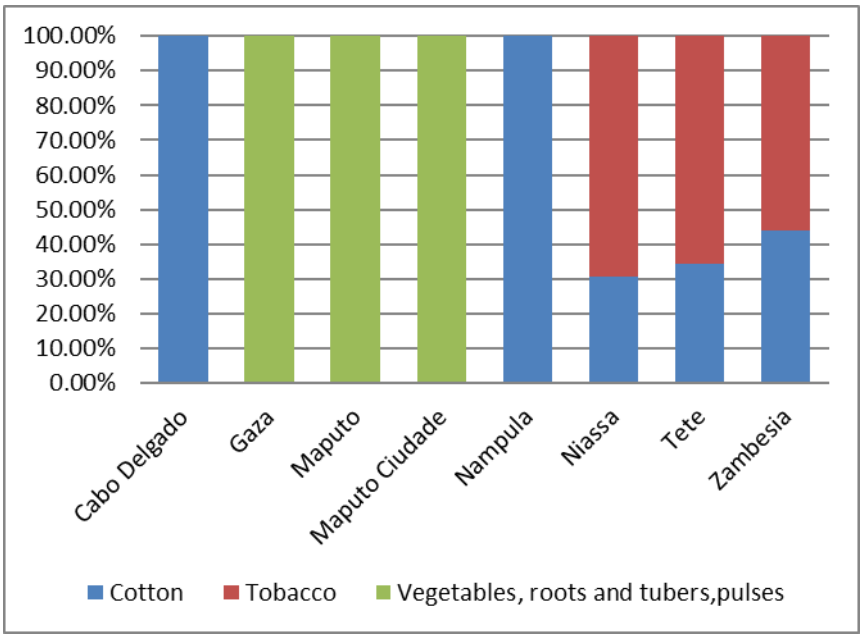


Figure 3 crop distribution per province

3.3. Use of pesticides

3.3.1. Use of pesticides

The majority of the respondents where applying themselves the pesticide, and this is true for all provinces surveyed. Therefore they were providing personal replies on their use of pesticides.
The surveys revealed that most of the farmers surveyed applied pesticides- only 17 of the 325 said they did not.

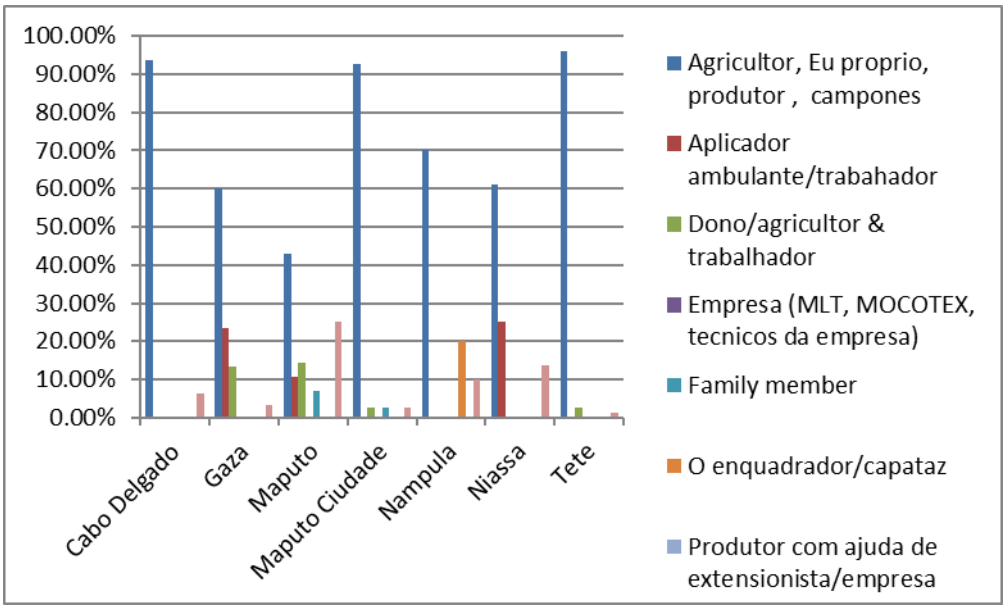


Figure 4 applicators of pesticide

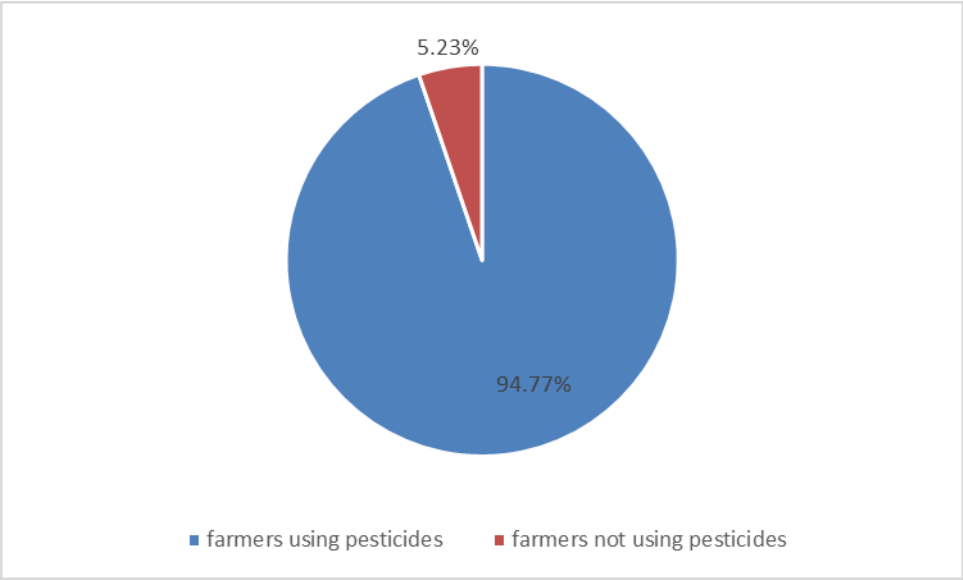


Figure 5 use of pesticide for farmer's part of the survey

3.3.2. Use of Highly Hazardous Pesticides (HHPs)

Farmers using HHPs (as per FAO-WHO 7 criteria) include almost 30% of the surveyed farmers. The HHP formulation that is most used is by far including methamidophos compound which is used by a great share of farmers particularly for vegetable crops. In addition, farmers reported overspraying vegetable crops as many as 14 timesper growing season.

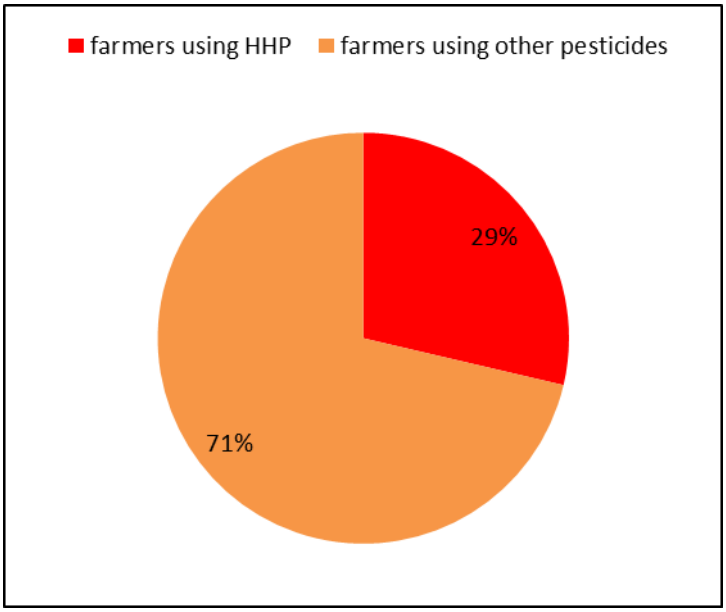


Figure 6 HHP users (out of farmers who apply pesticides)

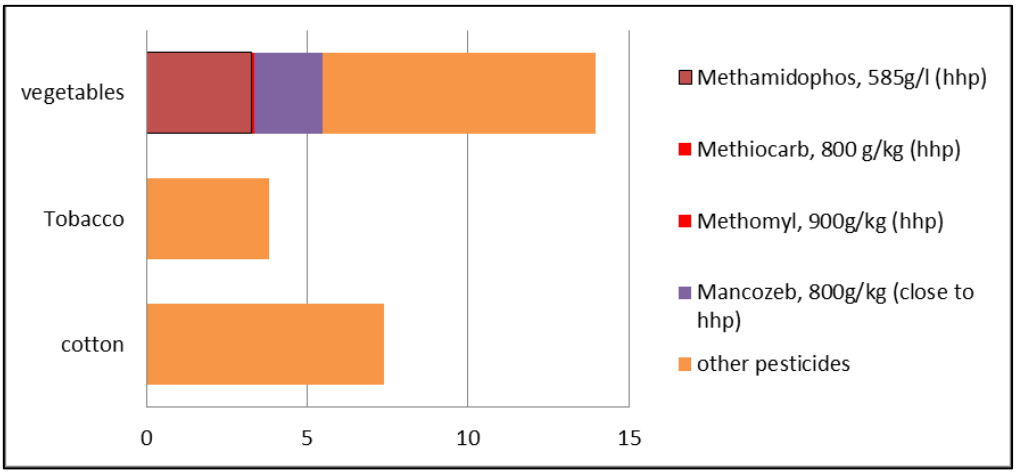


Figure 7 average applications of pesticides for farmers surveyed per crop

3.3.3. Training of farmers on pesticide use

At least half farmers did not receive training on pesticide use while making use of pesticides including HHPs.

Row Labels	Não	Sim	null	Grand Total
Cabo Delgado	60.94%	32.81%	6.25%	100.00%
Gaza	73.33%	26.67%	0.00%	100.00%
Maputo	46.43%	46.43%	7.14%	100.00%
Maputo Ciudade	55.00%	42.50%	2.50%	100.00%
Nampula	80.00%	20.00%	0.00%	100.00%
Niassa	47.22%	44.44%	8.33%	100.00%
Tete	43.84%	53.42%	2.74%	100.00%
Zambesia	5.88%	88.24%	5.88%	100.00%
Grand Total	**50.15%**	**45.54%**	**4.31%**	**100.00%**

3.3.5. Pesticide application equipment

The majority of pesticide applicators used manual sprayer (36%), followed by electric sprayer (with batteries); 33% and followed by inappropriate equipment such as watering can (13.5%) or other (unknown) means (12.5%).

Table 4 Pesticide application equipment

Provinces	Balde	Outros	Pulverizador de dorso manual	Pulverizador que funcionam a pilhas (e.x. Micro-Ulva)	Regador	no data
Cabo Delgado	0.00%	0.00%	0.00%	93.75%	0.00%	6.25%
Gaza	3.33%	0.00%	96.67%	0.00%	0.00%	0.00%
Maputo	0.00%	0.00%	100.00%	0.00%	0.00%	0.00%
Maputo Ciudade	0.00%	0.00%	97.50%	0.00%	0.00%	2.50%
Nampula	0.00%	0.00%	0.00%	100.00%	0.00%	0.00%
Niassa	0.00%	61.11%	5.56%	25.00%	0.00%	8.33%
Tete	0.00%	0.00%	24.66%	6.85%	60.27%	8.22%
Zambesia	0.00%	55.88%	2.94%	41.18%	0.00%	0.00%
Grand Total	**0.31%**	**12.62%**	**36.00%**	**33.23%**	**13.54%**	**4.31%**

3.3.6. Farmer reports of undue pesticide contamination

Farmers responses to the question: “are you receiving pesticides on clothes or skin, or in your eyes during using pesticides?” are summarised in the tables and figures below. At the national level (as sum) about half farmers surveyed reported that they noticed to receive pesticide on their clothes, bare skin or eyes when using pesticides, with some differences between provinces for different crops.

Table 5 Farmer reports of noticing of being contaminated by pesticides while using them

Provinces	Não, nunca	Sim	Sim, algumas vezes	Sim, muitas vezes	null
Cabo Delgado	20.31%	0.00%	62.50%	17.19%	0.00%
Gaza	66.67%	0.00%	23.33%	10.00%	0.00%
Maputo	28.57%	3.57%	60.71%	3.57%	3.57%
Maputo Ciudade	50.00%	17.50%	32.50%	0.00%	0.00%
Nampula	25.00%	0.00%	50.00%	25.00%	0.00%
Niassa	69.44%	0.00%	25.00%	2.78%	2.78%
Tete	63.01%	0.00%	26.03%	9.59%	1.37%
Zambesia	88.24%	0.00%	11.76%	0.00%	0.00%
Grand Total	**51.38%**	**2.46%**	**36.62%**	**8.62%**	**0.92%**

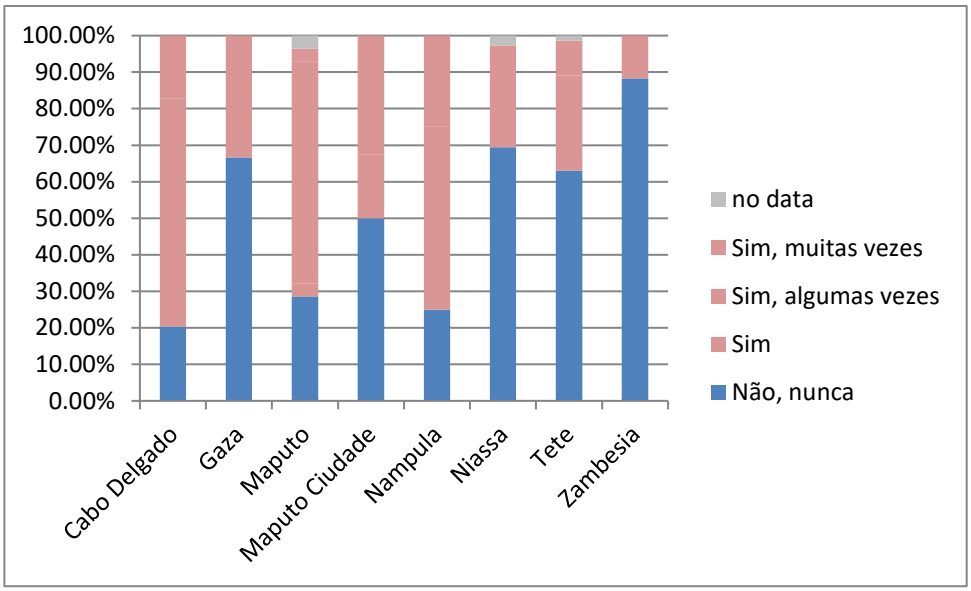
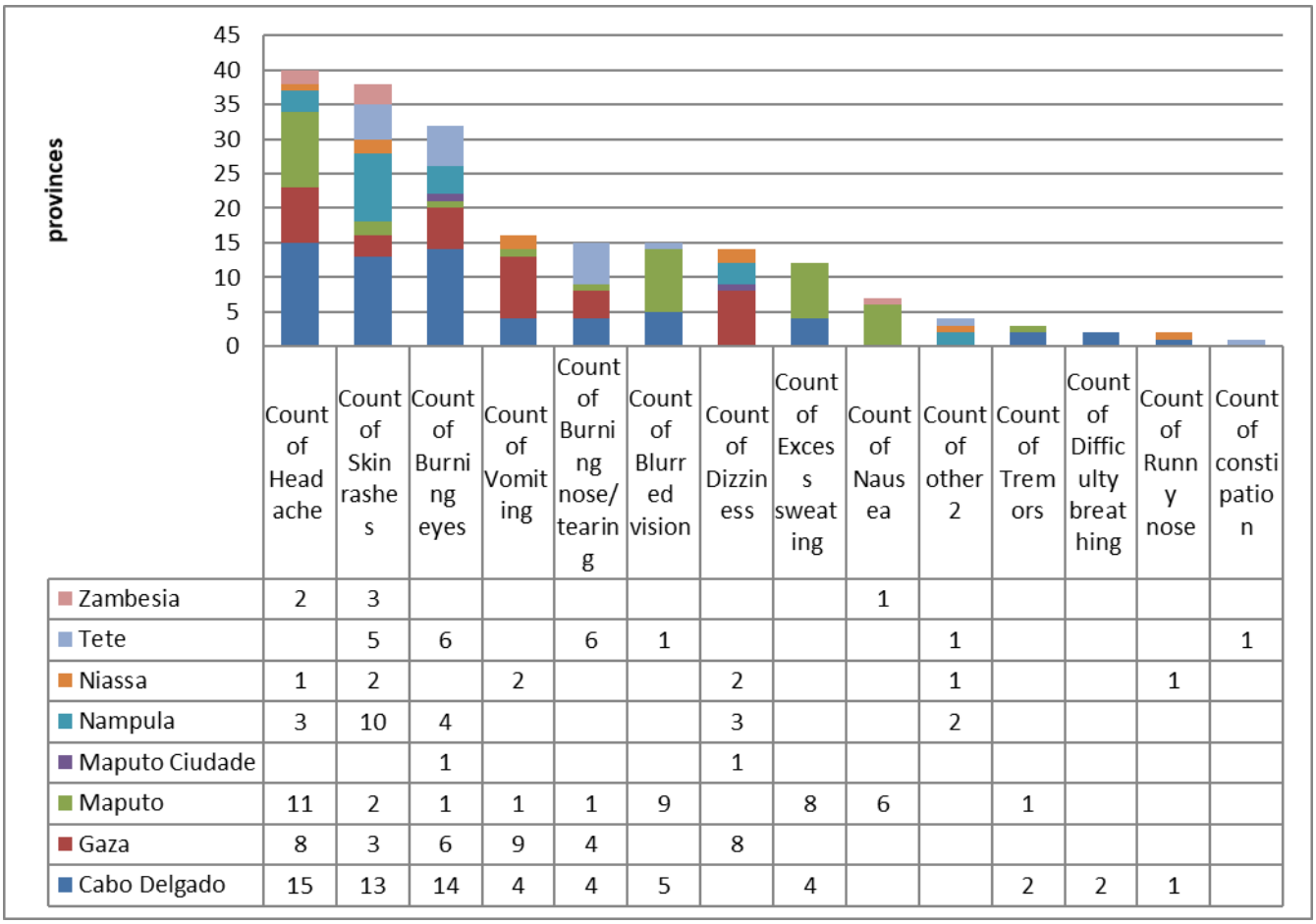


Figure 8 Farmer reports of noticing of being contaminated by pesticides while using them

3.3.7. Main health symptoms associated with pesticide use by farmers

Main health symptoms associated with pesticide use by farmers noticing symptoms were headaches, skin rashes, burning eyes, vomiting, burning nose, blurred vision, dizziness and excess sweating.



provinces	Count of Head ache	Count of Skin rashes	Count of Burning eyes	Count of Vomiting	Count of Burning nose/ tearing	Count of Blurred vision	Count of Dizziness	Count of Excess sweating	Count of Nausea	Count of other 2	Count of Tremors	Count of Difficulty breathing	Count of Runny nose	Count of constipation
Zambesia	2	3							1					
Tete		5	6		6	1				1				1
Niassa	1	2		2			2			1			1	
Nampula	3	10	4				3			2				
Maputo Ciudade			1				1							
Maputo	11	2	1	1	1	9		8	6		1			
Gaza	8	3	6	9	4		8							
Cabo Delgado	15	13	14	4	4	5		4			2	2	1	

Figure 9 Reported health symptoms of farmers per province after or during having used pesticides

3.3.8. Farmer health management of the symptoms associated with pesticide use

The great majority of farmers who noticed to experience symptoms during or right after pesticide use did not see a doctor or nurse or receive any check in a health care facility.

Table 6 health care of farmers experiencing potential symtoms of pesticide poisoning when using pesticides

Provinces	Não	Sim	null
Cabo Delgado	78.13%	1.56%	20.31%
Gaza	36.67%	0.00%	63.33%
Maputo	82.14%	3.57%	14.29%
Maputo Ciudade	45.00%	0.00%	55.00%
Nampula	85.00%	15.00%	0.00%
Niassa	83.33%	5.56%	11.11%
Tete	53.42%	0.00%	46.58%
Zambesia	91.18%	2.94%	5.88%
Grand Total	**67.38%**	**2.46%**	**30.15%**

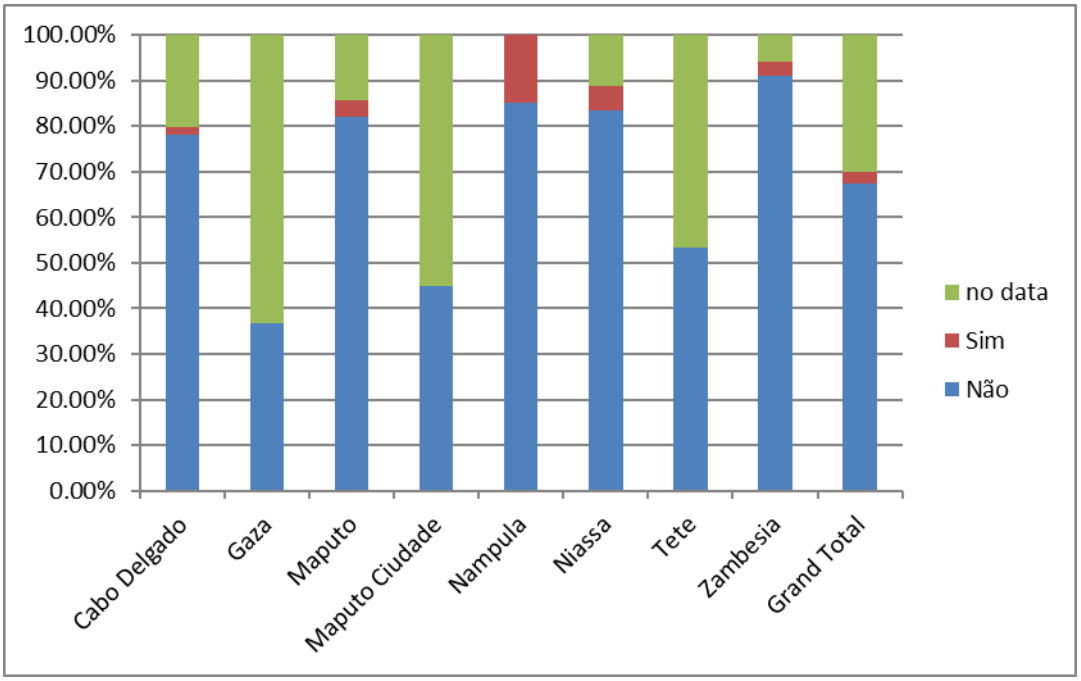


Figure 10 health care of farmers experiencing potential symtoms of pesticide poisoning when using pesticides

3.3.9. Use of Personal Protective Equipment by pesticide applicators including HHPs

Almost none of the farmers owned or wore adequate personal protective equipment. This is showns in the figures and tables below.

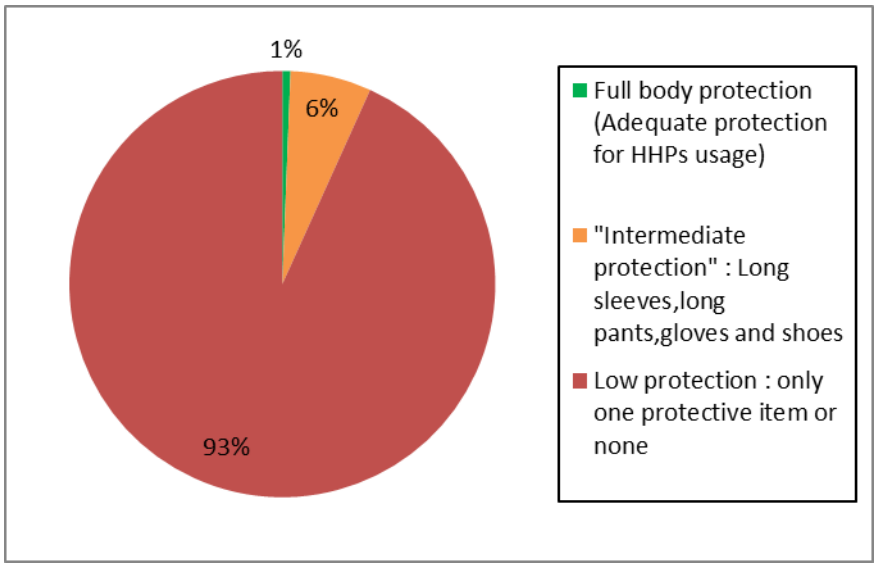


Figure 11 ***PPE usage for all farmers applying pesticides***

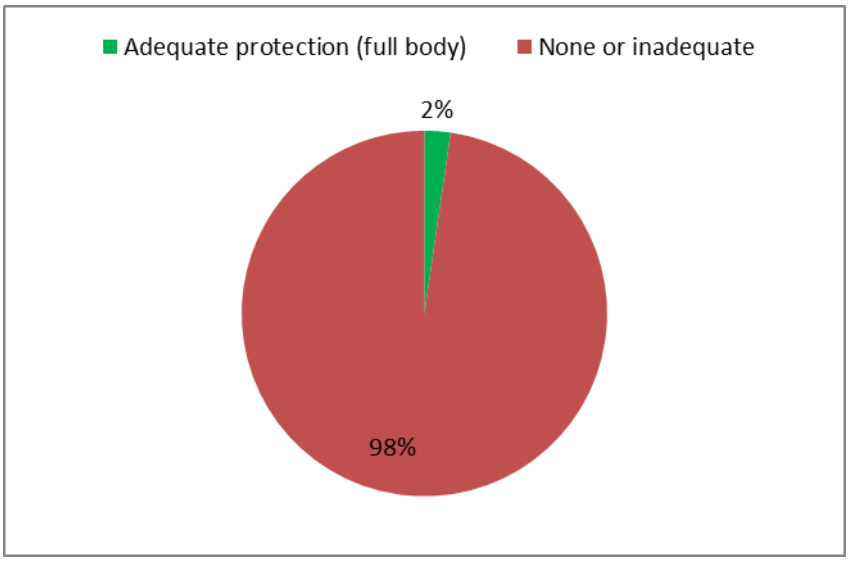


Figure 12 PPE usage for farmers applying HHPs

Table 7 Figure 14 clothes worn by pesticide applicators

Long pants	Shirt with long	Rubber boots	Gloves	bare feet or flip	T-shirt	Shorts	Shoes	Rubber mask	Overalls	Dust mask	Eyes glasses or	Other
63%	53%	39%	34%	34 %	29 %	17%	20%	15%	7%	3%	3%	2%

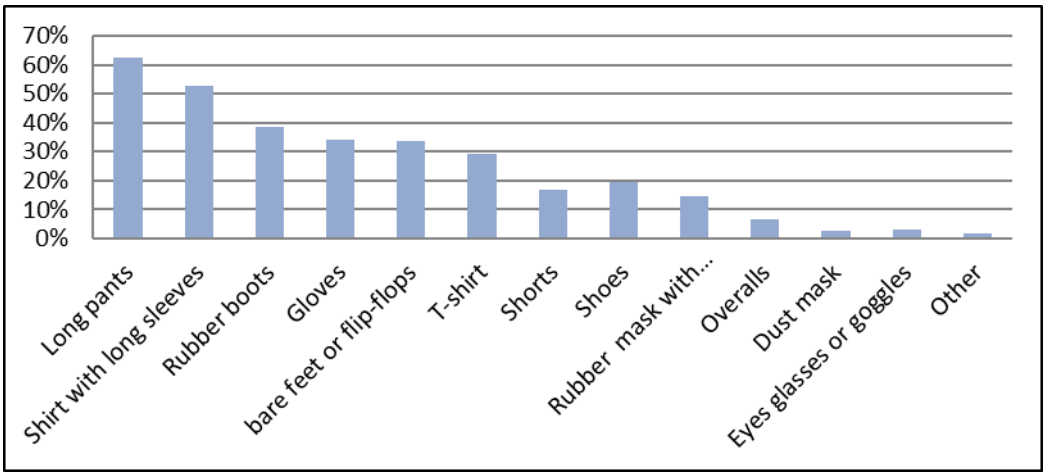


Figure 13 Clothes worn by pesticide applicators

3.3.10. Extent of protection of pesticide applicators by body part

Table 8 Protection used per body part by pesticide applicators

Row Labels	other	overalls	Rubber mask with filter	Dust mask	no mask?	Eye glasses or goggles	no eye protection?	gloves	no gloves?	t-shirt	Shirt with long sleeves	no shirt?	shorts	long pants	Rubber boots	Shoes	Bare feet
Grand Total	2	6	14	2	84	50	50	3	96	16	28	50	60	32	37	19	32

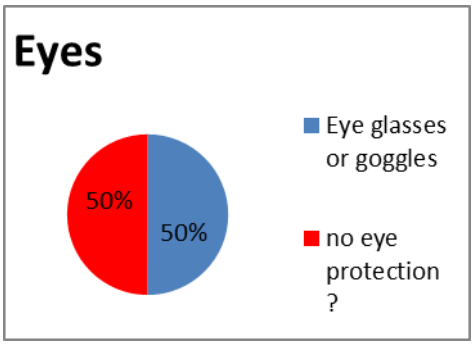


Figure 14 eye protection of pesticide applicators

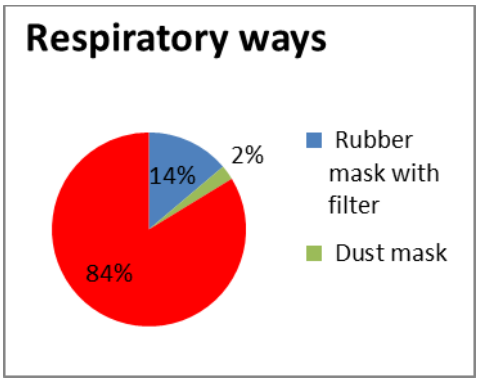


Figure 15 respiratory protection of pesticide applicators

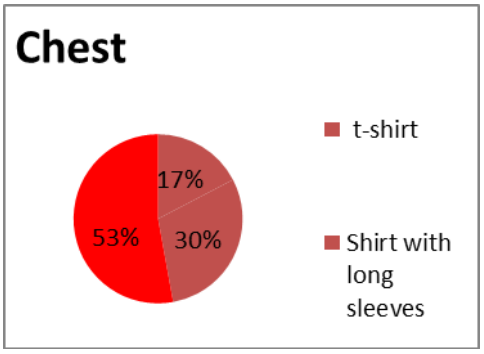


Figure 16 dermal chest protection of pesticide applicators

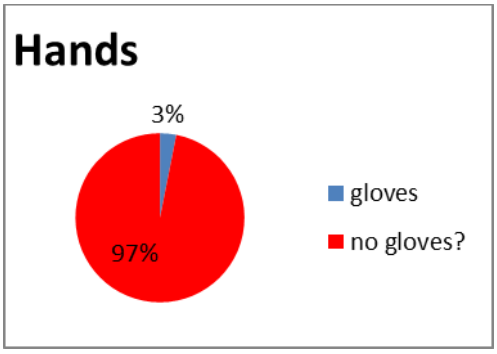


Figure 17 dermal hand protection of pesticide applicators

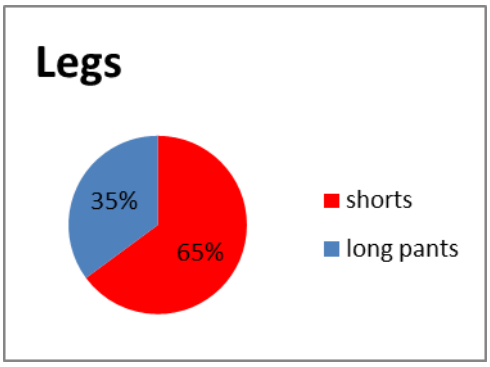


Figure 18 dermal leg protection of pesticide applicators

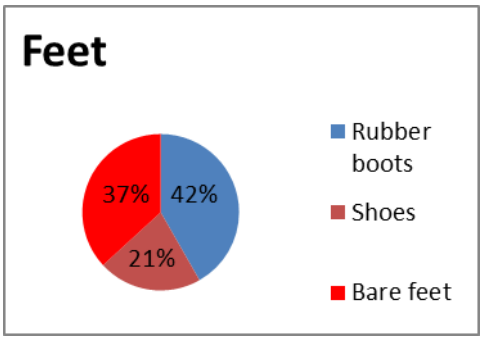


Figure 19 dermal feet protection of pesticide applicators

3.3.11. Pesticide label reading and understanding

Almost half of the farmers declared they did not read pesticide labels, includinguse instructions such as proper dosage and protective measures, the main reason being illiteracy. One out of four farmers poorly understood the colour band on pesticide labels that indicates acute toxicity. Tables and figures below show details by province and crops.

Table 9 percentage of farmers declaring to read the pesticide label per province

Provinces	Não	Sim	null	Grand Total (# of famers responding to this question	
Cabo Delgado	82.81%	10.94%	6.25%	64	
Gaza	86.67%	10.00%	3.33%	30	
Maputo	67.86%	32.14%	0.00%	28	
Maputo Ciudade	62.50%	37.50%	0.00%	40	
Nampula	95.00%	5.00%	0.00%	20	
Niassa	88.89%	5.56%	5.56%	36	
Tete	49.32%	46.58%	4.11%	73	
Zambesia	64.71%	35.29%	0.00%	34	
Grand Total	**71.38%**	**25.54%**	**3.08%**	**325**	

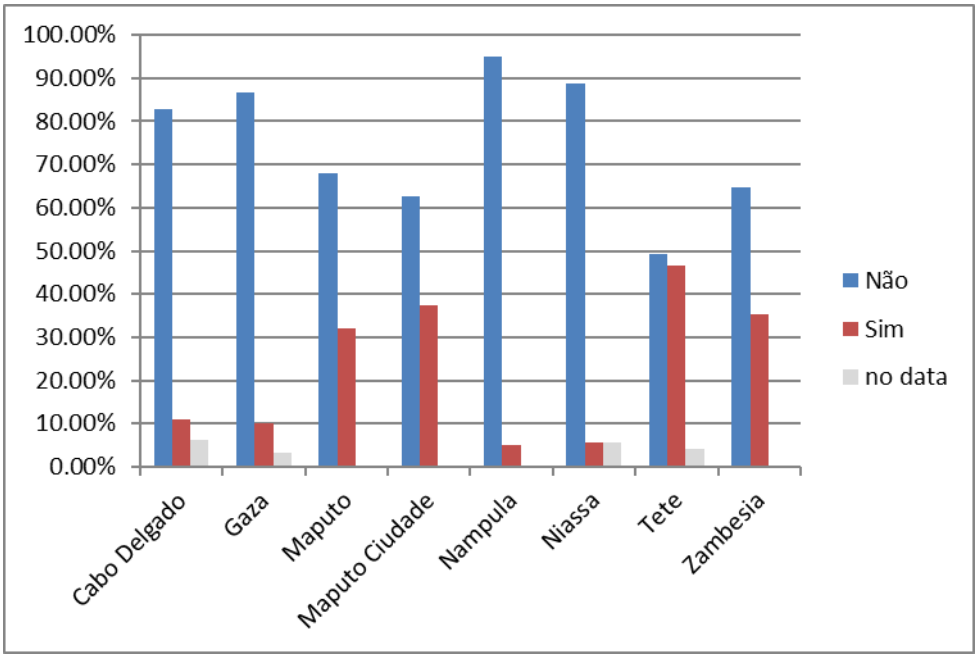


Figure 20 percentage of farmers declaring to read pesticide label per prvicince

Table 10 percentage of farmers declaring to read the label per crop and province

Row Labels	Não	Sim	null
Cotton	**41.48%**	**53.33%**	**5.19%**
Cabo Delgado	56.25%	37.50%	6.25%
Nampula	30.00%	70.00%	0.00%
Niassa	36.36%	45.45%	18.18%
Tete	28.00%	68.00%	4.00%
Zambesia	20.00%	80.00%	0.00%
Tobacco	**43.48%**	**55.43%**	**1.09%**
Niassa	56.00%	44.00%	0.00%
Tete	52.08%	45.83%	2.08%
Zambesia	5.26%	94.74%	0.00%
Vegetables, roots and tubers,pulses	**31.63%**	**66.33%**	**2.04%**
Gaza	20.00%	80.00%	0.00%
Maputo	21.43%	75.00%	3.57%
Maputo Ciudade	47.50%	50.00%	2.50%
Grand Total	**39.08%**	**57.85%**	**3.08%**

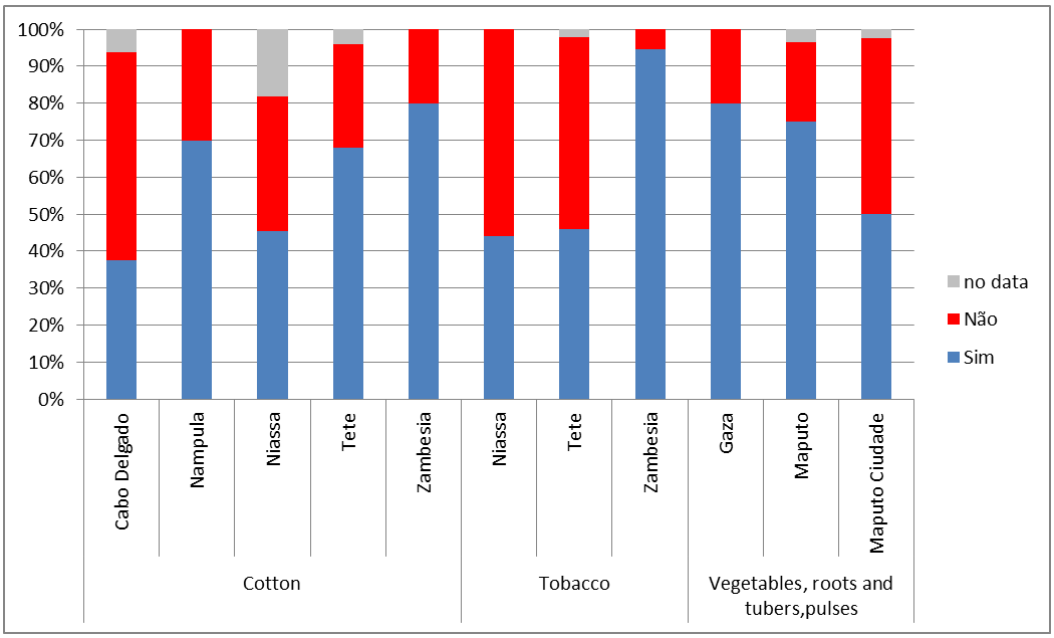


Figure 21 percentage of farmers read the label per province and crops

Table 11 farmers reporting to understand the pesticide label dosage

Row Labels	null	Não	Sim	Sim, com ajuda do técnico da empresa
Cabo Delgado	**6.25%**	**0.00%**	**93.75%**	**0.00%**
Cotton	6.25%	0.00%	93.75%	0.00%
Gaza	**0.00%**	**26.67%**	**73.33%**	**0.00%**
Vegetables, roots and tubers,pulses	0.00%	26.67%	73.33%	0.00%
Maputo	**7.14%**	**7.14%**	**85.71%**	**0.00%**
Vegetables, roots and tubers,pulses	7.14%	7.14%	85.71%	0.00%
Maputo Ciudade	**0.00%**	**37.50%**	**62.50%**	**0.00%**
Vegetables, roots and tubers,pulses	0.00%	37.50%	62.50%	0.00%
Nampula	**0.00%**	**85.00%**	**15.00%**	**0.00%**
Cotton	0.00%	85.00%	15.00%	0.00%
Niassa	**5.56%**	**83.33%**	**11.11%**	**0.00%**
Cotton	18.18%	72.73%	9.09%	0.00%
Tobacco	0.00%	88.00%	12.00%	0.00%
Tete	**2.74%**	**46.58%**	**50.68%**	**0.00%**
Cotton	4.00%	48.00%	48.00%	0.00%
Tobacco	2.08%	45.83%	52.08%	0.00%
Zambesia	**2.94%**	**5.88%**	**88.24%**	**2.94%**
Cotton	6.67%	13.33%	80.00%	0.00%
Tobacco	0.00%	0.00%	94.74%	5.26%
Grand Total	**3.38%**	**33.23%**	**63.08%**	**0.31%**

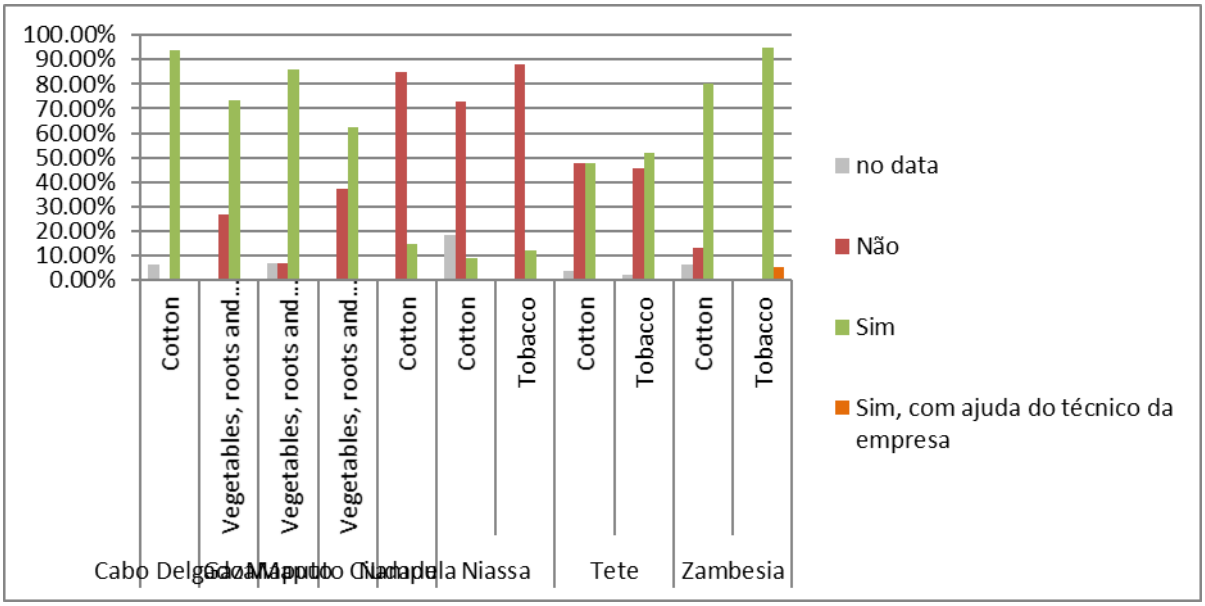


Figure 22 farmers reporting to understand the pesticide label dosage

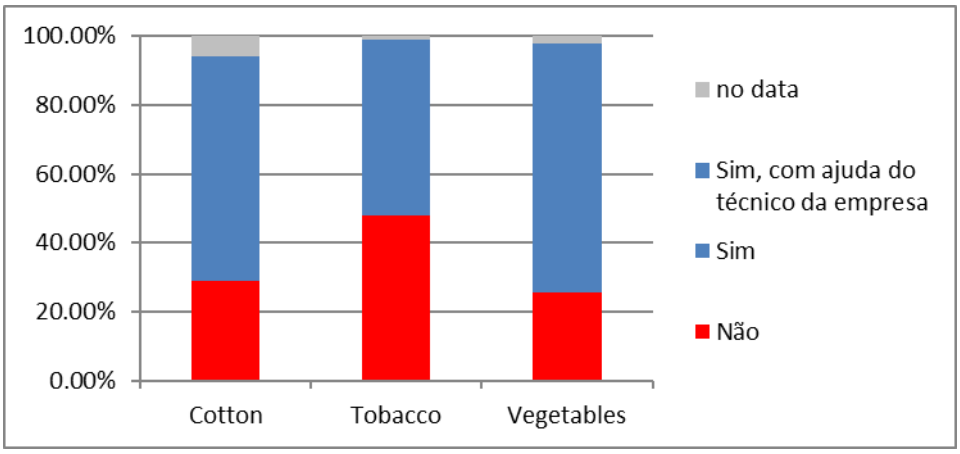


Figure 23 farmer reporting understanding the pesticide dosage instruction on the label per crop

3.3.4. Pesticide storage practices

About a third of farmers are storing pesticides inside their house

Provinces	Number of farmers storing the pesticide Inside the house	Number of farmers storing outside the house	Number of farmers
Cabo Delgado	33	21	60
Gaza	4	20	29
Maputo	1	25	28
Maputo Ciudade		38	38
Nampula	3	14	20
Niassa	16	16	34
Tete	50	15	70
Zambesia		33	34
Grand Total	**107**	**182**	**313**

Figure 24 pesticide storage practices per province

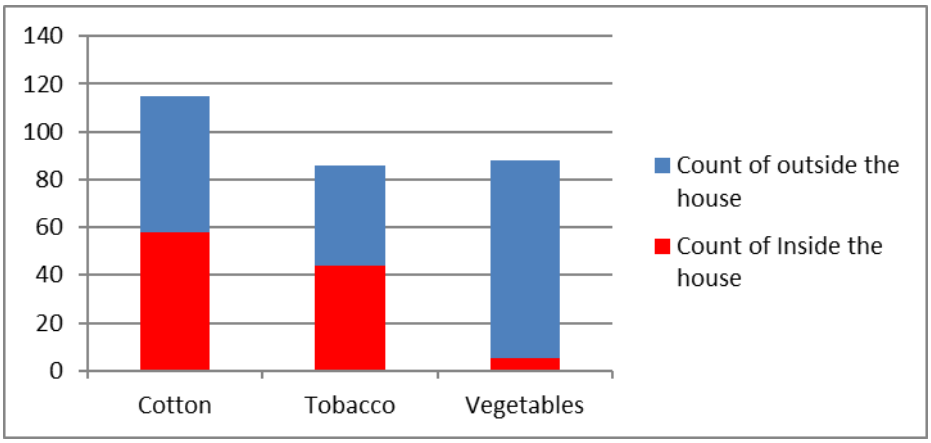


Figure 25 pesticide storage practices per crop

Preliminary discussion and conclusions

The survey results showed that the use of pesticides in general, and of HHPs in particular, was likely to result in undue exposure of farmers in the Mozambique.

Half of the farmers interviewed in the survey had not received any sort of training in using agrochemicals, and even those who had often lacked a good understanding of the risks involved through poor label reading and understanding and poor wearing of PPE. Many farmers in Mozambique do not have the required literacy and numeracy rate to even be able to understand the label. In addition PPE is often difficult to find, and expensive. As a result of all those reasons, the great majority of farmers survey (93%) did not wear appropriate protection to handle any HHPs and potentially neither a big share of the pesticides used.

For what concerns risk mitigation, it is difficult to enforce risk reduction measures that depend on wearing the appropriate PPE in these conditions. A further risk assessment is suggested by the survey and IPM programme targeting especially vegetables and cotton would improve the sustainability of the agricultural sector of Mozambique.

References

Amera T & Abate A (2008) An assessment of the pesticide use practice and hazards in the Ethiopian Rift Valley. Africa Stockpiles Programme. Institute for Sustainable Development (ISD), Addis Ababa & Pesticide Action Network-UK, London. At: http://www.pan-uk.org/archive/Projects/Obsolete/MDTF%2008-09/ETH%20An%20Assessment%20of%20Pesticide%20Use,%20Practice%20and%20Hazards%20in%20the%20Ethiopian%20Rift%20Valley.pdf

Come AMW & Van der Valk H (2014) Reducing risks of highly hazardous pesticides in Mozambique. Step 1 – Shortlisting highly hazardous pesticides. Project report – Update 5 May 2014. Food and Agriculture Organization of the United Nations, Rome

FAO (1997) **Chapter 4 – Questionnaire design. *In:* Marketing Research and Information Systems. Marketing and Agribusiness Texts – 4. Food and Agriculture Organization of the United Nations, Rome. At: http://www.fao.org/docrep/w3241e/w3241e00.HTM**

Rotterdam Convention (undated) Severely Hazardous Pesticide Formulation report form. Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade. Geneva & Rome. At: http://www.pic.int/Procedures/SeverelyHazardousPesticideFormulations/FormsandInstructions/tabid/1192/language/en-US/Default.aspx

WHO (2001) Pesticide Exposure Record. International Programme on Chemical Safety. World Health Organization, Geneva. At: http://www.who.int/ipcs/poisons/pesticides/en/

REPORT

2ND FAO/WHO JOINT MEETING ON PESTICIDE MANAGEMENT

and

4TH SESSION OF THE FAO PANEL OF EXPERTS ON PESTICIDE MANAGEMENT

6 – 8 October 2008
Geneva

Food and Agriculture Organization of the United Nations

World Health Organization

Table of contents

Abbreviations

ADI	Acceptable Daily Intake
ASP	Africa Stockpiles Programme
CCPR	Codex Committee on Pesticide Residues
CIEN	Chemicals Information Exchange Network
CMR	Carcinogenic, Mutagenic and Reproductive toxicant
FAO	Food and Agriculture Organization of the United Nations
GCDPP	Global Collaboration for Development of Pesticides for Public Health
GHS	Globally Harmonized System of Classification and Labelling of Chemicals
GLP	Good Laboratory Practice
GMP	Global malaria Programme
HHP	Highly Hazardous Pesticide
HQ	Headquarters
IARC	International Agency for Research on Cancer
ICC	International Chamber of Commerce
ICCM	International Conference on Chemicals Management
ICSC	International Chemical Safety Card
IFCS	Inter-governmental Forum on Chemical Safety
IGO	Inter-governmental Organization
IOMC	Inter-Organization Programme for the Sound Management of Chemicals
IPCS	International Programme on Chemical Safety
IPM	Integrated Pest Management
IVM	Integrated Vector Management
JMPR	Joint Meeting on Pesticide Residues
JMPS	Joint Meeting on Pesticide Specifications
MEA	Multilateral Environmental Agreement
MRL	Maximum Residue Limit
NGO	Non-governmental Organization
OECD	Organization for Economic Co-Operation and Development
PAN	Pesticide Action Network
PIC	Prior Informed Consent
PIM	Poisons Information Monograph
POP	Persistent Organic Pollutant
SAICM	Strategic Approach to International Chemicals Management
UN	United Nations
UNDP	United Nations Development Programme
UNEP	United Nations Environment Programme
UNITAR	United Nations Institute for Training and Research
WHO	World Health Organization
WHOPES	World Health Organization Pesticide Evaluation System

1. Introduction

The 2nd FAO/WHO Joint Meeting on Pesticide Management and 4th Session of the FAO Panel of Experts on Pesticide Management, were held at WHO Headquarters in Geneva from 6 to 8 October 2008.

The FAO Panel of Experts on Pesticide Management is the official statutory body that advises the Organization on matters pertaining to pesticide regulation and management, and alerts it to new developments, problems or issues that otherwise merit attention. The Panel in particular counsels FAO on the further implementation of the revised version of the *International Code of Conduct on the Distribution and Use of Pesticides*[1] (the Code of Conduct). Members of the WHO Panel of Experts are drawn from the WHO Panel of Experts on Vector Biology and Control, or are academic or government experts invited to advise the Organization on policies, guidelines and key actions to support Member States on sound management of pesticides.

Experts invited to this meeting have been selected for their personal expertise and experience in specific aspects of pesticide management, both in agriculture and in public health, and do not represent the position of governments or institutions they may belong to. They are appointed in their personal capacity by either FAO or WHO. In addition, representatives from other Inter-Governmental Organizations (IGOs), pesticide industry and Non-Governmental Organizations (NGOs) also attended the meeting as observers.

Dr Morteza Zaim welcomed all participants on behalf of WHO and expressed his great pleasure in hosting the joint meeting for the first time in Geneva. He thanked all present for kindly having responded to the invitation to participate in the meeting.

Mr Mark Davis, of FAO, noted the absence of Dr Gero Vaagt, former Senior Officer of the FAO Pesticide Management Group, who had been called to other duties. He recalled the long involvement of Dr Vaagt in the organization of this Panel and noted that his experience would be greatly missed. Mr Davis underlined the importance of the guidance which the Panel is providing, in particular to developing countries, which are in the complicated situation of having to balance trade, health and environmental interests.

All participants in the meeting are listed in Annex 1.

2. Opening of the meeting

Dr Lorenzo Savioli, Director Control of Neglected Tropical Diseases, gave the opening address on behalf of Mr Hiroki Nakatani, Assistant Director General of WHO. He welcomed the Panel members from FAO and WHO and colleagues from other UN organizations and the World Bank to the meeting, as well as representatives of industry associations and public interest groups who attended the meeting as observers.

[1] http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/code/en/

Dr Savioli reminded the participants that the Panel has an advisory role to FAO and WHO on policies, guidelines and key actions to support Member States on the sound management of pesticides. He stressed that the strengthening of capacity for judicious and effective management of pesticides is a priority for WHO and that the collaboration with FAO provides an opportunity to ensure complementarity, harmonized and coordinated guidance and support to Member States and other stakeholders on this important issue.

The Director underlined that Integrated Vector Management (IVM) is being promoted by WHO as a key strategy for the sound management of pesticides. Capacity building in the field of public health pesticides is an important element of IVM, in particular given the increased use of insecticides in the health sector in many vector-borne disease endemic countries where resources and infrastructure for such activities are often inadequate.

Dr Savioli noted that important guidance documents are being prepared by the Panel and requested the meeting to ensure that these are pragmatic and useful to the main target groups, which are governments of developing countries and countries with economies in transition. He emphasized that the Code of Conduct serves as a framework and guiding document for both FAO and WHO and invited the Panel to carefully review the Code and advise whether any improvements can be made to the document to better address the specific needs of public health pesticides.

Finally, Dr Savioli, wishing the meeting success and stating he looked forward to its recommendations, declared the 2nd FAO/WHO Joint Meeting on Pesticide Management open.

3. Election of the chairperson and rapporteurs

Dr Vibeke Bernson was elected Chairperson of the meeting, and Dr Gamini Manuweera and Dr Sandhya Kulshrestha were appointed rapporteurs.

4. Adoption of the agenda

One additional issue was included under agenda item 13: counterfeiting and illegal trade in pesticides.

The definitive agenda was adopted as shown in Annex 2.

5. Developments since the previous session of the Panel

A brief summary was presented of some important developments with respect to pesticide management that had taken place since the 1st Joint Meeting in October 2007.

5.1 WHO

Chemical safety

WHO Chemical Safety is in the process of updating the Poisons Information Monographs (PIMs) on dieldrin, endosulfan, paraquat and aluminium phosphide. PIMs are concise but comprehensive, internationally peer-reviewed documents about individual agents or groups of agents to which poisoning exposures may occur. The PIMs are primarily intended to facilitate the work of poison information specialists and clinicians in dealing with poisoning cases. They summarize the physico-chemical and toxicological properties of the substance, the clinical features of poisoning and patient management. These will be available on the INTOX and INCHEM websites[2].

Chemical Safety has also developed International Chemical Safety Cards (ICSCs). ICSCs summarize essential product identity data and health and safety information on pure chemicals for use by workers and employers, agriculture and for the public at large. There are now approximately 150 ICSCs on pesticides, available through the WHO web page of the International Programme on Chemical Safety (IPCS)[3].

Chemical Safety is undertaking a risk assessment of the use of DDT in indoor residual spraying for malaria prevention. The draft document will be released for public and peer review, followed by an expert meeting.

Food safety

The 2008 FAO/WHO Joint Meeting on Pesticide Residues (JMPR) was held in Rome, Italy, in September 2008. The meeting evaluated 26 pesticides, of which six were new compounds and six were re-evaluated within the periodic review programme of the Codex Committee on Pesticide Residues (CCPR).

JMPR consists of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and the WHO Core Assessment Group. During the Meetings, the FAO Panel of Experts is responsible for reviewing residue and analytical aspects of the pesticides under consideration, including data on their metabolism, fate in the environment and use patterns, and for estimating the maximum residue levels that might occur as a result of the use of the pesticides according to good agricultural practices. The WHO Core Assessment Group is responsible for reviewing toxicological and related data and for estimating, where possible, acceptable daily intakes (ADIs) for humans of the pesticides under consideration. Relevant information is accessible on the respective JMPR websites of FAO and WHO[4].

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[2] http://www.inchem.org and http://www.intox.org

[3] http://www.who.int/ipcs/publications/icsc/en/index.html

[4] http://www.who.int/ipcs/food/jmpr and http://www.fao.org/ag/AGP/AGPP/Pesticid/JMPR

Evidence, research and action on mental and brain disorders

Pesticide ingestion accounts for over 60 percent of suicides in many rural areas of China and South-East Asia and there is evidence of increased pesticide self-poisoning in Central and South American, as well as African countries. The WHO Team of Evidence, Research and Action on Mental and Brain Disorders of the WHO Department of Mental Health and Substance Abuse held a meeting in Nonthaburi, Thailand, in December 2007 to launch the global public health initiative *The Impact of Pesticides on Health: Preventing Intentional and Unintentional Deaths from Pesticide Poisoning*. The meeting identified actions for safer access to pesticides through community interventions.

The Team also published *Prevention of suicidal behaviours: Feasibility demonstration projects on community interventions for safer access to pesticides*[5]. The document provides draft protocols for the demonstration of feasibility of community-level interventions for safer access to pesticides and the identification of potential sites where to conduct those demonstration projects. The Team also convened a meeting on *Prevention of Suicidal Behaviours: Clinical Management of Acute Pesticide Intoxication*, in Nonthaburi, Thailand, in December 2007. The purpose of this meeting was to do an in-depth review of guidelines on the clinical management of acute pesticide intoxication and to develop clinical guidance for health care workers at different levels of the health care system (i.e., primary health care, district hospitals and specialized units) and a strategy for implementation.

Global Malaria Programme

The Global Malaria Programme (GMP) has produced an update on the WHO Position statement on DDT: The *Use of DDT for Malaria Control*, which includes increased focus on occupational and environmental safety guidance.

The GMP has been collaborating with UNEP and the Secretariat of the Stockholm Convention on Persistent Organic Pollutants (POPs), in providing technical support to countries for capacity building in the use of DDT according to the provision of the Convention. In this context, the Secretariat of the Convention has signed a memorandum of understanding with WHO to support countries in fulfilling their requirements for reporting to the Secretariat on the production and use of DDT for disease vector control.

Two national workshops on DDT reporting were held in 2008, respectively in Rabat, Morocco and in Sana'a, Yemen. Both workshops were preceded by a field visit conducted on assessment and support for safe storage of DDT. In July 2008 a three day inter-regional workshop was held in Bangkok, Thailand to improve the relevant processes for data collection, reporting systems and DDT stocks management in each of the participating countries, i.e., China, Democratic People's Republic of Korea, India, Myanmar, Papua New Guinea and Solomon Islands. As part of these regional and country workshops support was also given to countries to assess the capacities of countries for environmentally sound management of DDT stocks and wastes and discuss the introduction of alternatives to DDT and the strategies to be used to reduce the reliance on DDT.

[5] http://www.who.int/mental_health/resources/suicide/en/index.html

WHOPES

The WHO Pesticide Evaluation Scheme (WHOPES) finalized the testing and evaluation of 5 pesticide products and developed recommendations on their use in public health[6]. The reports of the WHOPES Working Group meetings provide critical reviews of existing literature as well as of studies organized and supervised by WHOPES. These reports are widely distributed among national control programmes, registration authorities and other stakeholders and are intended to facilitate the registration and safe and effective use of such products by Member States.

The 7th FAO/WHO Joint Meeting on Pesticide Specifications (JMPS), held in Braunschweig, Germany, in June 2008, reviewed data package of 19 manufacturers of pesticides (ten for FAO specifications; two for WHO specifications; and seven for joint FAO/WHO specifications) and made recommendations for the development of quality standards for these products.

In collaboration with FAO, WHOPES developed a training manual on the development of pesticide specifications. This tool provides a step-by-step approach to acquiring the knowledge and skills for basic decision-making on the development of pesticide specifications, including the determination of equivalence, following the principles, criteria and procedures detailed in the *Manual on development and use of FAO and WHO specifications for pesticides*[7]. The planned training activities of the two Organizations are expected to support capacity building of the national programmes in the implementation of the Code of Conduct, especially as it relates to Article 6.1.4.

The sixth meeting of the Global Collaboration for Development of Pesticides for Public Health (GCDPP) was held at WHO headquarters, in April 2008. The meeting was attended by representatives of industry, national and government-supported agencies, regional and international organizations, and universities and research institutions, as well as several WHO resource persons, mainly from pesticide registration authorities. The meeting discussed the draft FAO/WHO guidelines on registration of pesticides and advised WHO on the refinement of the guidelines so that they are pragmatic and useful for the main target groups.

WHOPES is in the process of peer review of three generic risk assessment models for application of insecticides in indoor residual spraying, space spraying and mosquito larviciding, as well as three efficacy guidelines for mosquito skin repellents, ground-applied space spray products and household insecticide products. All six guidelines are expected to be published by mid-2009.

Housed in the WHO Vector Ecology and Management Unit, WHOPES has supported the activities of the Unit in supporting Member States in incorporating the principles IVM into their national policies. IVM is highly promoted by WHO for the optimal use of resources for vector and public health pest control and as a key strategy for sound management of pesticides.

WHOPES has also, in collaboration with WHO Regional Offices, initiated situation analyses and needs assessments for strengthening capacity on sound management of pesticides in 12

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[6] http://www.who.int/whopes/recommendations/wgm/en/

[7] http://whqlibdoc.who.int/publications/2006/9251048576_eng_update2.pdf

priority countries in Asia, Africa and South America, through multi-sector and multi-stakeholder approaches. WHOPES also attended the WHO/EURO meeting on Sound Management of Pesticides – Risk Reduction, in Bonn, Germany, in August 2008. The meeting was attended by representatives of 18 Member States, mainly from Eastern Europe, the Caucasus and Central Asia, and recommended on actions to reduce risks associated with the use of such chemicals in agriculture and health.

5.2 FAO

Organizational changes

The Panel was informed that the Plant Production and Protection Division, which hosts the pesticide management programme at FAO, is going through a process of restructuring which should lead to closer integration of crop production and protection activities. Issues related to pesticide management used to be handled by the Pesticide Management Group, but will now be under a Programme Entity responsible for the reduction of risks associated with pesticide use in agriculture to protect human health and the environment, which has three main objectives:

- implementation of the Code of Conduct, including the progressive elimination of highly hazardous pesticides. This objective also covers the work of the JMPR and the JMPS;
- national capacity building for implementation of the Code of Conduct. This objective covers, among other activities, human health risk assessment, strengthening of laboratory capacity, the development of national action plans, implementation of IPM, the safeguarding of obsolete pesticides stocks, etc.;
- communication, knowledge management and associated capacity building services in support of pesticide risk reduction, which includes such activities as the development of guidelines in support of the Code of Conduct, the deployment of pesticide stock management systems, the publication of the joint FAO/WHO training manual on pesticide specifications, information tools on herbicide resistance, etc..

Furthermore, the departure of the Senior Officer Pesticide Management at FAO has led to a reassignment of tasks to other staff within AGP. However, it has also led to a reduction in capacity to implement some of the planned activities related to pesticide management, including some recommendations made previously by the Panel. It is expected that this post will be filled again by mid-2009.

Food safety

The Codex Committee on Pesticide Residues (CCPR) met for its 40th Session, in Hangzhou, China, in April 2008. In addition to the adoption of (draft) Maximum Residue Limits (MRLs) and the revocations of some existing MRLs, the CCPR discussed options for setting globally harmonized MRLs through Codex. This might be achieved by the definition of Codex MRLs before most national MRLs have been set. The implications of such a system on the work of the CCPR and the JMPR would be considerable, though, and these will be further evaluated before the next session. The report of the CCPR is available on the Codex web site[8].

[8] http://www.codexalimentarius.net/web/archives.jsp?year=08

In addition to the work carried out by the JMPR in 2008 referred to under section 5.1, the attention of the Panel drawn to the ongoing FAO/WHO-IPCS project to update principles and methods for the risk assessment of chemicals in food[9].

Minor uses

A Global Minor Use Summit was organized jointly by FAO, the US Department of Agriculture (USDA), the US Environmental Protection Agency (USEPA), and IR-4 Project, at FAO headquarters in December 2007. The summit focussed on finding solution for constraints regarding the generation of data for the registration of pesticides, and other regulatory issues, for minor use or specialty crops.

The summit discussed such issues as the generation of residue data, the promotion of extrapolation of data between different uses (e.g., through zoning or crop grouping), strengthening information and data sharing, and the development of harmonized, global guidance. The final recommendations of the summit can be found on FAO's web site[10].

Obsolete pesticides

Regarding the management and disposal of obsolete pesticides, the Panel was informed that a second phase of the Africa Stockpiles Programme (ASP) is being developed. Noticeably, a much greater emphasis will likely be placed on the importance of sound pesticide management for the prevention of accumulation of obsolete pesticide stocks.

In addition, FAO is in the process of setting up new projects on the management and disposal of obsolete pesticides in Eastern Europe, the Caucuses and Central Asia; the Middle East; the Andean countries and Paraguay; and India and Vietnam (with UNDP).

Rotterdam Convention

The number of Parties to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (the Rotterdam Convention) continues to increase its scope and impact. The number of Parties increased to 126, while national implementation plans for the Convention have been developed for 52 countries, and is continuing.

The Chemical Review Committee, in March 2008, recommended the inclusion of two new pesticides into its Annex III (the PIC procedure): aldicarb and alachlor. Furthermore, the upcoming Conference of Parties of the Convention, later in October 2008, will consider the inclusion of the pesticides TBT and endosulfan into Annex III.

Trends in international agriculture

The year 2008 has seen the emergence and increased importance of a number of global issues which have a direct impact of agricultural production, such as spiralling food prices, the promotion of bio-fuels and the consequences of climate change. These trends have focused international attention on agriculture again, after a long period of relative neglect. The implications of these global trends on (increased) pesticide use are already being noted. This underlines the importance of continued efforts to ensure sound pesticide management.

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[9] http://www.who.int/ipcs/food/principles/en/

[10] http://www.fao.org/ag/AGP/AGPP/Pesticid/

Monitoring implementation of the Code of Conduct

The previous session of the Joint Meeting discussed two *ad hoc* cases of monitoring observance of the Code of Conduct.

In response to the provisions of the Guidelines on Monitoring and Observance of the Code of Conduct, and in particular its Annex I, FAO sent out an invitation to provide a Regular Monitoring Report on implementation of the Code of Conduct to all its member countries, in July 2008. The deadline for receipt of reports was set at 30 October 2008.

Results of this monitoring exercise will be analysed in the course of 2009, and a report on implementation of the Code of Conduct in FAO member countries should be available at the next session of the Joint Meeting. The report should assist FAO, WHO and the Panel in identifying and/or strengthening priorities for further implementation of the Code of Conduct.

5.3 UNEP

UNEP Chemicals presented its activities for strengthening sound management of pesticides, much of which is carried out in support of SAICM and chemicals-related multilateral agreements. They include activities related risk assessment, management and communication, such as:

- facilitating development of tools for guidance and training in methods for risk assessment and management to be used in capacity building in developing countries and economies in transition;
- promoting the development, exchange and communication of information on reduction of chemicals exposures and effects of chemicals on in particular for sensitive groups and ecosystems;
- supporting activities to minimize effects of natural disasters and industrial accidents involving chemicals;
- mainstreaming of chemicals management into national development agendas.

Pesticide risks

A particular issue with respect to pesticides which UNEP intends to focus on over the next few years are the environmental risks of pesticides in the tropics. In this respect, limited funding has been programmed for the period 2009 – 2011.

Information systems

Several information systems have been put in place, which are of particular relevance for pesticide management:

- the *POPs Laboratory Databank*, a global database of laboratories capable of analyzing POPS. The database provides information, for each laboratory, of the type of analyses that are carried out, the matrices in which POPs can be detected, methods being used, and quality assurance aspects[11];

[11] http://www.chem.unep.ch/databank/Home/Welcome.aspx

- the *Information System on DDT in Disease Vector Control*, which is operated in collaboration with the WHO Global Malaria Programme and the Stockholm Convention[12]. The system provides relevant up-to-date information and guidance on DDT and its alternatives in disease vector control. It was especially developed as a tool for exchanging data, experiences and expertise on the management and use of DDT within and between regions;
- the *Information System on POP Termiticides and Alternatives*, which aims to provide easy access to relevant information and guidance materials on termites and options for their management without POP termiticides[13];
- the *Chemical Information Exchange Network* (CIEN), which was set up as a mechanism to help networking and collaboration among various stakeholders responsible for the environmentally sound management of chemicals[14]. Twelve countries in Africa now have national CIEN web sites to facilitate national information exchange on chemicals;

5.4 Other organizations

The representative of UNITAR informed the meeting about its activities on capacity building for chemicals and waste management. UNITAR is assisting 25 countries in implementing SAICM. It also has a collaborative programme with the Rotterdam Convention, in particular to develop national action plans for its implementation.

The participants were also informed about activities related to pesticide risk reduction carried out by the OECD. A number of seminars has been organised on specific topics, in which non-OECD countries have taken part, the latest of which was the workshop on *Risk Reduction through Better Worker Safety and Training*. Its report has been published earlier in 2008[15].

The Pesticide Action Network (PAN) brought to the attention of the meeting that it had taken up the issue of risk reduction from highly hazardous pesticides (HHPs). A community monitoring exercise had been started to collect information of human health effects caused by pesticides. Furthermore, a first draft of a list of HHPs is presently being elaborated by PAN.

[12] http://www.chem.unep.ch/ddt/Default.html

[13] http://www.chem.unep.ch/termites/Default.html

[14] http://jp1.estis.net/communities/cien/

[15] http://www.oecd.org/department/0,3355,en_2649_34383_1_1_1_1_1,00.html

6. Highly hazardous pesticides

6.1 Identifying highly hazardous pesticides

The previous session of the Panel defined a number of criteria to define HHPs. Following publication of these criteria, feedback was received with regard to the clarity of the criteria and their completeness. Therefore, a number of criteria were revisited by the Panel.

WHO classification

A presentation was made by the WHO on the *WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification*[16], in particular the approach taken for the inclusion of certain chronic hazards (the "CMR" criteria: carcinogenicity, mutagenicity and reproduction toxicity). At present, pesticides classified by the International Agency for Research on Cancer (IARC) as having a high likelihood of being carcinogenic, are specifically identified in the WHO Classification. Reproductive toxicity is taken into account on a case-by-case basis, but not all pesticides listed in the classification have been evaluated against this hazard.

Concern was expressed that CMR hazards have not been, and are presently not, systematically evaluated for all pesticides listed in the WHO Classification. It therefore, contrary to acute hazards, may not provide a complete classification of CMR hazards. However, the only other global hazard classification, the *Globally Harmonized System for the Classification and Labelling of Chemicals* (GHS)[17], while providing criteria for CMR hazards, does not evaluate individual pesticides against these criteria. Systematic evaluation of individual pesticides against the CMR criteria of the GHS, and inclusion of its results in the WHO Classification, would according to the Panel be extremely useful.

The Panel underlined the longstanding use and great importance of the WHO Classification for many aspects of pesticide management and regulation, in particular in developing countries. It noted its wide use in registration, classification and labelling, among others.

The Panel reiterated its previously expressed concern that that the acute toxicity classifications of the WHO system and of the GHS have not yet been harmonized. It therefore recommended that WHO, as soon as possible, harmonize its criteria for acute toxicity with those of the GHS. The Panel further recommended that WHO should assess the feasibility of incorporating the GHS CMR criteria, and possibly other relevant endpoints, into its Classification. Pesticides listed in the Classification would subsequently need to be evaluated against these criteria, so that the WHO Classification can be considered comprehensive and complete, not only for acute hazards but also for the most important chronic hazards. The Panel recognized, however, that such evaluations would require considerable resources.

Endocrine disrupting pesticides

Endocrine disrupting effects were not incorporated into the list of criteria for HHPs as defined by the previous session of the Panel. A presentation was therefore made by PAN on the status of knowledge about endocrine disrupting pesticides.

[16] http://www.who.int/ipcs/publications/pesticides_hazard/en/

[17] http://www.unece.org/trans/danger/publi/ghs/ghs_welcome_e.html

It was stressed in this presentation that endocrine disruption by chemicals should not be considered an emerging issue anymore. Much scientific work has been carried out on the effects of endocrine disruption and the toxicological and physiological explanatory mechanisms. A summary of these mechanisms, as well as the resulting adverse effects, was presented to the Panel.

PAN noted that a number of countries have started taking action in regulating endocrine disrupting chemicals, including pesticides. As a first step, several countries, such as the European Union, Japan and the United States of America have started listing potential endocrine disrupting chemicals and identifying those that require further regulation. Furthermore, the OECD has initiated a research programme which is expected to lead, shortly, to a battery of new and revised testing guidelines to detect endocrine disruptors.

It was recognized in the presentation that there still is no full understanding of all the mechanisms by which pesticides affect the endocrine system, and the adverse effects this may cause. However, PAN was of the view that there is sufficient information on endocrine disrupting pesticides, with assay guidelines well developed by OECD in conjunction with the European Union, Japan and the United States of America, to move forward and regulate at least those pesticides already identified by the European Union. As a result, PAN urged FAO and WHO to include endocrine disruption as a criterion for HHPs.

The Panel welcomed the considerable advancements in the development of harmonized testing guidelines and evaluation criteria for endocrine disrupting chemicals. However, it noted that the OECD harmonized testing guidelines had not yet been published, and the European Union list of likely endocrine disrupting chemicals requiring regulation had not yet been formally adopted. Furthermore, there is still much discussion about the variety in effects that may be caused by endocrine disruptors, questions regarding potency, and effective approaches to assess their actual risk. The Panel also noted that endocrine disruption is not a toxicity endpoint as such and often will lead to toxic effects such as cancer or reproductive effects. Such effects would be covered by the criteria for HHPs.

The Panel, therefore, felt it was premature to include specific reference to endocrine disruptors as a separate category of highly hazardous pesticides. However, the Panel recognized that endocrine disruption can be an important mechanism of pesticide hazard expression. It was recommended that this issue be closely followed, and that the Panel should review the extent to which the existing criteria address endocrine disrupting pesticides at one of its future sessions.

Criteria for HHPs

Based on its discussions, and with the aim to ensure that its criteria for HHPs are clear and unequivocal, the Panel recommended that the criteria published at its 2007 session be slightly revised, and read as follows.

Highly hazardous pesticides should be defined as having one or more of the following characteristics:

- pesticide formulations that meet the criteria of classes Ia or Ib of the *WHO Recommended Classification of Pesticides by Hazard*;

  or

- pesticide active ingredients and their formulations that meet the criteria of carcinogenicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

  or

- pesticide active ingredients and their formulations that meet the criteria of mutagenicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

  or

- pesticide active ingredients and their formulations that meet the criteria of reproductive toxicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

  or

- pesticide active ingredients listed by the *Stockholm Convention* in its Annexes A and B, and those meeting all the criteria in paragraph 1 of annex D of the Convention;

  or

- pesticide active ingredients and formulations listed by the *Rotterdam Convention* in its Annex III;

  or

- pesticides listed under the *Montreal Protocol*;

  or

- pesticide active ingredients and formulations that have shown a high incidence of severe or irreversible adverse effects on human health or the environment.

With respect to the last criterion, the Panel requested WHO, FAO and UNEP to develop workable criteria on how to determine whether pesticide active ingredients and their formulations have shown a high incidence of severe or irreversible adverse effects on human health or the environment.

Pesticide industry representatives indicated that criteria to identify highly hazardous pesticides which are entirely hazard-based would not be supported by them, and risk assessment should be the basis for regulatory decision making.

6.2 Priority activities for risk reduction

The Panel recalled the recommendation made by the 131st session of the FAO Council, in 2006, with respect to FAO's contribution to SAICM, which read:

In view of the broad range of activities envisaged within SAICM, the Council suggested that the activities of FAO could include risk reduction, including the progressive ban on highly hazardous pesticides, promoting good agricultural practices, ensuring environmentally-sound disposal of stock-piles of obsolete pesticides and capacity-building in establishing national and regional laboratories.

The previous session of the Panel made a number of recommendations with respect to risk reduction of HHPs. FAO informed the meeting that regrettably little progress had been made with implementation of these recommendations, to a large extent due to limitations in personnel (see section 5.2). FAO stressed, however, that risk reduction of HHPs would remain a high priority in its programme, as recommended by the FAO Council.

The previous Panel recommendation that FAO and WHO, as a first step, prepare as list of HHPs based on the criteria identified, had not been taken up. FAO indicated it would be very hesitant to develop such a list, since its relationship to existing Multilateral Environmental Agreements (MEAs) that have more extensive identification procedures, in particular the Rotterdam Convention, might cause confusion in implementation at country level. In addition, preparing a list of individual pesticides classified as a HHP will likely result in long and complicated discussions, which may divert attention from the main task of reducing the risks posed by HHPs.

FAO therefore suggested that the first step of implementing the criteria defined by the Panel may be to develop guidance for registrars on how to apply the criteria for the national authorization of pesticides. Such guidance would also include available relevant data sources needed to use the criteria, and advice on elements and procedures for decision making, in particular with respect to viable alternatives for HHPs. As a second step, FAO and WHO could then actively engage regulators at the national level and assist them in implementing risk mitigation measures for HHPs.

The Panel stressed that registrars in many developing countries need clear guidance on what should be considered HHPs and what type of risk reduction measures can be taken. At present, most countries concerned already lack manpower and technical expertise to carry out proper hazards assessment for pesticides, let alone complete risk assessments.

The Panel revisited its previous recommendations made on priority activities for risk reduction. It noted that most of these recommendations still stand, but suggested to make a number of amendments to further clarify actions that should be taken to reduce risks that are posed by HHPs.

The Panel noted that many HHPs are currently in use, and reiterated that substituting them by less hazardous pest management options will often take time. However, as a general principle, the Panel recommended that HHPs should not be registered for use unless:

i. governments establish a clear need;

ii. no alternatives, based on a risk – benefit analysis, are available; and

iii. control measures as well as good marketing practices are sufficient to ensure that the product can be handled with acceptable risk to human health and the environment.

The Panel considered that the following activities should be a priority for FAO and WHO, with the aim to reduce the risks from HHPs, which explicitly could include a progressive ban of these compounds:

- FAO and WHO, as a first step, should make available to countries information on HHPs based on the criteria above, update it periodically in cooperation with UNEP, and make it widely known;
- FAO, in collaboration with WHO, should invite governments and the pesticide industry to develop plans of action to reduce risks from HHPs by taking regulatory or technical

action, either at the national or the regional level as appropriate, taking into account the work undertaken in existing MEAs such as the Stockholm Convention, Rotterdam Convention and the Montreal Protocol;

- FAO, in collaboration with WHO, should collect information on alternatives for HHPs, both reduced risk pesticides and other pest management approaches, in cooperation with all relevant stakeholders, and share experiences among countries;
- FAO, in collaboration with WHO, should seek assistance from donors for countries which wish to act to reduce risks from HHPs with the aim of preparing, implementing and enforcing action plans and search for alternatives;
- FAO should mobilize internal and external resources in order to implement, as a priority, the recommendations of the FAO Council with respect to HHPs.

The Panel underlined that effective risk reduction from HHPs is mainly carried out at the national level, and that national governments thus have the prime responsibility in this respect. It therefore recommended that FAO, in collaboration with WHO, invite national governments to ensure that at least the following risk reduction measures for HHPs are taken into account:

- identify HHPs with help of the criteria explained above;
- review the need for the use of HHPs, while simultaneously reviewing use conditions, mitigation measures and comparative risk assessment;
- where a specific need is identified for a HHP and no viable alternatives are available, governments should be advised to take all the necessary precautions, mitigation measures and apply restrictions, that may include the use only under certain conditions or by specifically certified users, severe restrictions, or a possible phase-out;
- promote the use of alternative pest management strategies and, in case they are not available, promote research for development of alternative strategies;
- promote the substitution principle for HHPs;
- ensure the provision of sufficient advice and information to users.

Finally, the Panel noted that the Global Guide to Resources on Acute Toxic Pesticides, which had been prepared by the Intergovernmental Forum on Chemical Safety (IFCS) to assist its recommendations on acutely toxic pesticides, is still being updated regularly[18.] The Panel suggested that FAO and WHO, as well as national government, could also use this guide to further identify and implement priority activities for risk reduction of HHPs.

[18] http://www.who.int/ifcs/champions/guide_resources/en/index.html

7. Guidelines in support of the Code of Conduct

As an introduction to the discussions on the various guidelines being developed in support of the Code of Conduct, the Panel was informed of newly published or translated guidelines since the its previous session, in October 2007:

- the publication, in May 2008, of the joint FAO/WHO *Guidelines on Management Options for Empty Pesticide Containers.*[19]
- the translation into French and Spanish of the FAO *Guidelines on Monitoring and Observance of the Code of Conduct*.[20]
- the translation into Arabic of the FAO *Guidelines on Efficacy Evaluation for the Registration of Plant Protection Products*.[21]
- the publication of the FAO Legislative study No. 97 – *Designing National Pesticide Legislation*.[22]

The Panel was also informed that, because of legal requirements at WHO and the wish to operate a consistent guideline drafting procedure within both organizations, FAO and WHO have decided that guidelines in support of the Code of Conduct would in the future only be drafted by independent experts. FAO and WHO underlined that this procedure would be adhered to avoid any appearance of a conflict of interest, and not because there had been any reservation with respect to the technical quality of previous guidelines. Guidelines presently in the process of being drafted are not affected by this change of policy. Pesticide industry associations and public interest groups would continue to be invited to participate in Task Groups for specific guidelines as observers, and provide inputs in the drafting process.

8. Drafting status of guidelines under development

The Panel was presented with the drafting status of a number of guidelines that are presently being developed.

8.1 Guidelines on resistance management for pesticides

The Panel reviewed a first working draft of the *Guidelines on Resistance Management for Pesticides* at its previous session. Additional comments on this draft had been received subsequently and had been incorporated into a second draft by the drafter in close collaboration with the Task Group chair. The second draft had been reformatted by FAO and was being completed by the drafter.

The Panel requested the Task Group chair and the drafter to finalize the draft by January 2009, to be circulated for review by the Task Group and by a limited number of independent

[19] http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/code/frame/implement/obsolete/en/

[20] http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/code/frame/monitor/en/

[21] http://www.fao.org/agriculture/crops/core-themes/theme/pests/pm/code/frame/implement/regpes/en/

[22] http://www.fao.org/legal/legstud/list-e.htm

peer reviewers. External peer reviewers should be selected based on their expertise in pesticide resistance management, both in agriculture and in public health, by FAO and WHO in consultation with the Task Group chair. The Panel recommended that comments received be taken into account in finalizing this draft, and that it subsequently be circulated among Panel members and observers for review, by June 2009. A final version of the guideline should be presented to the Panel for endorsement by October 2009.

8.2 Guidelines on registration of microbial pest control agents

With respect to the *Guidelines on Registration of Microbial Pest Control Agents*, the Panel took note of the fact that a draft had been prepared based on the outline agreed during its previous session. This draft was circulated among the Task Group members and comments were incorporated by the drafter. The second draft will require reformatting, to be in line with the agreed guideline format.

The Panel requested that this draft be finalized and reviewed by the Task Group by January 2009, and subsequently be sent for external peer review. External peer reviewers should be selected based on their expertise in the registration of microbial pest control agents, both in agriculture and in public health, by FAO and WHO in consultation with the Task Group chair. The Panel recommended that the peer review be taken into account in finalizing this draft, and it be circulated subsequently among Panel members and observers for comments, by May 2009. A new version of the guideline should be presented to the Panel for endorsement, by October 2009.

8.3 Guidance on pest and pesticide management policy development – agriculture.

A draft of the *Guidance on Pest and Pesticide Management Policy Development (Agriculture)* had been discussed by the Panel at its previous session. Subsequently, additional comments were provided which differed substantially from each other and did not represent a clear consensus on the changes to be made. This resulted in a new draft of the document, which had not yet been circulated among the Task Group or full Panel.

The Panel discussed the status and process of development of this draft guideline. It requested FAO to circulate the newly revised draft among the Task Group members for review, by January 2009, to assess whether previous comments have been incorporated in an acceptable manner. Since the latest comments were all provided Task Group members, the Panel recommended that the Task Group consider calling an external independent peer review of the guidance document if certain key elements would remain unresolved. The Panel recommended that a final draft then be prepared, and circulated among Panel members for endorsement by June 2009. If no major comments were to be received on the final draft, FAO was requested to finalize the guidance document and subsequently proceed with publication prior to the Panel's next session.

9. Review of outlines for new or revised guidelines

The Panel was presented with one draft outline for a new guideline to be developed.

9.1 Guidelines on retail establishments for pesticides

A revised scope and outline was presented of the *Guidelines on Retail Establishments for Pesticides*, based on the suggestions made the Panel during its previous session. The Panel confirmed its previous recommendation that the guideline should focus on providing advice to governments on the establishment of a proper system and setting minimum requirements of pesticide distribution and sales within the country. Guidance to be provided to retailers was considered to be the main responsibility of individual governments and of the private sector itself.

The Panel underlined the very important role that retailers play in the pesticide management chain, in particular in developing countries, where they tend to be the prime source of information for pesticide users, not only on the products themselves but also on pest management in general. The effective organization and regulation of retail outlets should therefore be a priority and the guideline should provide minimum requirements in this respect.

The Panel made a number of suggestions regarding the contents of guideline, which included:

- ensuring that distribution and sales of all types of pesticides, including agricultural, public health and domestic use products are covered;
- taking into account different types of retail outlets which may cater for different groups of pesticide users (e.g., general public, farmers, professional pest control operators);
- addressing forms of retail specific to many developing countries, such as travelling salesmen and mixed retail shops (e.g., 'one-stop shops' selling all agricultural inputs and materials, or even other types of goods);
- including options for retailer licensing, and the problem encountered in various countries that license holders may not be the actual shopkeepers;
- addressing in sufficient detail elements on labelling, packaging, storage and disposal;
- stressing the need to avoid the risk of food contamination during storage;
- covering all articles of the Code of Conduct which are relevant of pesticide distribution and sales.

In addition, the Panel underlined the importance of training of and information provision to pesticide distributors and retailers, and of effective enforcement, and requested that this be taken into account in the guideline.

The Panel requested that FAO and WHO prepare a detailed annotated table of contents for this guideline by March 2009, and circulate it among Panel members and observers for comments. The Panel further recommended that the development of the guideline be initiated as soon as possible afterwards, so that a complete draft can be distributed for discussion at its next session.

10. Review of new and revised guidelines

The Panel was presented with three draft guidelines presently under development.

10.1 Guidelines on the development of a reporting system for health and environmental incidents resulting from exposure to pesticides

A draft version of the *Guidelines on the Development of a Reporting System for Health and Environmental Incidents Resulting from Exposure to Pesticides* had been discussed during the previous session of the Panel. Comments made by the Panel were incorporated and the draft went subsequently through an additional review round by a number of Panel members, observers and external reviewers. A final draft was then prepared and had been distributed to the Panel for endorsement.

The Panel commended the drafter for her excellent work in finalizing this guideline. The Panel recognized the importance of having a feedback system on possible adverse impact of pesticides within the country as a basis for effective interventions through policy and other options. While recognizing that the operation of a thorough and effective pesticide incident reporting and monitoring system is very complex and will require considerable resources, the Panel underlined that this guideline can provide guidance on how to initiate such a system.

The Panel endorsed in principle the present version of the guideline, but requested that a number of clarifications be made to certain sections of the text. These included:

- adding and/or amending certain definitions;
- providing a good description of the circumstances of pesticide exposure, and the addition of certain elements to the report of suspected pesticide poisoning cases;
- including a recommendation for mandatory reporting of health and environmental incidents;
- providing more guidance on the verification of incident reports.

The Panel recognized that cases of pesticide poisoning as a result of suicide attempts will have very different policy implications from occupational and accidental cases. However, it recommended that reporting and assessment of suicide cases also be included in the guideline.

The Panel noted that for the guidelines to be effective, many countries will likely need capacity building in various aspects of incident reporting and analysis. The Panel also stressed the need of field-testing this guideline and obtaining feedback about the feasibility of its recommendations and its usefulness, and noted the willingness of individual members and of UNEP to do so. It was underlined that a reporting system is only one of the building blocks in protecting human health and the environment as part of sound pesticide management.

The Panel requested that a definitive draft be circulated to its members for final endorsement by November 2008, and that FAO and WHO, after formatting and editing, proceed with publication of the guideline no later than March 2009.

10.2 Guidelines on registration of pesticides

Based on the outline agreed upon at the previous session of the Panel, a draft of the *Guidelines on Registration of Pesticides* had been prepared. This initial draft had been discussed at the 6th GCDPP Meeting in April 2008, in which most of the members of the Task Team for this guideline participated. The comments and suggestions provided during the meeting were subsequently incorporated in a revised draft, which had been circulated among Panel members and observers.

The Panel was reminded of the fact that the purpose of the guideline is to provide general advice on the principles and process as well as requirements for registration of pesticides, including institutional and administrative organization. It should be considered as an umbrella document with more detailed guidance on technical elements of the registration process (such as data requirements, testing methods or risk assessment procedures) to be provided in separate guidelines.

The Panel expressed its appreciation regarding the advanced status of development of the document. It stressed that an effective pesticide registration system is a vital element for sound management of pesticides in a country, and requires a multi-disciplinary approach in implementation.

The Panel considered that the overall scope and contents of the guideline were appropriate for its purpose, and raised a number of issues that might be considered when finalizing the document. These included:

- limiting the section on the responsibilities of various stakeholders to those that are directly involved in pesticide registration;
- considering to extend the definition of 'pesticide' to the one used by the JMPS, so that public health and domestic use pesticides are more clearly included;
- explaining different types of registration in more detail;
- providing more information on registration by equivalence;
- clarifying and correcting the section on data protection, by limiting it to a description of principles but avoiding to take a specific position, as this was not done in the Code of Conduct;
- ensuring that issues regarding transparency of the registration process and public information are properly covered;
- providing more guidance on the use of existing data and data exchange between registration authorities;
- including experimental permits, and providing more detail on registration options for minor uses and biopesticides;
- providing additional guidance on comparative risk assessment and the substitution principle;
- clarifying the various options and requirements for fast-track registration.

The Panel further confirmed that genetically modified organisms or natural enemies of pests would not be covered by the guideline. It requested FAO and WHO to carry out a legal review of the guideline to avoid inconsistencies or errors.

The Panel recommended to extend the commenting period until 31 December 2008, after which a new draft should prepared and circulated among Panel members for endorsement, no later than March 2009. The Panel requested that, if no major comments are received, FAO and WHO, after formatting and editing, proceed with publication of the guideline.

10.3 Guidelines on pesticide advertising

With respect to the *Guidelines on Pesticide Advertising*, the Panel took note of the new draft which had been prepared by the Task Group chair and the written comments provided on this document.

The draft of the guidelines as presented to the Panel suggests that for certain types of advertisements, the provisions of Article 11.2 do not necessarily need to be observed. This would be the case, for instance, for small promotional items such as pens which may not have enough space to show the required wording. While recognizing that such physical constraints could exist for certain types of promotional items, the Panel underlined that no exemptions should be made in this guideline for provisions in the Code of Conduct. Therefore, the Panel recommended that the provisions of Article 11 in the Code of Conduct would need to apply to all forms of pesticide advertising, and that the guidelines reflect this clearly.

The Panel discussed the need to provide further guidance on Article 11.2.18 of the Code of Conduct which states that *Pesticide industry should ensure that advertisements and promotional activities should not include inappropriate incentives to encourage the purchase of pesticides*. The previous session of the Panel recommended that examples be given of what can be considered appropriate and inappropriate incentives or gifts, to assist regulators in the application of this article to their national situation. Examples were subsequently provided in the new draft of the guideline.

The draft guidelines provide a general definition of 'inappropriate' which reads: *In general terms, an incentive may be considered appropriate if it is in line with the objectives of the Code of Conduct, and inappropriate if it runs counter to these objectives, i.e. if it encourages the purchasing of a pesticide for another reason than to make the best choice to control a pest or disease*. This definition was considered by some observers as too narrow, as the 'best choice' could be interpreted as being limited to biological reasons, but excluding convenience of use, price, etc. Such an interpretation would then disallow advertising to encourage 'brand change'. It was suggested to modify the latter part of the phrase into: *make the best choice for cost-effective control a pest or disease.* However, the Panel considered this an equally narrow interpretation, and suggested clarify that the best choice will need to be made for agronomic, economic, environmental and health reasons.

Concern was expressed about the use of specific examples in the guidelines, as they can never be exhaustive, and are highly dependent on social, economic, cultural and religious circumstances. A replacement text was therefore presented to the Panel of a more generic nature. The Panel discussed both the draft guideline text and the proposed replacement and concluded that inclusion in the guidelines of explicit examples of inappropriate incentives

would be helpful to national regulators. It considered that the draft guideline clearly stresses that the exact interpretation of this article is subjected to the national or local situation.

The Panel therefore concluded that a list of examples of inappropriate (but not of appropriate) incentives of gifts should be provided in the guideline, such as, but not necessarily limited to:

- incentives or gifts which are not related to the product advertised;
- incentives or gifts with a value higher than the product advertised, unless it is related to the judicious use of the product in question (e.g., personal protective equipment, sprayer maintenance equipment);
- incentives or gifts in exchange of the product label, as this leads to unlabeled products in the hands of the end-user.

The suggestion made to refer in the guidelines to the International Chamber of Commerce (ICC) Code of Advertising and Marketing Communication Practice[23] (and in particular Chapter A on Sales promotion) as minimum general provisions regarding the use of incentives, was supported by the Panel.

The guideline leaves it at the discretion of governments and other stakeholders to notify FAO or WHO of cases of non observance of the provisions of the Code of Conduct on advertising. FAO and WHO may decide to review such notifications. It was suggested that a summary of such complaints and the outcome of the review should be made publicly available by FAO or WHO. The Panel did not support this suggestion, since the *ad hoc* monitoring procedure of observance of the Code of Conduct, set up by FAO, is not a formal international complaints procedure[24.]

CropLife International noted that, at this point in time, it could not agree with the Panel recommendations on this guideline, but would provide a definitive statement on its acceptance after having reviewed the final draft.

The Task Group was requested to incorporate the recommendations made during the meeting, as well as any editorial comments as far as appropriate. The Panel further requested that the final draft of the guidelines be reviewed again for any legal inconsistencies.

The Panel recommended that the Task Group prepare a new draft of the document by January 2009, for subsequent circulation among the Panel members for endorsement. The Panel requested that, if no major comments are received, FAO and WHO, after formatting and editing, proceed with publication of the guideline no later than June 2009.

[23] http://www.iccwbo.org/policy/marketing/id8532/index.html

[24] http://www.fao.org/ag/AGP/AGPP/Pesticid/Code/Guidelines/Monitoring.htm

11. Guidelines proposed for updating

The Panel discussed two guidelines which had been proposed for updating during a previous session.

11.1 Guidelines on pesticide legislation

The Panel was presented with the recently published *FAO Legislative Study on Designing National Pesticide Legislation,* and commended its quality and clarity.

The Panel underlined that the existing FAO guidelines on pesticide legislation are outdated and do not cover all pesticide uses addressed in the Code of Conduct, and reiterated its previous recommendation to develop updated guidelines on this issue. The Panel discussed in which ways the presented legislative study could be used as a basis for the elaboration of a new guideline on pesticide legislation, which would need to cover all areas of pesticide use, including public health and domestic uses.

The Panel recommended that FAO and WHO initiate the development of an outline for a new guideline on pesticide legislation, to be presented for consideration by the Panel at its next session.

11.2 Guidelines on good labelling practice for pesticides

The Panel was informed that no progress had yet been made in updating this document. The Panel stressed the importance of effective labelling of pesticides as a prime tool for communication with the user.

The Panel revisited its previous recommendation to present the WHO and GHS classifications for pesticides in a parallel manner in the guidelines, since these two systems had not yet been harmonized. It agreed, however, that clear advice on pesticide labelling needs to be provided to countries and a double-track system should be avoided. Furthermore, countries have started implementing GHS and require specific guidance on how to apply this to pesticide labelling.

The Panel noted that while the GHS is to become the global standard for classification and labelling of chemicals, the FAO guidelines and WHO classification of pesticides have long history of use in many countries, and that users have grown accustomed to this approach. The Panel therefore supported the proposal to update the guideline, taking into account the GHS but ensuring that the existing guideline is not changed more than absolutely necessary.

The Panel requested that a first draft be circulated among Panel members and observers by January 2009.

12. Implementation of the Code of Conduct

Although a large number of activities are being carried out by international organizations, national governments, the private sector and civil society organizations, which contribute to the implementation of the Code of Conduct, continued efforts to promote the sound management of pesticides are still needed, in particular in developing countries and countries with economies in transition. The Panel was therefore invited to discuss ways and means of strengthening implementation of the Code over the next few years.

A number of issues were put forward, regarding a possibly reorientation of implementation of the Code, among them:

- increased focus on national implementation, by favouring the development of national projects and programmes;
- better orientation of guidance and guidelines to the needs to developing countries and including systematic verification of their usefulness;
- closer integration of pest management, pesticide management, sustainable intensification of crop production, integrated vector management, chemicals management, environmental issues;
- mainstreaming of awareness building on the Code in the regular work of FAO, WHO and UNEP.

It was proposed to develop a programme for implementation of the Code of Conduct, which would build on a strategic approach based on four main elements: **i.** *normative work* at the international level (e.g., guidelines, policies, forums), which would guide to **ii.** *capacity building* on technical and policy issues (e.g., training, information exchange) at national and regional levels, which would lead to **iii.** *implementation* projects and programmes, primarily at the national level, which in turn would require **iv.** *feedback* mechanisms to assess effectiveness of implementation. By having the feedback direct the normative work again, a 'strategic loop' for implementation of the Code of Conduct could be developed.

The Panel welcomed the initiative to attempt to increase attention and resources for implementation of the Code of Conduct, and agreed that activities at national and regional levels are in particular required. The Panel endorsed the general concept to develop a programme for implementation of the Code of Conduct along the lines set out during the meeting.

The Panel stressed the importance of ensuring the involvement of all stakeholders, since the success of the Code of Conduct is borne by the fact that all major stakeholders have underwritten it. New stakeholders, such as the food sector, should therefore be actively engaged to participate in the programme. Furthermore, the Panel recommended that opportunities be sought to work with other organizations which are members of the Inter-organization Programme for the Sound Management of Chemicals (IOMC) to strengthen work on training, capacity building and implementation of the Code of Conduct.

The Panel stressed the importance of integration of the programme with initiatives such as the *Strategic Approach to International Chemicals Management* (SAICM) and the *2nd International Conference on Chemicals Management* (ICCM-2), with a view to facilitating a more effective implementation of the Code of Conduct.

While FAO, WHO and UNEP are already accessing their regular budgets to fund implementation activities, this will certainly be greatly insufficient to develop an effective programme. The Panel therefore called upon FAO, WHO, UNEP and other meeting participants to identify sources and secure funds for implementation of the programme. The Panel recommended that particular attention be paid to presenting the programme in ways that are attractive to governments and potential donors.

The Panel indicated that its members could contribute to the development of a programme for implementation of the Code of Conduct by identifying important needs and gaps that require attention and key entry points that could help get such a programme started up. Furthermore, the Panel could act as 'steering committee' which would oversee implementation and monitor its effectiveness.

13. Counterfeit pesticides

At the request of CropLife International, the Panel discussed the problem of counterfeit and illegal pesticides.

The Panel was informed of the increasing importance of counterfeit pesticide products, which are estimated to amount to 5-7 percent of the products in Europe and 20-30 percent in developing countries. Apart from causing economic losses to the legitimate pesticide industry, forged pesticides may endanger farmers' livelihoods and health, put the food chain and consumers at risk, and may cause damage to the environment. Counterfeiting also undermines the national regulatory systems. CropLife expressed its concern that legitimate pesticides tend to be strictly regulated but problems of illegal and counterfeit products still get relatively limited attention in many countries.

The Panel recognized the importance of the problems caused by the trade in counterfeit pesticides, and noted that it appears to be related, to a large extent, to weak inspection and control systems in many (developing) countries. Strengthening import and export controls, and developing effective systems of quality control which are also feasible in resource-poor countries, are needed to get to grips with this problem. This will require involvement of many players and stakeholders.

The Panel indicated that it would like to further discuss possible ways of reducing the trade and adverse impact of counterfeit pesticides at a next session.

14. Review of the Code of Conduct

The Panel discussed the scope and objectives of the *International Code of Conduct on the Distribution and Use of Pesticides,* in particular its coverage of public health and domestic pesticides. The Panel noted that the Code of Conduct clearly addresses all pesticides and all areas of use. However, it was recognized that its provisions, definitions and the included references appear to focus more on the management of agricultural pesticides.

The Panel recognized that an even more complete Code of Conduct, which might be jointly published by FAO, WHO and possibly UNEP, would likely increase its visibility and impact. However, concern was expressed at initiating a formal revision of the Code of Conduct, as experience has shown that this would require much time and resources, which might better be used for actual implementation of the Code of Conduct. Any possible updating of the Code of Conduct should therefore be limited in scope and not attempt to amend issues expected to generate much discussion.

The Panel recommended that FAO and WHO start the process to ensure that the Code of Conduct, and its implementation tools, adequately addresses all pesticides, and in particular public health pesticides. As a first step, WHO was requested to prepare a working document indicating which articles of the Code of Conduct might need to be amended or completed to ensure full coverage of public health and domestic pesticides.

15. Recommendations

Based on the working documents reviewed, the presentations made and the discussions held during the meeting, the Panel made the following recommendations:

Highly hazardous pesticides

1. To make further progress on the initiative for the reduction of risks posed by HHPs, the Panel reviewed the recommendations from its 2007 meeting and **agreed** that these recommendations **be adopted with the modifications** as incorporated in the following text:

2. HHPs **should be defined** as having one or more of the following characteristics:

   - pesticide formulations that meet the criteria of classes Ia or Ib of the *WHO Recommended Classification of Pesticides by Hazard*;

   or

   - pesticide active ingredients and their formulations that meet the criteria of carcinogenicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

   or

- pesticide active ingredients and their formulations that meet the criteria of mutagenicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

or

- pesticide active ingredients and their formulations that meet the criteria of reproductive toxicity Categories 1A and 1B of the *Globally Harmonized System on Classification and Labelling of Chemicals* (GHS);

or

- pesticide active ingredients listed by the *Stockholm Convention* in its Annexes A and B, and those meeting all the criteria in paragraph 1 of annex D of the Convention;

or

- pesticide active ingredients and formulations listed by the *Rotterdam Convention* in its Annex III;

or

- pesticides listed under the *Montreal Protocol*;

or

- pesticide active ingredients and formulations that have shown a high incidence of severe or irreversible adverse effects on human health or the environment.

3. The Panel **noted** advancements in the development of harmonized testing guidelines and evaluation criteria for endocrine disrupting chemicals, but felt it was premature to include specific reference to endocrine disruptors as a separate category of highly hazardous pesticides. However, the Panel **recognized** that endocrine disruption can be an important mechanism of pesticide hazard expression. It was **recommended** that the extent to which the existing criteria address endocrine disrupting pesticides be reviewed by the Panel at one of its next sessions.

4. The Panel further **recommended** that WHO, FAO and UNEP develop criteria for determining whether pesticide active ingredients and their formulations have shown a high incidence of severe or irreversible adverse effects on human health or the environment.

5. The Panel discussed how to address the current use of highly hazardous pesticides, and **recommended** that these should not be registered for use unless:

   a) governments establish a clear need;

   b) no alternatives, based on a risk – benefit analysis, are available; and

   c) control measures as well as good marketing practices are sufficient to ensure that the product can be handled with acceptable risk to human health and the environment.

6. The Panel discussed priority activities related to risk reduction from HHPs, including a progressive ban, and **recommended** that:

   a) FAO and WHO, as a first step, make available to countries information on HHPs based on the criteria above, update it periodically in cooperation with UNEP, and make it widely known;

b) FAO, in collaboration with WHO, invite governments and the pesticide industry to develop plans of action to reduce risks from HHPs by taking regulatory or technical action, either at the national or the regional level as appropriate, taking into account the work undertaken in existing Multilateral Environmental Agreements such as the Stockholm Convention, Rotterdam Convention and the Montreal Protocol;

c) FAO, in collaboration with WHO, collect information on alternatives for HHPs, both reduced risk pesticides and other pest management approaches, in cooperation with all relevant stakeholders, and share experiences among countries;

d) FAO, in collaboration with WHO, seek assistance from donors for countries which wish to act to reduce risks from HHPs with the aim of preparing, implementing and enforcing action plans and search for alternatives;

e) FAO mobilize internal and external resources in order to implement, as a priority, the recommendations of the FAO Council with respect to HHPs.

7. The Panel further **recommended** that FAO, in collaboration with WHO, invite national governments to ensure that at least the following risk reduction measures for highly hazardous pesticides (HHPs) are taken into account:

a) identify HHPs with help of the criteria explained above;

b) review the need for the use of HHPs, while simultaneously reviewing use conditions, mitigation measures and comparative risk assessment;

c) where a specific need is identified for a HHP and no viable alternatives are available, governments should be advised to take all the necessary precautions, mitigation measures and apply restrictions, that may include the use only under certain conditions or by specifically certified users, severe restrictions, or a possible phase-out;

d) promote the use of alternative pest management strategies and, in case they are not available, promote research for development of alternative strategies;

e) promote the substitution principle for HHPs;

f) ensure the provision of sufficient advice and information to users.

WHO Classification of pesticides by hazard

8. Given the great importance of the *WHO Recommended Classification of Pesticides by Hazard* for various aspects of pesticide management and regulation, including registration, classification and labelling, in particular in many developing countries, the Panel **expressed its concern** that that the classifications of the WHO system and of the GHS have not yet been harmonized, which impedes the provision of clear guidance on classification and labelling of pesticides.

9. The Panel therefore **recommended** that WHO, as a matter of urgency, harmonize its criteria on acute toxicity with those of the GHS. The Panel further **recommended** that WHO assess the feasibility to incorporate the GHS criteria on carcinogenicity, mutagenicity and reproductive toxicity, and other relevant endpoints, into its Classification and ensure that all pesticides listed have been evaluated against these criteria.

Implementation of the Code of Conduct

10. The Panel discussed the need to strengthen the implementation of the *International Code of Conduct on the Distribution and Use of Pesticides* and **recognized** the importance of its implementation at, in particular, national and regional levels. The Panel **endorsed** the general concept to develop a programme for implementation of the Code of Conduct as presented, and **recommended** that it include a strategy to involve the food sector as an important stakeholder.

11. The Panel **stressed** the importance of integration with initiatives such as the *Strategic Approach to International Chemicals Management* (SAICM) and the *2nd International Conference on Chemicals Management* (ICCM-2), with a view to facilitating a more effective implementation of the Code of Conduct. Furthermore, the Panel **recommended** that opportunities be sought to work with organizations which are members of the Inter-organization Programme for the Sound Management of Chemicals (IOMC) to strengthen work on training, capacity building and implementation of the Code of Conduct.

12. The Panel **called upon** FAO, WHO, UNEP and other meeting participants to identify sources and secure funds for implementation of the programme. The Panel **recommended** that particular attention be paid to presenting the programme in ways that are attractive to governments and potential donors.

13. The Panel **requested** to be kept informed of developments in the elaboration and implementation of the programme.

Guidelines in support of the Code of Conduct

14. The Panel reviewed the drafting status of a number of guidelines which are being developed in support of the Code of Conduct, and made the following recommendations.

    a) With respect to the *Guidelines on Resistance Management for Pesticides*, the Panel took note of the ongoing work to develop a new draft of this guideline, along the lines set out during its previous session. The Panel **requested** the Task Group chair and the drafter to finalize the draft by January 2009, to be circulated for review by the full Task Group and independent peer reviewers. The Panel **recommended** that comments received be taken into account in finalizing this draft, and that it subsequently be circulated among Panel members and observers for review, by June 2009. A final version of the guideline should be presented to the Panel for endorsement by October 2009.

    b) With respect to the *Guidelines on Registration of Microbial Pest Control Agents*, the Panel took note of the fact that a draft had been prepared for this document, based on the outline agreed during its previous session. The Panel **requested** that this draft be finalized and reviewed by the Task Group by January 2009, and subsequently be sent for external peer review. The Panel **recommended** that the peer review be taken into account in finalizing this draft, and it be circulated subsequently among Panel members and observers for comments, by May 2009. A new version of the guideline should be presented to the Panel for endorsement, by October 2009.

c) With respect to the *Guidance on Pest and Pesticide Management Policy Development*, the Panel noted the status of development of this draft and **requested** that, after internal review by FAO, the draft be circulated and commented on by the Task Group, by January 2009, to assess whether previous comments have been incorporated in an acceptable manner. The Panel **recommended** that the Task Group consider calling an external independent peer review of the guidance document if certain elements would remain unresolved. The Panel **recommended** that a final draft be circulated among Panel members for endorsement by June 2009 and that FAO, if no major comments were received, finalize the guidance document and subsequently proceed with publication prior to its next session.

15. The Panel reviewed the draft outline of one guideline which is being developed in support of the Code of Conduct, and made the following recommendations.

    a) With respect to the outline for the *Guidelines on Retail Establishments for Pesticides*, the Panel **underlined** the importance of proper regulation of retail outlets, and **recommended** drafting a guideline focused on providing advice to the governments in the establishment of a proper system of sale of pesticides within the country, including public health and household pesticides. The Panel **provided** several **suggestions** on its content, which included taking into account different types of retail establishments which may sell pesticides; addressing in sufficient detail elements on labelling, packaging, storage and disposal; and stressing the need to avoid food contamination during storage. The Panel **requested** that FAO and WHO prepare a detailed annotated table of contents for this guideline by March 2009, and circulate it among Panel members and observers for comments. The Panel further **recommended** that the development of the guideline be initiated as soon as possible afterwards, so that a complete draft can be distributed for discussion at its next Session.

16. The Panel reviewed a number of draft guidelines that were developed in support of the Code of Conduct, and made the following recommendations.

    a) With respect to the *Guidelines on the Development of a Reporting System for Health and Environmental Incidents Resulting from Exposure to Pesticides*, the Panel **recognized** the importance of having a feedback system on possible adverse impact of pesticides within the country as a basis for effective interventions through policy and other options. The Panel **endorsed in principle** the present version of the guideline, but requested that a number of clarifications be made to certain sections of the text. The Panel **requested** that a definitive draft be circulated to its members for final endorsement by November 2008, and that FAO and WHO, after formatting and editing, proceed with publication of the guideline no later than March 2009.

    b) With respect to the *Guidelines on Registration of Pesticides*, the Panel **stressed** that an effective pesticide registration system is a vital element for sound management of pesticides in a country, and requires a multi-disciplinary approach in implementation. The Panel **made suggestions** for improvements to various sections of the draft, including the responsibilities of various actors for pesticide registration; the issue of data protection, transparency and public information; registration by equivalence; comparative risk assessment and the substitution principle. The Panel **recommended** to extend the commenting period until 31 December 2008, after

which a new draft should prepared and circulated among Panel members for endorsement, no later than March 2009. The Panel **requested** that, if no major comments are received, FAO and WHO, after formatting and editing, proceed with publication of the guideline.

c) With respect to the *Guidelines on Pesticide Advertising*, the Panel took note of the new draft which had been prepared by the Task Group chair and the comments provided on this document. The Panel **recommended** that the provisions of Article 11 in the Code would need to apply to all forms of advertising. The Panel further discussed the issue of inappropriate incentives and **concluded** that a list of examples should be provided in the guideline, taking into account the comments made. The Panel **recommended** that the Task Group prepare a new draft of the document by January 2009, for subsequent circulation by among the Panel members for endorsement. The Panel **requested** that, if no major comments are received, FAO and WHO, after formatting and editing, proceed with publication of the guideline no later than June 2009.

17. The Panel reviewed a number of draft guidelines which had been proposed for updating, and made the following recommendations.

a) With respect to *Guidelines on Pesticide Legislation*, the Panel took note of the *FAO Legislative Study on Designing National Pesticide Legislation* and **commended** its quality. The Panel **underlined** that existing FAO guidelines on pesticide legislation are outdated and do not cover all pesticide uses addressed in the Code of Conduct. The Panel discussed in which ways the study could be used as a basis for the elaboration of a new guideline on pesticide legislation, covering all areas of pesticide use, including public health and domestic uses. The Panel **recommended** that FAO and WHO initiate the development of an outline for a new guideline on pesticide legislation, to be presented for consideration by the Panel at its next session.

b) With respect to the Guidelines *on Good Labelling Practice for Pesticides*, the Panel took note of the status of updating this document. The Panel **stressed** the importance of effective labelling of pesticides as a prime tool for communication with the user. The Panel **agreed** that clear advice on labelling needs to be provided to countries, and that parallel presentations of the WHO and GHS classifications for pesticides in the same guideline should be avoided. The Panel **recommended** that the guideline be updated, taking into account the GHS but ensuring that the existing guideline is not changed more than absolutely necessary, and that a first draft be circulated among Panel members and observers by January 2009.

Review of Code of Conduct

18. The Panel discussed the scope and objectives of the *International Code of Conduct on the Distribution and Use of Pesticides* and **noted** that, while these clearly address all pesticides, the provisions of the Code of Conduct and the included references appear to lean to the management of agricultural pesticides. The Panel therefore **recommended** that FAO and WHO start the process to ensure that the Code of Conduct, and its

implementation tools, adequately addresses all pesticides, and in particular public health pesticides.

16. Closure of the meeting

The 2nd FAO/WHO Joint Meeting on Pesticide Management, and the 4th Session of the FAO Panel of Experts on Pesticide Management, was closed by Mr Mark Davis, Senior Officer a.i. of the Pesticide Management Group of FAO and by Dr Morteza Zaim, Scientist in charge of the WHO Pesticide Evaluation Scheme. They thanked all participants for their valuable inputs in the discussions and expressed their satisfaction about the progress that was made.

The meeting was informed that Dr Vibeke Bernson, who had chaired the meeting over the last few years, would be retiring at the end of 2008. Her pleasant but very efficient way of chairing the meetings has greatly contributed to their success. Her contribution to the Panel was gratefully acknowledged.

Finally, the meeting also took note of the fact that FAO Panel members will come to the end of their 4-year term in the course of 2009, but before the next session. Therefore, Mr Davis extended his sincere gratitude, on behalf of FAO, to all for having accepted to sit on the Panel and for having shared their experience and expertise. He presented an FAO memorial medal to each FAO Panel member as an expression of the appreciation of the Organization.

Annex 1 – List of participants

FAO PANEL MEMBERS

Mr Jonathan Akhabuhaya
Chief Research Scientist
Tropical Pesticides Research Institute
PO Box 3024
Arusha
Tanzania
Tel: (+255) 27 250 5871
Fax: (+255) 27 250 58 71
E-mail: akhabuhaya@yahoo.co.uk

Ms Cathleen McInerney Barnes
Office of Pesticide Programs (7506-P)
United States Environmental Protection Agency
Washington, D.C. 20460
U.S.A.
Tel: (+1) 703 305 7101
Fax: (+1) 703 308 1850
E-mail: barnes.cathleen@epa.gov

Dr Vibeke Bernson
Advisor to the Director General in International Affairs
Swedish Chemicals Agency
Box 2
S-172 13 Sundbyberg
Sweden
Tel: (+46) 8 519 41139
Fax: (+46) 8 735 7698
E-mail: vibeke.bernson@kemi.se

Mr Julio Sergio de Britto
General Coordination of Pesticides
Ministry of Agriculture, Livestock and Food Supply
Esplanada dos Ministerios
Bloco D, Anexo A, Sala 345
Brasilia 70043-900
Brazil
Tel: (+55) 61 321 82 808
Fax: (+55) 61 322 55 341
E-mail: julio.britto@agricultura.gov.br

Dr Gu Bao-Gen
Deputy Director General
Institute for the Control of Agrochemicals
Ministry of Agriculture (ICAMA)
22, Maizidian Street, Chaoyang District
Beijing 100025
China
Tel: (+86) 10 6419 4079
Fax: (+86) 10 6593 7005
E-mail: gubaogen@agri.gov.cn
or ggbbgg868@yahoo.com.cn

Mr Halimi Bin Mahmud
Deputy Director
Pesticides Board
Pesticides Control Division
Department of Agriculture
4-6 Floors, Wisma Tani
Jalan Mahameru, 50 632
Kuala Lumpur
Malaysia
Tel: (+603) 2030 1480
Fax: (+603) 2691 7551
E-mail: halimi_mahmud@yahoo.com
or halimi@doa.gov.my

Dr Gamini Manuweera
Registrar of Pesticides
Office of the Registrar of Pesticides
PO Box 49 Peradeniya
Sri Lanka
Tel: (+94) 811 238 8076
Fax: (+94) 811 238 8135
E-mail: pest@slt.lk

Dr Maristella Rubbiani
Director
Dangerous Preparations Unit
National Center for Chemicals
Viale Regina Elena 299
00161 Rome
Italy
Tel: (+39) 06 499 02353
Fax: (+39) 06 493 87068
E-mail: maristella.rubbiani@iss.it

Dr Gary Whitfield
Science Director – Integrated Pest Management
Agriculture & Agri-Food Canada
Greenhouse and Processing Crops Research Centre, R. R. #2
2585 County Road #20
Harrow, Ontario, N0R 1G0
Canada
Tel: (+519) 738 2251 402
Fax: (+519) 738 3756
E-mail: whitfieldg@agr.gc.ca

Dr Wolfgang Zornbach
Deputy Head
Plant Protection Division
Federal Ministry of Food, Agriculture and Consumer Protection,
Rochusstrasse 1
D-53123 Bonn
Germany
Tel: (+49) 228 529 4317
Fax: (+49) 228 529 5535 95
E-mail: wolfgang.zornbach@bmelv.bund.de

WHO PANEL MEMBERS

Dr Cristina Alonzo
Chemical Safety Unit
Department of Environmental Health
Ministry of Public Health
4to piso, Anexo B.
Avenida 18 de Julio 1892
Montevideo
Uruguay
Tel: (+598) 2 402 8032
Fax: (+598) 2 402 8032
E-mail: aloncris@adinet.com.uy

Dr Sandhya Kulshrestha
Central Insecticides Board and Registration Committee
Dte of PPQ&S
Dept of Agriculture & Cooperation
Ministry of Agriculture
N.H. – IV, Faridabad (Haryana)
India
Tel: (91) 129 241 3002
Fax: (+91) 129 2412125
E-mail: sandhyak@nic.in
skulsh57@yahoo.co.in

Dr Irma R Makalinao
Professor and Graduate Program Chair
Department of Pharmacology and Toxicology
College of Medicine
University of the Philippines Manila
547 Pedro Gil St Ermita
Manila 1000
Philippines
Tel/Fax: (+63) 521 8251
E-mail: irmakalinao@gmail.com

Mr Somchai Preechathaveekid
Director
Hazardous Substances Control Division
Food and Drug Administration (FDA)
Ministry of Public Health
Tiwanon Road, Nonthaburi 11000
Thailand
Tel: (+662) 5918481, 5907300
Fax: (+662) 591 8483
E-mail: psomchai@health.moph.go.th

Dr Tiina Santonen
Risk Assessment Team
Finnish Institute of Occupational Health
Topeliuksenkatu 41 a A
FO 00250 Helsinki
Finland
Tel: (+358) 30 474 2666
Fax (+358) 30 474 2110
E-mail: tiina.santonen@ttl.fi

INTERGOVERNMENTAL ORGANIZATIONS

ILO

Dr Peter Hurst
Occupational Safety and Health Specialist
International Programme on the Elimination of Child Labour (IPEC)
International Labour Organization
4 route des Morillons
CH-1211 Geneva 22
Tel: (+41) 22 799 8274
Fax: (+41) 22 799 8771
E-mail: hurst@ilo.org

UNEP

Dr Agneta Sundén-Byléhn
Senior Scientific Affairs Officer
United Nations Environment Programme
Maison Internationale de l'Environnement
11-13, Chemin des Anemones
CH-1219 Châtelaine
Geneva
Switzerland
Tel: (+41) 22 917 8193
Fax: (+41) 22 797 3460
E-mail: asunden@chemicals.unep.ch

Mr Cyrille-Lazare Siéwé
Scientific Affairs Officer
Division of Technology, Industry & Economics (DTIE)
Chemicals Branch, IEH I
United Nations Environment Programme
Maison Internationale de l'Environnement
11-13, Chemin des Anémones
CH-1219 Châtelaine
Geneva
Switzerland
Tel: (+41) 22 917 8437
Fax: (+41) 22 797 3460
E-mail: csiewe@chemicals.unep.ch

UNITAR

Mr Jan van der Kolk
Training Advisor
United Nations Institute for Training And Research
c/o Eco Conseil
Van Deventerlaan 41
2271 TV Voorburg
The Netherlands
Tel: (+31) 70 3861141
E-mail: janvanderkolk@ecoconseil.nl

WORLD BANK

Dr Abdelaziz Lagnaoui
Senior IPM Policy Advisor
The World Bank
1818 H Street, NW
Washington, DC 20433
U.S.A.
Tel: (+1) 202 458 2806
Fax: (+1) 202 477 0565
E-mail: alagnaoui@worldbank.org

OBSERVERS

AGRO-CARE

Mr Pedro Correia
President
AGRO-CARE
Inventus Quimicos Lda
Rue Egas Moniz 11
PT-2765-218 Estoril
Portugal
E-mail: Inventus@mail.telepac.pt

Mr Roman Macaya
President
Asociación Latinoamericana de la Industria Nacional de Agroquímicos (ALINA)
Apartado 1325-1250
Escazu
Costa Rica
Tel: (+506) 2573 7751
Fax: (+506) 2573 7285
E-mail: roman_macaya@yahoo.com

CROPLIFE INTERNATIONAL

Dr Richard Brown
Head of Product Stewardship
Syngenta Crop Protection AG
Schwarzwaldalleee 215
P.O. Box
CH-4002 Basel
Switzerland
Tel: (+41) 61 323 7525
Fax: (+41) 61 323 7680
E-mail:
richard_anthony.brown@syngenta.com

Dr Bernhard Johnen
Director, International Regulatory Policy, Crop Protection,
CropLife International
Avenue Louise 326, Box 35
B-1050 Brussels
Belgium
Tel: (+32) 2 542 0410
Tel: (+32) 2 541 1668
Fax: (+32) 2 542 0419
E-mail: bernhard@croplife.org

INTERNATIONAL UNION OF FOOD (IUF)

Mr François Meienberg
c/o Berne Declaration
P.O. Box
CH 8026 Zurich
Switzerland
Tel: (+41) 44 277 7004/277 7001
E-mail: food@evb.ch

PESTICIDE ACTION NETWORK

Dr Meriel Watts
Pesticide Action Network – Aotearoa
New Zealand
Tel: (+47) 9 372 2034
E-mail: merielwatts@xtra.co.nz

Ms Carina Weber
Director
Pesticide Action Network – Germany
Nernstweg 32
D-22765 Hamburg
Germany
Tel: (+49) 40 399 1910/ 399 1923
Fax: (+49) 40 390 7520
E-mail: carina.weber@pan-germany.org

WHO – Secretariat

Dr Alexandra Fleischmann
Scientist, Management of Substance Abuse (MSA)
World Health Organization
Avenue Appia 20, CH - 1211
Geneva 27
Switzerland
Tel: (+41) 22 791 3625
E-mail: fleischmanna@who.int

Ms Stephanie Guillaneux
Technical Officer, Global Malaria Programme (GMP)
World Health Organization
Avenue Appia 20, CH - 1211
Geneva 27
Switzerland
Tel: (+41) 22 791 1088
E-mail: guillaneuxs@who.int

Dr Kazuyo Ichimori
Scientist, Vector Entomology and Management (VEM)
World Health Organization
Avenue Appia 20, CH - 1211
Geneva 27
Switzerland
Tel: (+41) 22 791 2767
E-mail: ichimorik@who.int

Dr Lorenzo Savioli
Director, Neglected Tropical Diseases
World Health Organization
Avenue Appia 20, CH - 1211
Geneva 27
Switzerland
Tel: (+41) 22 791 2664
E-mail: saviolil@who.int

Ms Johanna Tempowski
Scientist, Evidence and Policy on Emerging Issues (PHE)
World Health Organization
Avenue Appia 20, CH - 1211
Geneva 27
Switzerland
Tel: (+41) 22 7913571
E-mail: tempovskij@who.int

Dr Morteza Zaim
Scientist, WHO Pesticide Evaluation Scheme (WHOPES)
World Health Organization
Avenue Appia 20, CH - 1211
Geneva 27
Switzerland
Tel: (+41) 22 791 3841
E-mail: zaimm@who.int

FAO – Secretariat

Mr Clifton Curtis
Consultant
c/o The Varda Group
3409 Quebec St., NW
Washington DC 20016
U.S.A.
Tel: (+1) 202 362 0476
E-mail: clifton@vardagroup.org

Mr Mark Davis
a.i. Senior Officer Pesticide Management
Plant Protection Service
Food and Agriculture Organization of the United Nations
Viale delle Terme di Caracalla
00153 Rome
Italy
Tel: (+39) 06 570 55192
Fax: (+39) 06 570 56347
E-mail: Mark.Davis@fao.org

Mr Harold van der Valk
Consultant
Vissersdijk 14
4251 ED Werkendam
The Netherlands
Tel: (+31) 183 500410
E-mail: harold.vandervalk@wxs.nl

Ms Jessica Vapnek
Legal Officer
Development Law Service
Food and Agriculture Organization of the United Nations
Viale delle Terme di Caracalla
00153 Rome
Italy
Tel: (+39) 06 570 56605
E-mail: Jessica.Vapnek@fao.org

Annex 2 – Agenda

1. Opening of the meeting and welcome address

2. Appointment of Chairman and Rapporteurs

3. Adoption of agenda

4. Introduction of meeting procedure, working arrangements and housekeeping matters.

5. Summary of developments and actions taken after the first joint meeting in October 2007.

6. Highly hazardous pesticides – status of implementation of recommendations made after the first joint meeting in October 2007.

7. Draft Guidelines agreed for publication in the previous meeting – status report
   a. Guidelines on management options for empty pesticide containers.
   b. Guidelines on pesticide advertising.
   c. Guidance on pest and pesticide management policy development – agriculture.

8. Draft Guidelines under development – status report
   a. Guidelines on resistance management for pesticides.
   b. Guidelines on registration microbial pest control agents.

9. Draft outlines for Guidelines – for review
   a. Guidelines on retail establishments of pesticides.

10. Draft Guidelines – for review.
    a. Guidelines on the development a reporting system for health and environmental incidents resulting from exposure to pesticides.
    b. Guidelines on registration of pesticides.

11. Guidelines proposed for updating – issues regarding content
    a. Guidelines on pesticide legislation
    b. Guidelines on good labelling practice for pesticides

12. Implementation of the revised version of the International Code of Conduct – future orientation of activities.

13. Any other matters.

Hazards of pesticides imported into Mozambique, 2002-2011

Joost Lahr
Roel Kruijne
Jan Groenwold

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Contents

Summary

Together with the government of Mozambique, The Food and Agriculture of the United Nations (FAO) is implementing a project to identify the most Highly Hazardous Pesticides (HHPs) in Mozambique based on import data and to reduce risks of these pesticides by recommendations for mitigation measures. In the framework of this project Alterra, Wageningen UR, has conducted a desk top study to assess the hazards associated with pesticides imported in Mozambique from 2002 to 2011. The objectives of the study were (1) to conduct an evaluation of historical trends in the use of pesticides in Mozambique based on pesticide import data compiled by the Ministry of Agriculture over the period 2002 – 2011, (2) to assess trends in human health and environmental hazards and potential risks of the pesticides imported in Mozambique, and (3) to identify pesticides or pesticide use patterns (as far as feasible) contributing most to these hazards.

In order to analyse trends in potential hazards of pesticide use on human health and the environment, hazard based indicators were used for occupational health, aquatic organisms, bees and groundwater. When true exposure assessment data are not available, hazard based indicators can be used to rank pesticides relatively to each other from high to low hazard. FAO supplied data to Alterra of pesticides imported into Mozambique from the years 2002 to 2011, as well as information on pesticides with a registration in Mozambique. It is not clear if the pesticide import data for 2002 used in this study are complete.

The most important results of the study are:

- The volume of pesticides imported increased almost threefold, from 670 tonnes in 2003 to 2592 tonnes in 2011. Agricultural production increased by 40 % from 9.9 million tonnes in 2002 to 13,9 million tonnes in 2011, whereas the agricultural area increased only by 1.4%;
- The types of pesticides imported in the country are very consistent over time. The majority of products consists of insecticides, followed by the herbicides and fungicides;
- The volume of highly hazardous products imported over time decreased and the volume of products with a (very) low hazard increased;
- Only few pesticide products with a known chronic hazard to human health were imported in the country, although carcinogenic products were imported at the rate of 100 tons per year;
- A considerable number of the pesticides imported into the country are acutely toxic to fish, aquatic invertebrates, algae and bees. However, the less hazardous pesticides represent a much higher volume of imports;
- The Environmental Toxic Load (ETL) (relative hazard corrected for surface of agricultural area) to aquatic organisms (fish, aquatic invertebrates and algae) increases from 2002 to 2010, but decreases for all three groups of species in 2011;
- Overall, the hazard of the imported pesticides is more than two times higher to aquatic invertebrates and algae than to fish;
- The ETL to bees also increases from 2002 to 2008, but is considerably lower from 2009 to 2011;
- Only few active ingredients with a very high or high leaching potential are imported in the country.

The pesticides that contributed most to the overall human health hazards and environmental hazards are given in the following table. Active ingredients of primary or secondary concern were identified using criteria that combine both potential hazard of the pesticides and imported quantities in Mozambique. The table may be used to focus hazard reducing measures in the country.

Pesticides imported in Mozambique from 2002 to 2011 that are of concern in terms of potential human health and environmental hazard and annually imported quantity.

Type of hazard	Pesticide active ingredient of primary concern	Pesticide active ingredient of secondary concern
Human health		
Acute (WHO classification)	Class I pesticide products containing: Abamectin Aldicarb Aluminium phoshide Fenamiphos Methomyl Mevinphos Monocrotophos Oxamyl Terbufos	Class II pesticide products containing: Ametryn DDT Lambda-cyhalothrin
Chronic	Diuron (carcinogenic) Mancozeb (carcinogenic)	Dichlorvos (carcinogenic)
Environment		
Fish	Lambda-cyhalothrin	Aluminium phoshide Chlorpyrifos Cyfluthrin Cypermethrin Endosulfan
Aquatic invertebrates	-	Chlorpyrifos Cypermethrin DDT Dichlorvos Ethion Fenvalerate Lambda-cyhalothrin Pirimiphos-methyl
Algae	Acetochlor	Ametryn Paraquat
Bees	Imidacloprid	Bendiocarb Chlorpyrifos Cyfluthrin Cypermethrin Deltamethrin Lambda-cyhalothrin Profenofos Thiamethoxam
Leaching to groundwater	Methyl bromide Tebuthiuron	Atrazine Clomazone Hexazione Imidacloprid Propoxur

1 Introduction

1.1 Scope of the project

Together with the government of Mozambique, The Food and Agriculture of the United Nations (FAO) has been implementaing a project to identify the most Highly Hazardous Pesticides (HHPs) in Mozambique and to reduce risks of these pesticides by recommendations for mitigation measures.

In the framework of this project Alterra, Wageningen UR, has conducted a desk top study of the hazards associated with pesticides imported in Mozambique from 2002 to 2011.

1.2 Objectives

The objectives of the study were:

1. to conduct an evaluation of historical trends in the use of pesticides in Mozambique based on pesticide import data compiled by the Ministry of Agriculture over the period 2002 – 2011,
2. to assess trends in human health and environmental hazards and potential risks of the pesticides imported in Mozambique, and
3. to identify pesticides or pesticide use patterns (as far as feasible) contributing most to these hazards.

1.3 Approach

The potential risk related to the use of a specific pesticide is always determined by pesticide properties (hazard) and circumstances in which the pesticide is used (exposure). Therefore:

Risk = hazard × exposure

Hazard is determined by the toxicological properties of the pesticide. Environmental exposure is determined by pesticide use patterns, the physico-chemical properties of the active ingredient (a.i.) and the properties of the environment (e.g. soil, climate, surface water) of concern. Human occupational exposure is further determined by use of personal protective equipment, application equipment, skills and awareness of the operator, while dietary exposure is determined by many other factors like for instance composition of diet.

In order to analyse trends in potential hazards of pesticide use on human health and the environment, we used hazard based indicators for occupational health, aquatic organisms, bees and groundwater. When real exposure assessment data are not available, hazard based indicators can be used to rank pesticides relatively to each other from high to low hazard. These indicators, together with the quantitative information on pesticides use, can provide an indication of which pesticides are most likely to pose a potential problem. Such an approach has earlier been successful in identifying the trends in the hazards of pesticides used in cotton in different countries (De Blécourt et al., 2010). The actual risks posed by these pesticides, however, remain uncertain as realistic exposure profiles are not explicitly taken into consideration. This would need more location-specific data. But while perhaps less specific than risk indicators due to the lack of exposure data, hazard indicators are quite suitable for trend assessments and ranking exercises.

2 Methods

2.1 Datasets

FAO has supplied data to Alterra of pesticides imported into Mozambique from the years 2002 to 2011, as well as information on pesticides with a registration in Mozambique. Hereafter these spreadsheet files will be referred to as the Import data and the Registered pesticide data, respectively. Following an initial quality check conducted by Alterra, additional efforts by FAO and Alterra were needed in order to enhance the quality of these data, notably the Import data.

2.1.1 Import data

Text fields in the original Excel spreadsheet with Import data delivered by FAO contain Product names, Active ingredient names, Categories (i.e. the product group), Importer names, Units of Concentration, Units of Quantity, and the Monetary Units. These text fields were screened for typing errors, alternative spelling, abbreviations, etc.

Inconsistent entries were corrected when possible. Those which could not be corrected were removed from the dataset. For example, the active ingredient content is required for conversion of product volumes into active ingredient volumes. The import data included 11 bio pesticides and inorganic pesticides with an unknown formulation (i.e. a blank) or a value out of range in the content field. These import events had to be removed. In another five cases, a missing value for the content was replaced with the mean value of the content in the other imported products with exactly the same active ingredients. A numerical field was added to the text fields for identification. In some cases the number in the Concentration a.i. field was corrected in order to obtain a unique value for the content of the active ingredient of a formulated product

2.1.2 Pesticide properties

In order to make an analysis of the human and environmental hazards related to the agricultural use of pesticides in Mozambique, full consistency is required between the product formulation in the Import data and the active ingredients in the Registered pesticide data. On a few occasions, when the information in both datasets did not entirely match, we let the Import data prevail over the Registered pesticide data.

We gathered the toxicity and fate properties of the active ingredients and the products mentioned in the Import data from the following sources:

1. The Registered pesticide data, mainly for human toxicity data.
2. The internal compound database of the Alterra team Ecological Risk Assessment (ERA). This internal database is used for projects only and was last updated for the study on cotton (see De Blécourt *et al*., 2010).
3. A compound database available from the evaluation of the Dutch policy plan for sustainable use of pesticides (mainly for fate properties).
4. The Pesticides Properties DataBase PPDB (Footprint; 2013, 2007) database, for the classification of physical properties and environmental toxicity.

Some 80% of the properties required for the analysis were found in these sources. We used a routine for the repacement of missing values for compound properties, which consists of the following steps:

- When a parameter value for an active ingredient is not available, the mean value of all active ingredients from the same chemical class will be used (e.g., carbamate, organophosphate).

- When the mean of the parameter values for the active ingredients from the same chemical class cannot be calculated, the mean of all active ingredients from the same product group is used (insecticides, fungicides, etc.).
- When no mean values can be calculated, the parameter value is classified as unknown.

Accordingly, the status of each property will be either 1) original value, 2) estimated value based on chemical class, 3) estimated value based on product group, or 4) not available. This routine was developed in the framework of the European HAIR project on risk indicators for agricultural use of pesticides (Kruijne *et al*., 2011). It was developed and approved by the scientists in the HAIR consortium, but is has so far not been validated.

Annex 1 contains the fate properties and toxicity values for all active ingredients, including the source.

2.2 Trends in pesticide import

Trends in pesticide import in Mozambique from 2002 to 2011 were explored in terms of numbers (type) of pesticides and volume (amount) of pesticides. Trends in imported pesticide products and their active ingredients were based on the annual volume imported and the formulation of these products. Metabolites are not considered in this study.

In reality, the annual volume of products used in agricultural crops in the country may be different from the volume imported due to changes in stocks, exports to other countries, and non-agricultural uses. Gathering information on these flows and stocks was beyond the scope of this study. Moreover, the Import data or Registered pesticide data did not contain information on their use in e.g. agriculture, public health or veterinary use, so no formal distinction can be made. The import data provided are regarded as a proxy for actual use in Mozambique in the different sectors combined.

2.3 Hazard indicators

Hazard based indicators were used to rank products and active ingredients relative to each other from high to low hazard. Hazard is defined by the OECD (2003) as 'an inherent property of an agent or situation having the potential to cause adverse effects when an organism, system or (sub) population is exposed to that agent'. Hazard is determined by the toxicological properties of the formulated pesticide or its active ingredients. The hazard assessments conducted in this study do not estimate the actual risks in the field since true risks depend on many more factors that are not explicitly taken into account here such as pesticide formulation, soil properties, weather conditions during application, use of protective personal equipment, method of application, buffer strips and other mitigation techniques, the species that do actually occur in the field, etc.

In this study hazard assessments were performed for: 1) acute hazard to human health (WHO hazard classification), 2) chronic hazard to human health (carcinogenicity, mutagenicity and effects on reproduction), 3) hazard to aquatic organisms (fish, *Daphnia,* and algae), 4) hazard to bees, and 5) groundwater leaching potential. The basis of the indicators is described more fully below.

2.3.1 Acute hazard to human health

The classification of active ingredients according to their acute toxicity to human health originated from 'The World Health Organization recommended classification of pesticides by Hazard' (WHO, 2010). The hazard referred to is the acute hazard to health (that is, the potential effects of single or multiple exposures over a relatively short period of time) that might be encountered accidentally by any person handling the product in accordance with the directions for handling by the manufacturer or in accordance with the rules laid down for storage and transportation by competent international bodies. This definition does not include the regular handling of products in developing countries without personal protection equipment and consequent exposure.

The classification is primarily based on data on the acute oral and dermal toxicity to rats as standard testing species. Since 2009 it does not distinguish anymore between solid and liquid formulations. Provision is made for the classification of a particular compound to be adjusted if, for any reasons, the acute hazard to man differs from that indicated by the LD50 assessments alone. The WHO classification takes into consideration the toxicity of the technical compound and its common formulations. The criteria for classification are shown in Table 1.

Table 1: Categories of acute toxicity to human health according to the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) used for classification of formulations (WHO, 2010).

WHO Class		$LD50_P$ (mg/kg body weight)	
		Oral	Dermal
Ia	Extremely hazardous	< 5	< 50
Ib	Highly hazardous	5-50	50-200
II	Moderately hazardous	50-2000	200-2000
III	Slightly hazardous	2000-5000	2000-5000
U	Unlikely to present acute hazard	5000 or higher	

The classification of any product depends on the formulation concentration. If the concentration of the formulation is low, this may decrease the exposure and thus the acute risk (Equations 1, 2). Furthermore, for a solid formulation the exposure is usually lower compared to a liquid formulation since it is more difficult for a solid to pass through the skin.

Products containing a single active ingredient are classified based on the proportional toxicity and the categories shown in Table 1.

$$LD50_P = \frac{LD50_{ai}}{f_{ai}} \qquad \text{Eq. 1}$$

$LD50_P$ proportional LD50 for the product formulation (mg/kg body weight)
$LD50_{ai}$ oral acute LD50 or dermal acute LD50 of the active ingredient (mg/kg body weight)
f_{ai} content of the active ingredient (fraction)

Mixtures, i.e. products containing multiple active ingredients, are classified according to

$$LD50_P = \frac{1}{\sum \frac{f_{ai}}{LD50_{ai}}} \qquad \text{Eq. 2}$$

using the categories for oral toxicity shown in Table 1.

According to the WHO (2010), if both the oral acute LD50 and the dermal acute LD50 are available, the product should be classified based on the acute toxicity which results in the highest hazard class. The fields used for LD50 values in the Registered pesticide data were not entirely internally consistent. Fields contained numbers with both decimal points and comma's, text characters instead of numbers, combinations of both, lower limits, ranges, blanks and colours. This was too cumbersome to straighten out for 200 active ingredients in some 450 products. Numerical toxicity data were therefore partly gathered from the other sources used (see Annex 1). For practical reasons we decided only to use oral toxicity data. Oral LD50 data were more suitable to deal with the classification of mixtures. Often, there were no dermal data for all active ingredients in a mixture. Formulated mixtures of pesticides

cannot be classified on combined oral and dermal data (WHO, 2010). Moreover, the availability of dermal toxicity data is limited compared to oral toxicity, a fact that is recognised by the WHO (2010).

The consequence is that the oral toxicity criteria for classes Ia, Ib and II are slightly less strict than for purely dermal data. But oral toxicity is often higher than dermal toxicity, so in the majority of cases the use of oral toxicity data will lead to the most conservative classification. Another advantage is that all formulated pesticides are classified in a uniform way.

2.3.2 Chronic hazard to human health

According to the explanation provided with the HHP data, the classification of active ingredients of pesticides according to their chronic hazard to human health considering carcinogenicity, mutagenicity and reproductive toxicity according to the HHP data originated from at least four different sources including three different classification systems: the Globally Harmonized System (GHS) criteria, the classification system according to Directive 67/548/EEC and the US-EPA classification on carcinogenicity. The four different sources were needed in order to gather hazard classifications for as many active ingredients as possible:

- the active ingredient has been considered to be classified as a carcinogen of category 1A or 1B according to the GHS, a mutagen or reprotoxic ("yes"),
- the active ingredient is not classified as such ("no"), or
- the active ingredient was not evaluated by these sources (“n.e.”).

For this study we classified chronic hazard to human health according to the following decision rules:

- “yes” in case the active ingredient is toxic according to at least one of the sources mentioned,
- “no” in case the active ingredient is not qualified as toxic according to any of the sources and the active ingredient is qualified “not toxic” according to at least one of the sources.
- “n.e.” in case the active ingredient is neither toxic nor “not toxic” according to all sources.

2.3.3 Acute environmental hazard

The parameter used to classify the acute toxicity of active ingredients of pesticides to algae is the concentration that causes a 50% reduction in growth rate or final yield (EC50) of the test organisms in a standard algae test (usually 72h). The acute toxicity of pesticides to fish and the water flea *Daphnia* (representing aquatic invertebrates) is also expressed as acute EC50 or LC50 values (an LC50 is the concentration that kills 50% of the test organisms). The classification criteria of active ingredients according to acute toxicity to aquatic organisms is listed in Table 2. The classification was established by the US-EPA: http://www.epa.gov/oppefed1/ecorisk_ders/toera_analysis_eco.htm (retrieved in July 2009).

Table 2: Categories of acute toxicity to aquatic organisms (according to EPA, 2009)

LC50 or EC50 (mg/L)	Acute hazard to aquatic organisms
< 0.1	Very highly toxic
0.1 - 1	Highly toxic
1 - 10	Moderately toxic
10 - 100	Slightly toxic
> 100	Practically nontoxic

The classification of active ingredients according to their acute toxicity to bees is based on the dose per bee that kills 50% of bees (orally or by contact). The criteria for this classification are provided in Table 3. The classification originates from the ‘Manual for summarizing and evaluating the environmental aspects of plant protection products’ published by the Dutch National Institute for Public Health and the Environment (Mensink et al., 1995).

Table 3: Categories of acute toxicity to bees (Mensink et al., 1995)

LD50 (µg/bee)	Hazard to bees
< 0.1	Highly toxic
0.1 - 1	Toxic
1 - 10	Moderately toxic
10 - 100	Slightly toxic
> 100	Very slightly toxic

2.3.4 Environmental Toxic Load

The Environmental Toxic Load (ETL) indicator represents the average amount of toxic pressure by active ingredients of pesticides applied on one hectare of agricultural land in one year. Toxicity is mediated by the fact that only a small proportion of the pesticide volume will reach the organism. Dissipation processes like degradation and sorption are not taken into account. A similar approach has been used by Benbrook et al. (2002) and De Blécourt et al., 2010.

The ETL indicator is calculated separately for fish, *Daphnia*, algae and bees. The ETL is based on the total imported volume of active ingredients per year, the toxicity (either L(E)C50 for algae, *Daphnia* or fish or the LD50 for bees), and the total agricultural area in Mozambique. It is calculated as:

$$ETL_{yr} = \frac{\sum_{ai} \frac{V_{ai,yr}}{T_{ai}}}{A_{yr}} \qquad \text{Eq. 3}$$

ETL_{yr} Environmental Toxic Load indicator value for one year
$V_{ai,\,yr}$ volume of an active ingredient imported in a particular year (kg)
T_{ai} toxicity of the active ingredient; i.e. L(E)C50 of either fish, *Daphnia* or algae (mg/L), or the LD50 of bees (µg/bee)
A_{yr} total agricultural area in Mozambique in a particular year (ha)

The ETL cannot be used to assess the actual risk (i.e., the probability of an adverse effect on organisms) as a consequence of pesticide treatments because there is no exposure assessment involved in its calculation. For instance there is no prediction of an environmental concentration (PEC) in water that can be compared with a 'no effect concentration' for water organisms (PEC/NEC analysis). There is no thresholds of the ETL that signifies an absolute risk.

The ETL can therefore only be used to evaluate the impact of changes in relative environmental hazards between pesticides and between years. Furthermore, since toxicity data for bees (LD50) are expressed on the basis of µg/bee the ETL for bees cannot be compared to the ETL values for the aquatic organisms for which the toxicity (LC50 or EC50) is expressed in mg/L. However, since the same units for toxicity are used for algae, *Daphnia* and fish, it is justified to compare ETL's between these aquatic organisms. For instance it is possible to indicate if the pesticide import in Mozambique in a given year poses a higher overall potential hazard to algae than to fish. If the ETL for algae equals 10 and the ETL for fish equals 1000 in a certain year, the overall hazard of the pesticide import in Mozambique is 100 times greater for fish than for algae.

2.3.5 Groundwater leaching potential

The Groundwater Ubiquity Score or GUS (Gustafson, 1989) is an indication of the potential of the active ingredient of a pesticide to reach the groundwater before it is degraded. The GUS is an empirically derived value that relates to the persistence and sorption to soil organic matter of the active ingredient. The GUS index is calculated as follows

$$GUS = \log(DegT50_{soil}) \cdot (4 - \log K_{OC}) \qquad \text{Eq. 4}$$

GUS	potential of an active ingredient to reach the groundwater (-)
$DegT50_{soil}$	degradation half-life in soil (d)
K_{OC}	organic carbon sorption coefficient (L/kg).

The pesticide leaching potential is derived from the GUS. The ratings of active ingredients of pesticides range from very low to very high. The criteria are set out in Table 4.

Table 4: categories of groundwater leaching potential based on the GUS index.

GUS	Class	Groundwater leaching potential
< 1.0	1	Very low
1.0 – 2.0	2	Low
2.0 – 3.0	3	Moderate
3.0 – 4.0	4	High
> 4.0	5	Very high

2.4 Pesticides of concern

After the indicators were calculated and the analyses were done, criteria were established to select pesticides of concern. These are the pesticides that represent both an high hazard to human health and/or to the environment and that are imported in relatively large quantities in Mozambique for several years. The aim of this classification is to identify those pesticides and pesticide products for which the biggest gain in terms of reducing overall hazard to human health and/or the environment can be achieved by measures such as reducing their use in the country.

We distinguish two categories: 1) pesticides of primary concern, i.e., pesticides that contribute to a very large extent to the indicator values and that really stand out, and 2) pesticides of secondary concern that also contribute significantly but in a less dominant way. Both categories of pesticides are suitable to realise reductions of overall hazards by specific measures.

The criteria are applied per indicator or per group of indicators. This means that the pesticides of concern only stand out against other pesticides for a particular hazard. The overall hazard of imported hazards may be much bigger for, say, aquatic organisms than for human health, but such comparisons cannot be made based on the type of indicators that were used.

The criteria that were applied are listed on the following page.

Acute human health hazard (WHO classification of formulated products)

Primary concern:	All active ingredients occurring in WHO Class I formulated products imported from 2002 to 2011.
Secondary concern:	Active ingredients occurring in WHO Class II formulated products of which the imported volume (of formulated products) constitutes >5% of the total annually imported volume in 2 years or more.

Chronic human health

Primary concern:	Carcinogenic, mutagenic or reprotoxic active ingredients of which the imported quantity of a.i. constitutes >5% of the total quantity of annually imported a.i. in 2 years or more.
Secondary concern:	Carcinogenic, mutagenic or reprotoxic active ingredients of which the imported quantity of a.i. constitutes >1% of the total quantity of annually imported a.i. in 1 year or more.

Environmental Toxic Loads (fish, aquatic invertebrates, algae, bees)

Primary concern:	Active ingredients of which the imported quantity of a.i. constitutes >50% of the total annual ETL value in 2 years or more.
Secondary concern:	Active ingredients of which the imported quantity of a.i. constitutes >10% of the total annual ETL value in 1 year or more.

Groundwater Ubiquity Score (GUS)

Primary concern:	GUS class 5 active ingredients of which the imported quantity of a.i. constitutes >1% of the annual GUS index value in 2 years or more. And/or GUS class 4 active ingredients of which the imported quantity of a.i. constitutes >2% of the annual GUS index value in 2 year or more.
Secondary concern:	GUS class 5 active ingredients of which the imported quantity of a.i. constitutes >0.5% of the annual GUS index value in 1 year or more. and/or GUS class 4 active ingredients of which the imported quantity of a.i. constitutes >1% of the annual GUS index value in 1 year or more.

3 Results

3.1 Agricultural statistics

The dynamics in the total agricultural area in Mozambique according to FAOSTAT data (http://faostat3.fao.org/; accessed on July 1, 2013) are shown in Figure 1. The total agricultural area increased with 1,4% during the study period (2002-2011), i.e., from 48,7 million ha in 2002 to 49,4 million ha in 2011.

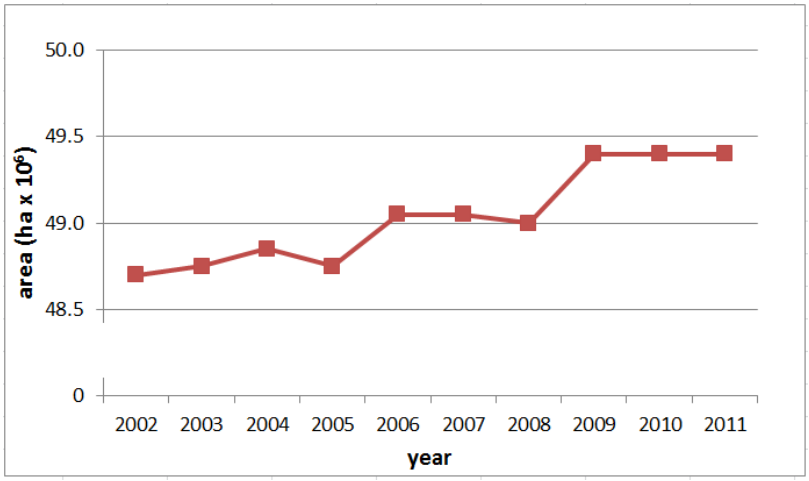

Figure 1: Total agricultural area in Mozambique in the years 2002 – 2011 (http://faostat3.fao.org/).

The total agricultural production according to FAOSTAT data (http://faostat3.fao.org/; July 1, 2013) is shown in Figure 2. These figures were calculated as the sum of eleven aggregated items[1]. The total agricultural production increased with 40% from 9,9 million tonnes in 2002 to 13,9 million tonnes in 2011. Because the cultivated area in the country did hardly increase over this period, it can be concluded that agriculture in Mozambique must have considerably intensified during this period.

[1] Cereals, Total; Citrus Fruit, Total; Coarse Grain, Total; Fibre Crops Primary; Fruit excl Melons, Total; Jute & Jute-like Fibres; Oilcrops Primary; Pulses, Total; Roots and Tubers, Total; Treenuts, Total; and Vegetables Primary.

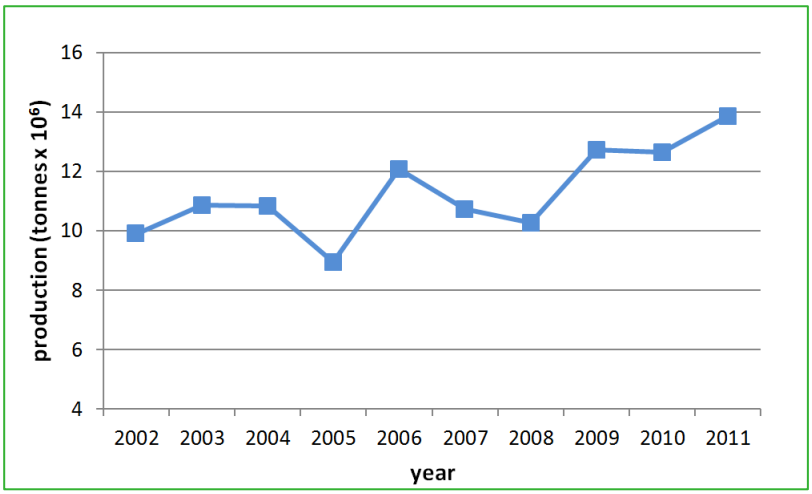

Figure 2: The total agricultural production in Mozambique in the years 2002 – 2011 (http://faostat3.fao.org/).

3.2 Pesticide imports

This section provides insights into trends in pesticide imports into Mozambique from 2002 to 2011. Trends are shown in the annual numbers and types (Section 3.2.1), the volume (Section 3.2.2) and the monetary value of imported pesticides (Section 3.2.3). In addition, the volume and the monetary value of imported pesticides are presented per unit of agricultural land and per unit weight of harvested product.

The Import data contain a relatively small number of import events for the first year, 2002. It seems logical that the dataset for this year is incomplete, but the authors have not received a confirmation of this. Since we cannot be entirely sure that the data of 2002 are representative for the entire year, we have decided to include the year 2002 in the graphs and tables but not to discuss the results for this particular year each time indicator values are lower compared to the other years.

3.2.1 Imported numbers of pesticides

Products

The annual number of formulated pesticide products imported is shown in Figure 3. The number fluctuates slightly and increases from 115 in the year 2003 to 157 in the year 2011.

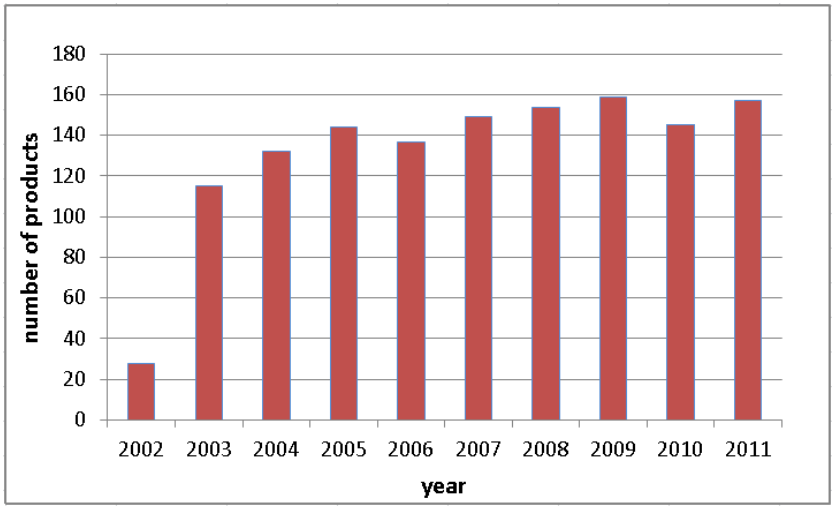

Figure 3: The annual number of formulated pesticide products imported in the years 2002 – 2011.

Product groups

The distribution of formulated pesticide products among the eight functional pesticide groups is shown in Figure 4. Insecticides constitute the major product group in all years, followed by herbicides and fungicides.

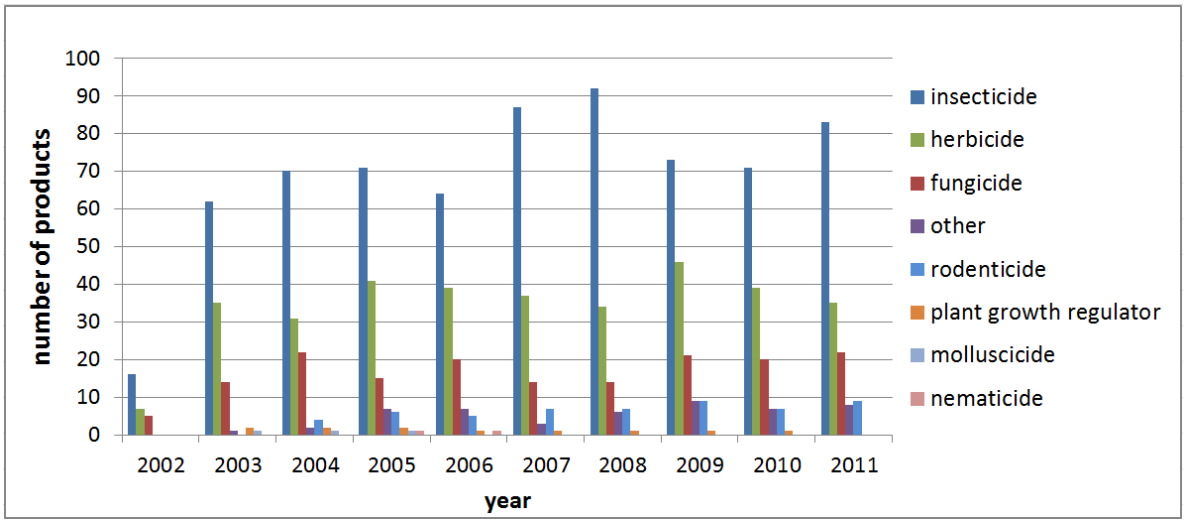

Figure 4: The number of formulated pesticide products per functional pesticide group imported yearly from 2002 to 2011.

Active ingredients

The formulated pesticide products imported in the period 2002-2011 contain 175 active ingredients assigned to 72 different chemical classes. The chemical classes with the largest number of active ingredients are the organophosphates (19 active ingredients), pyrethroids (16), carbamates (9), inorganic compounds (9), biopesticides (8), unclassified compounds (8), triazines (8) and triazoles (6). The annual number of chemical classes of active ingredients in the imported pesticides is shown in Figure 5. The numbers of the types of pesticides imported in the country increased up to 2005 and the fluctuated between c. 45 and 55.

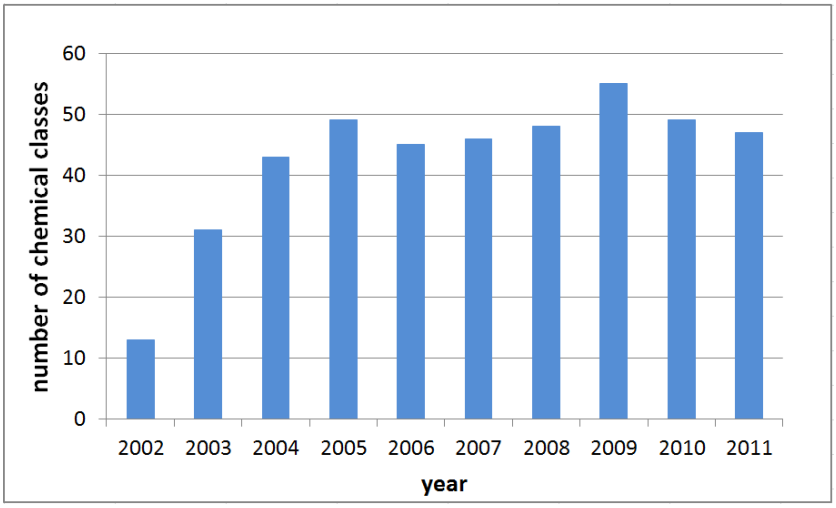

Figure 5: The number of chemical classes of the active ingredients imported annually in the years 2002 – 2011.

Importers

The annual number of active pesticide importers in Mozambique is shown in Figure 6. The numbers increase from 2002 to 2004, but decline in 2005 and 2006. From 2007 onwards the number increases again and the maximum number of importers is reached in the year 2010. Forty-four different importers were identified based on the Import data. The number of imported pesticide products per major importer is shown in Figure 7.

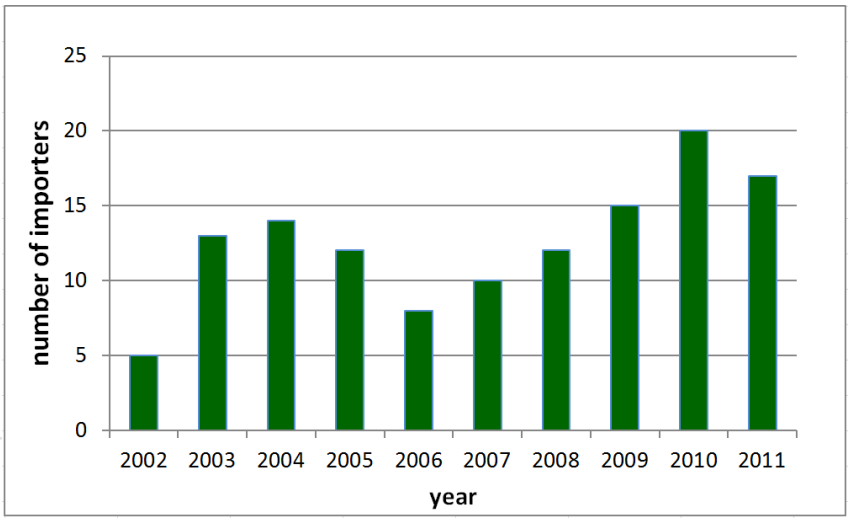

Figure 6: The number of pesticide importers responsible for the yearly imports from 2002 to 2011.

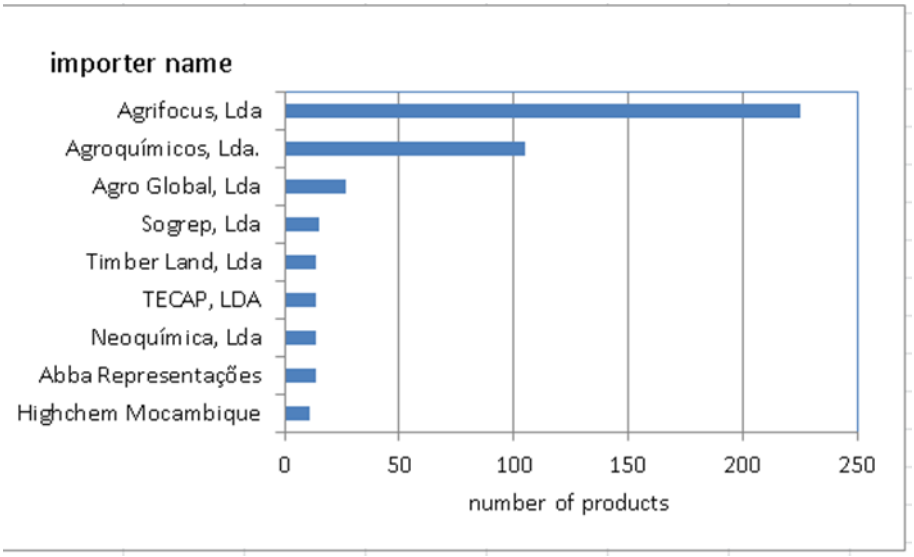

Figure 7: The total number of products imported by the major importers in the period 2002-2011.

3.2.2 Imported pesticide volume

Products

The annual volume of imported pesticides is shown in Figure 8. The imported volume increases until the year 2006. In the next year, 2007, the volume decreases by 37% to 1278 tonnes. As from 2008, the volume increases again to 2592 tonnes in the year 2011.

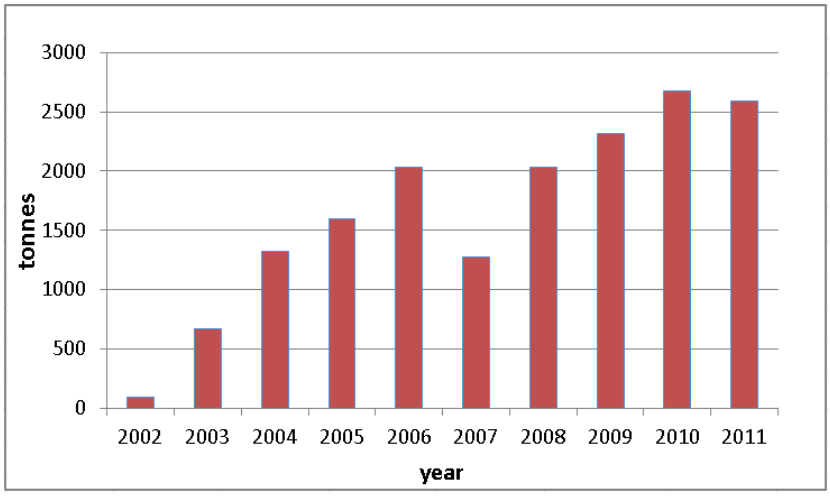

Figure 8: The annual volume of imported pesticide products in the years 2002 – 2011 (tonnes).

The volume of imported pesticides corrected for the total agricultural area (Figure 1) is shown in Figure 9, expressed in kg pesticides per hectare agricultural land. Because the total cultivated area changed only little during the study period, the pattern in Figure 9 is the same as in Figure 8.

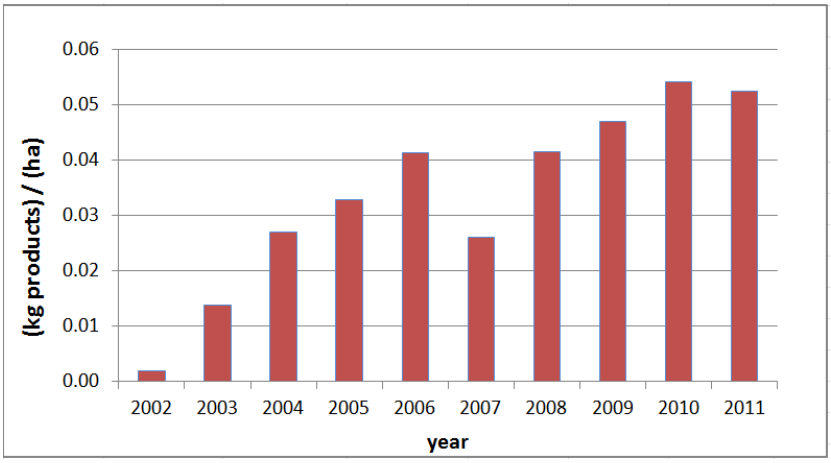

Figure 9: The annual volume of imported products corrected for the total agricultural area in the years 2002 – 2011 (kg/ha).

The volume of imported pesticides corrected for the total agricultural production (Figure 2) is shown in Figure 10. In the year 2007, the corrected volume of imported products decreases with 29% to 0.12 kg per ton harvested products. The figure clearly shows that although the total pesticide import per hectare in Mozambique is increasing (Figure 9), the pesticide import per tonne of harvested produce has been more or less constant from 2008 to 2011.

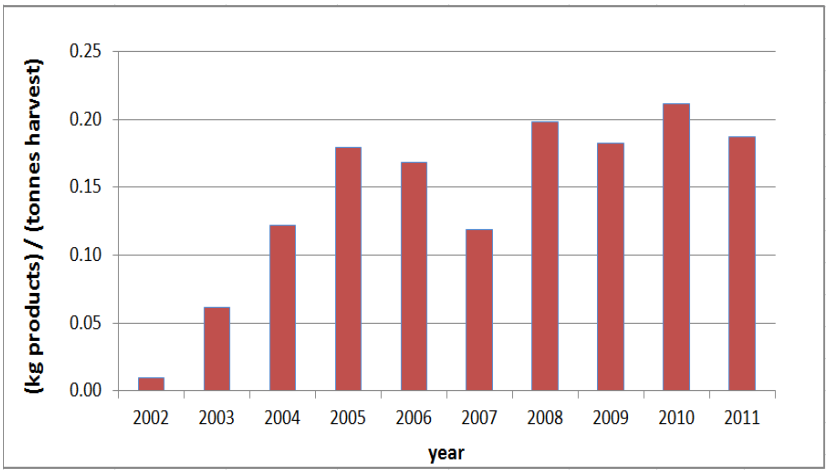

Figure 10: The annual volume of imported products corrected for the total agricultural production in the years 2002 – 2011 (kg products imported per ton of harvested products).

Product groups

The annual volume of imported products belonging to the eight functional groups is shown in Figure 11. Insecticides and herbicides constitute the major groups, followed by fungicides. The total amount of imported formulated pesticides increases in the first half of the decade and shows a dip in 2007. From 2008 to 2011 it is approximately the same. The annual volumes of insecticides and herbicides are more or less equal except in the years 2006 and 2008. In these two years, the volume of insecticides exceeds the volume of herbicides by some 50%.

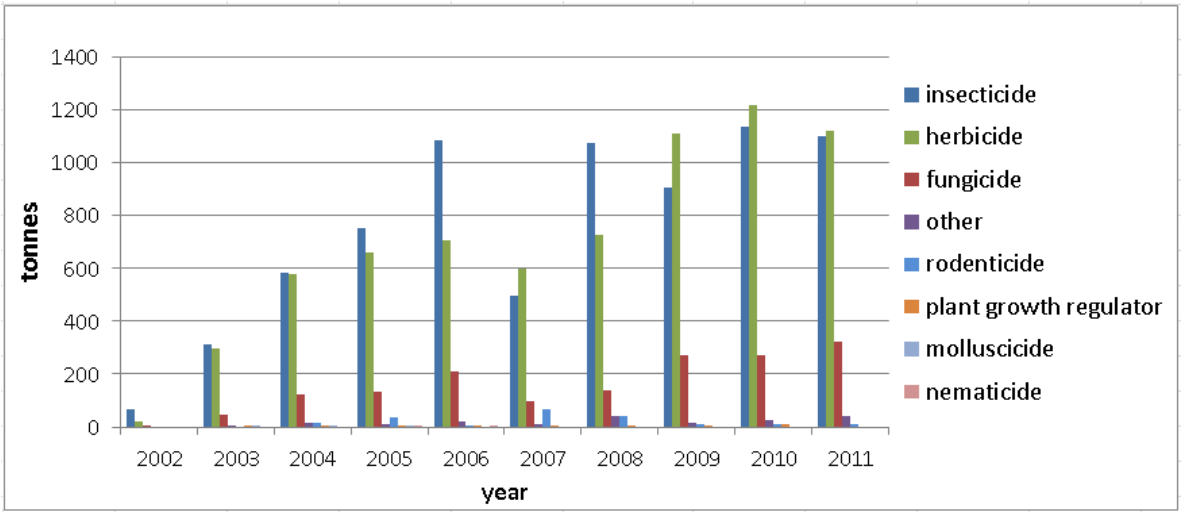

Figure 11: The annual volume per imported product group in the years 2002 – 2011 (tonnes)

The volume of imported pesticides belonging to the eight functional groups corrected for the total agricultural area (Figure 1) is shown in Figure 12. This parameter shows the same pattern as the uncorrected import data in Figure 11.

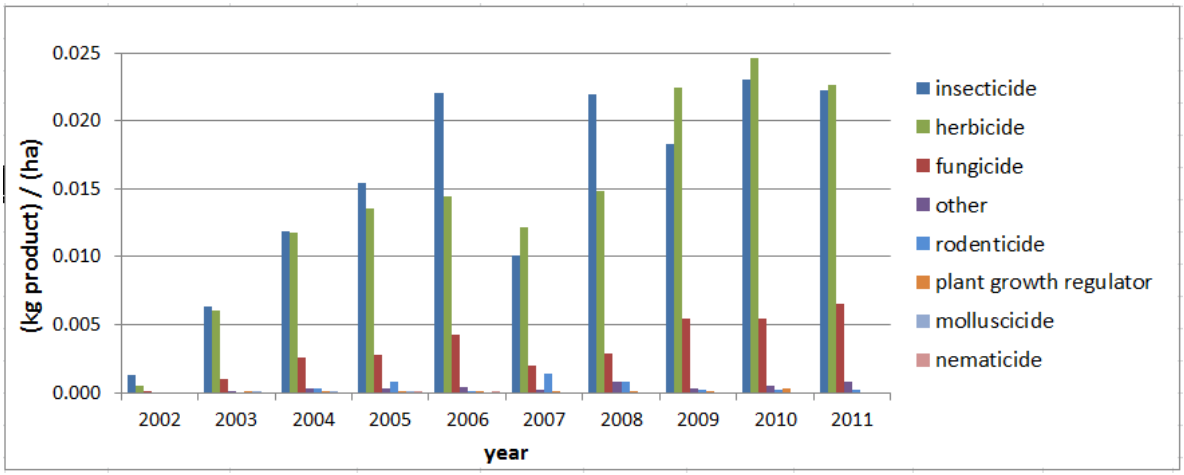

Figure 12: The annual volume per imported product group corrected for the total agricultural area in the years 2002 – 2011 (kg product/ ha)

The volume of imported pesticides corrected for the total agricultural production (Figure 2) is shown in Figure 13. The imports corrected for production still show the same pattern. A slight difference is that insecticide imports peak in 2008 instead of 2010.

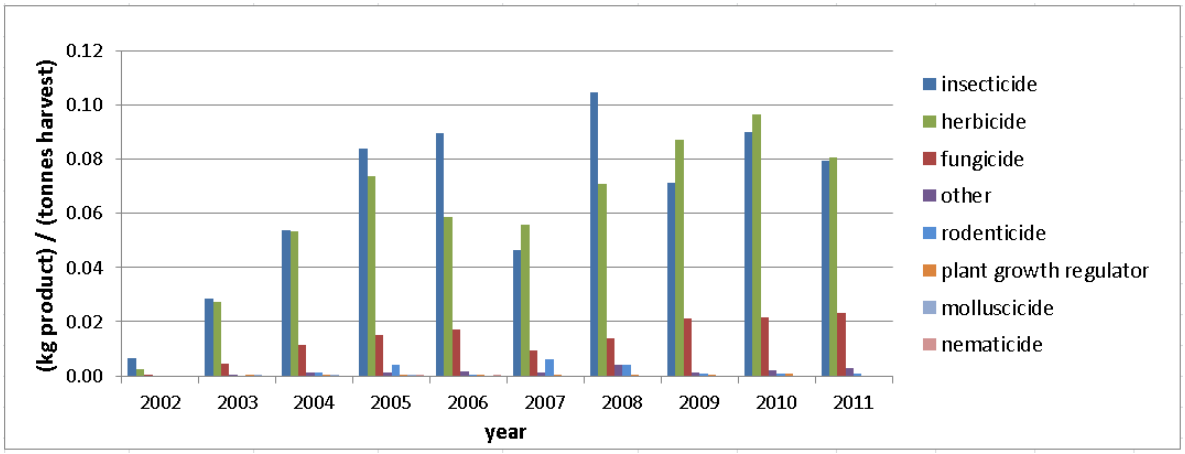

Figure 13: The annual volume per imported product group corrected for the total agricultural production in the years 2002 – 2011 (kg product / tonnes harvest)

Active ingredients

The annual volume of active ingredients per chemical class are shown in Figure 14. These are the major chemical classes based on the total volumes of products imported in the entire period 2002-2011. The volume of active ingredients in the chemical class of organochlorine compounds almost entirely consists of DDT (89% in the year 2005, 97% in 2006, and 100% in 2008). According to the Import data, DDT was only imported in these three years. There are conspicuous peaks in its import in 2006 and 2008, i.e., more DDT was imported that any other class of active ingredients. Endosulfan is the only other active organochlorine ingredient imported in the 10-year period. Another group of active ingredients that are reportedly imported in relative large quantities are the arsenates. Imports of these compounds keep on increasing from 2002 to 2011.

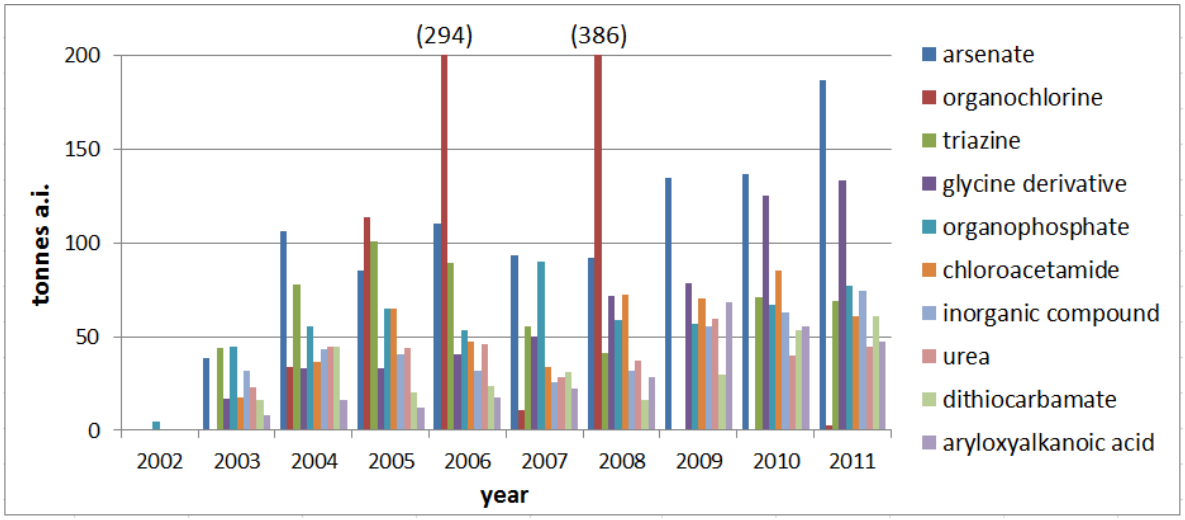

Figure 14: The annual volume per chemical class of active ingredients imported in the years 2002 – 2011 (in tonnes a.i.)

Importers

The five major importers in terms of their contribution to the total volume of imported products in the period 2002-2011 are shown in Figure 15. Agrifocus Lda is the major importer with almost 70% of the total volume of imported products in the entire period 2002-2011. The contributions of importers Agrifocus Lda and Sogrep Lda cover the entire period, whereas Abba Representações covers the years 2003-2011, Agroquímicos Lda covers the years 2002-2010, and Medimoc SA covers the years 2002-

2009. Contrary to these major importers, the majority of the other importers only contribute to the imported volume in one or two years over the 10-year period.

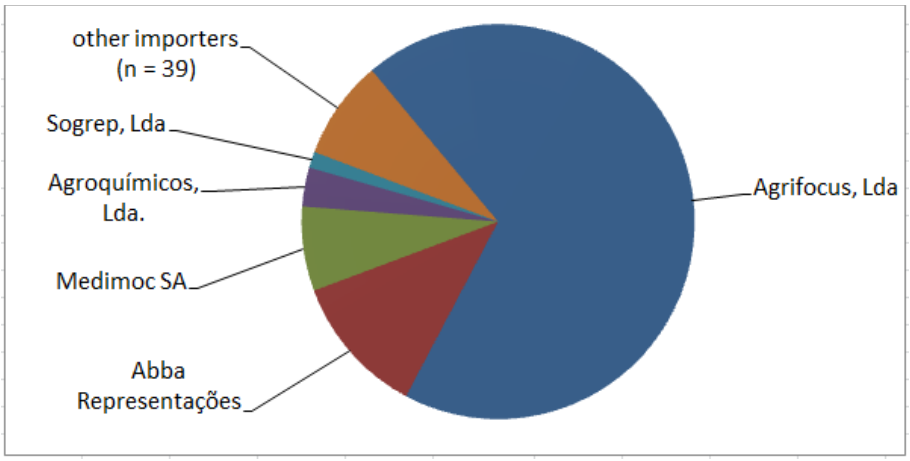

Figure 15: The five major pesticide importers according to the total volume of imported products in the period 2002-2011.

3.2.3 Monetary value

The monetary value of the imported quantity in the Import data is expressed in Metical or New Metical. In order to prepare the graphs and figures in this section, the monetary values in Metical (the years 2002 – 2005 and part of 2006) were converted into New Metical (1 Metical = 0.001 New Metical). The number of import events, the average price per L (or per kg) and the total monetary value of the imported product are shown in Table 5.

Table 5: The annual number of import events with the average price (in New Metical per L or per kg imported product)

Year	Number of import events	Average price per L or per kg in New Metical	Day rate US Dollar	Average price per L or per kg in US dollars	Total value of imports in New Metical (million)	Total value of imports in US dollar
2002	41	22	24.19	0.91	6.3	0.26
2003	263	100	24.02	4.17	115.2	4.80
2004	430	104	21.67	4.80	208.9	9.64
2005	493	112	26.68	4.20	309.5	11.60
2006	494	81	25.23	3.21	289.2	11.47
2007	431	123	25.79	4.77	202.7	7.30
2008	487	108	24.54	4.40	304.0	12.39
2009	563	191	27.40	6.96	459.6	16.78
2010	578	152	34.52	4.41	601.3	17.42
2011	590*	159	27.19	5.85	422.6	15.55

*For this year some import events were merged. Calculations were based on 461 import records.

Products

The annual monetary value of imported pesticides is shown in Figure 16 (in millions New Metical). The value of the imported pesticide products increases over the years with a dip in 2007 and a maximum in 2010. The annual value of imported pesticides corrected for the total agricultural area (Figure 1) is shown in Figure 17 (expressed in New Metical per hectare agricultural land) and the annual value of

imported pesticides corrected for the total agricultural production (Figure 2) is shown in Figure 18. The patterns for these corrected import data are comparable to the uncorrected imports.

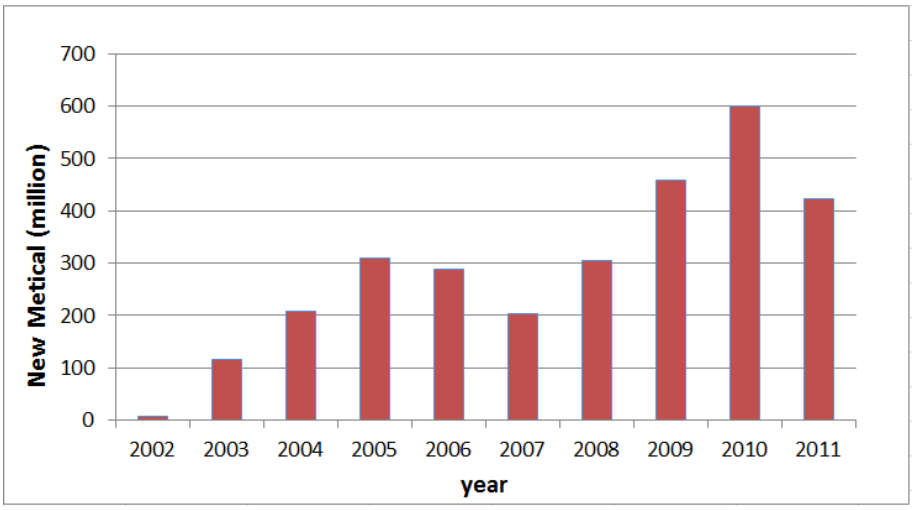

Figure 16: The annual value of imported products in the years 2002 – 2011 (million New Metical)

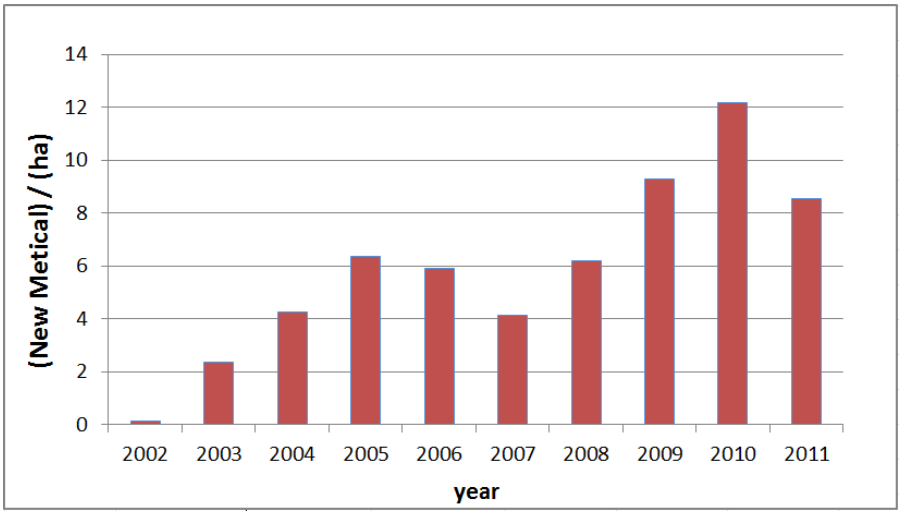

Figure 17: The annual value of imported products corrected for the total agricultural area in the years 2002 – 2011 (New Metical/ha)

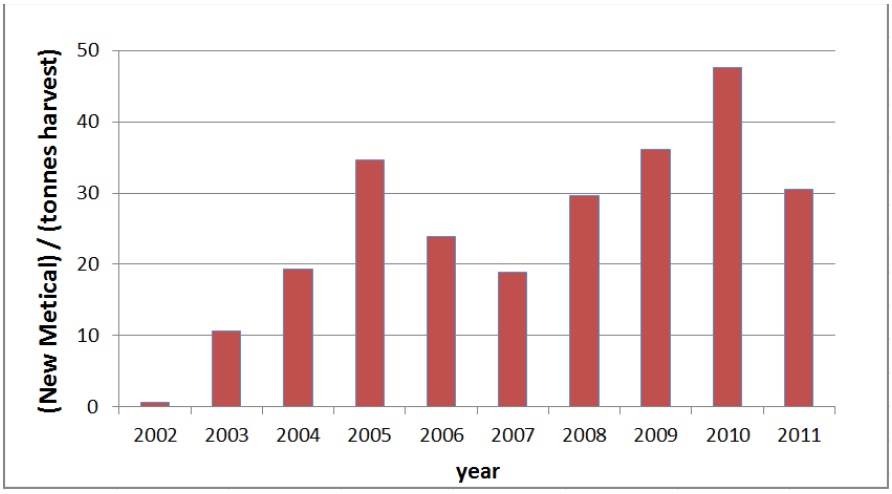

Figure 18: The annual value of imported products corrected for the total agricultural production in the years 2002 – 2011 (New Metical per ton harvested products)

Product groups

The annual value of imported products belonging to the major functional groups is shown in Figure 19. Imported insecticide products represent the highest imported value, followed by herbicides and fungicides. Since the imported volumes of insecticides and herbicides are comparable, imported insecticides must be more expensive than herbicides on average.

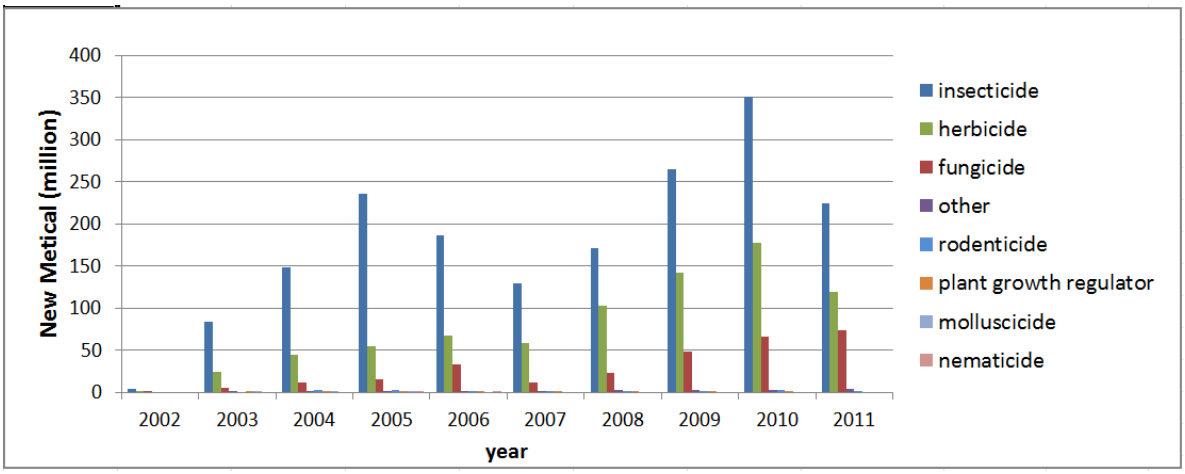

Figure 19: The annual monetary value per imported product group in the years 2002 – 2011 (million New Metical)

Importers

The five major importers according to the contribution to the total value of imported products in the period 2002-2011 are shown in Figure 20. These are also the importers with the major contribution in terms of volume (Figure 15).

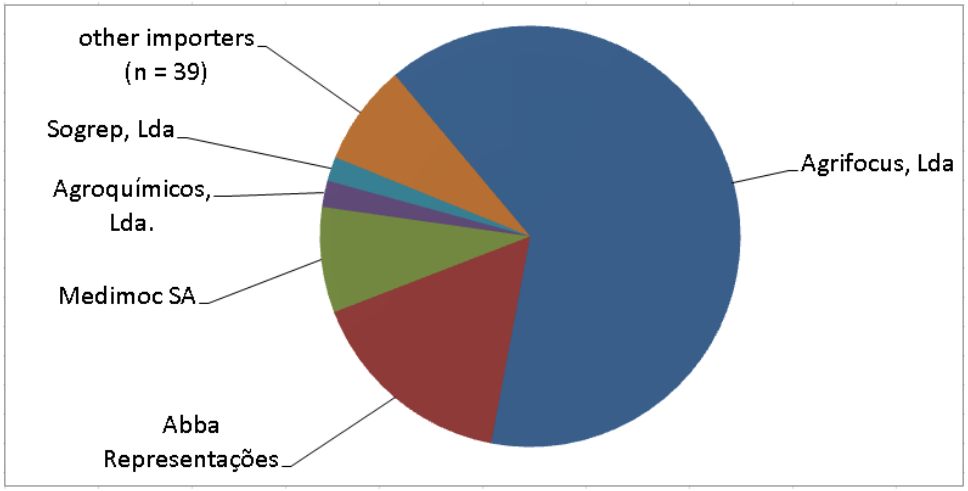

Figure 20: The five major pesticide importers according to the total value of imported products in the period 2002-2011 (in New Metical).

3.3 Acute hazard to human health

The classification of acute hazard to human health is made on a product basis according to Equations 1, 2 and the class boundaries shown in Table 1. The annual number of pesticide products per WHO

Class of acute hazard to human health is shown in Figure 21. Over the study period no products of the highest hazard class were imported (Ia, Extremely hazardous). The number of imported Highly hazardous pesticide products remains constant over the years at approximately 10 pesticides per year. The number and fraction of imported pesticide products unlikely to represent an acute hazard steadily increases over the ten years.

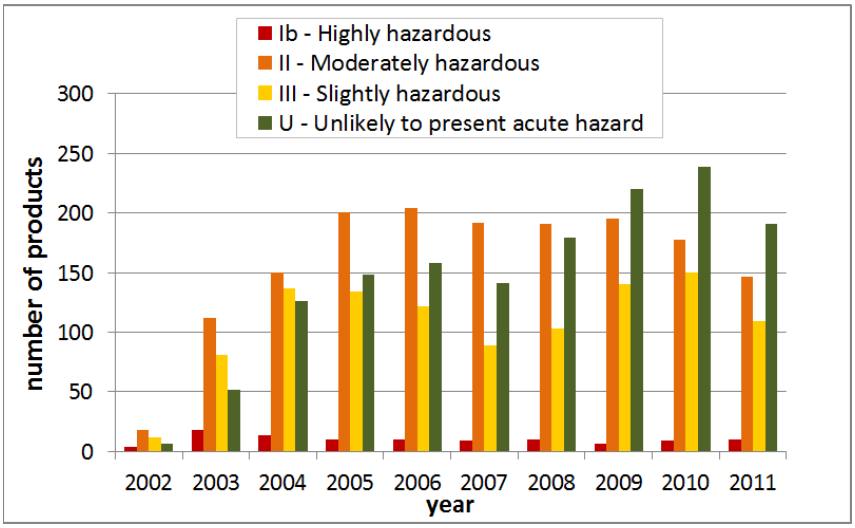

Figure 21: The annual imported number of pesticide products per WHO Class of acute hazard to human health in the period 2002-2011.

The annual volume of pesticide products per WHO Class of acute hazard to human health is shown in Figure 22. This graphs more clearly shows that fraction of imported volumes of moderately hazardous pesticides (Class II) of the total imported volume decreases whereas the fraction unlikely to present a hazard increases.

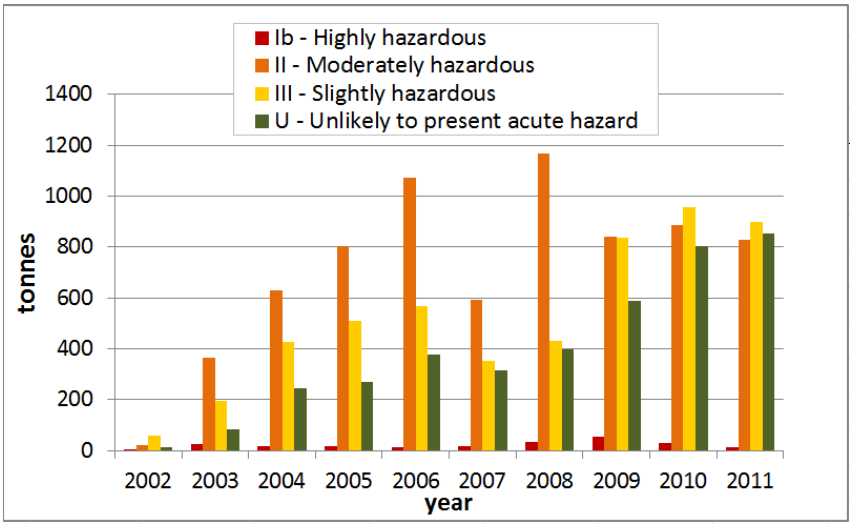

Figure 22: The annual volume of imported products per WHO Class of acute hazard to human health in the period 2002-2011 (tonnes).

In Table 2.1 in Annex 2 the imported pesticide products in WHO class Ib and II for each year are provided. The imported products in these classes change from year to year, but it can be seen that many of the Class Ib products contain only a few active ingredients under varying product names (also see Annex 5): abamectin (trade names: Agrometic, Moz Abamec Plus, Volcano), aldicarb (Temik, Volcano), aluminium phosphide (Moz Aluminium phoshide, Phosgard, Fumaphos, Falfume, Quickphos,

Volcano), fenamiphos (Nemacur, Volamiphos), Methomyl (Kuik), mevinphos (Universal), monocrotophos (Universal, Phoskill), oxamyl (Villa Platoon, Vydate) and terbufos (Rotam, Bongo). These pesticides of primary concern do only represent a small percentage of the yearly imports in Mozambique (<2% per product per year). Furthermore, the Class II products (moderately hazardous) representing >5% of total annual imports in two years or more (secondary concern) contained ametryn, DDT and lambda-cyhalothrin.

3.4 Chronic hazard to human health

The annual numbers and the volumes of imported pesticide per class of chronic hazard to human health are presented on active ingredient basis. The classification of chronic hazard to human health is taken from the Registered pesticide data (Section 2.3.2).

3.4.1 Carcinogenicity

The annual number of active ingredients per class of carcinogenicity is shown in Figure 23. The number of active ingredients in GHS Category 1A or 1B is less than ten per year and the majority of imported active ingredients are non-carcinogenic.

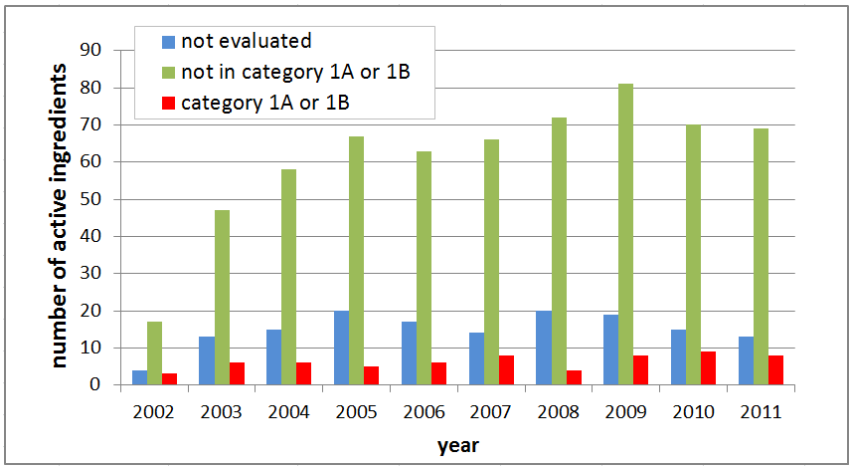

Figure 23: The annual number of imported active ingredients per class of carcinogenic hazard in the period 2002-2011.

The annual volume of active ingredients per class of carcinogenic hazard is shown in Figure 24. This graphs presents a slightly different picture than Figure 23. A relatively large volume of imported active ingredients is not evaluated in terms of carcinogenicity, especially those imported in 2006 and 2008. The imported amount of a.i. in GHS Category 1A or 1B is around 100 tonnes a year.

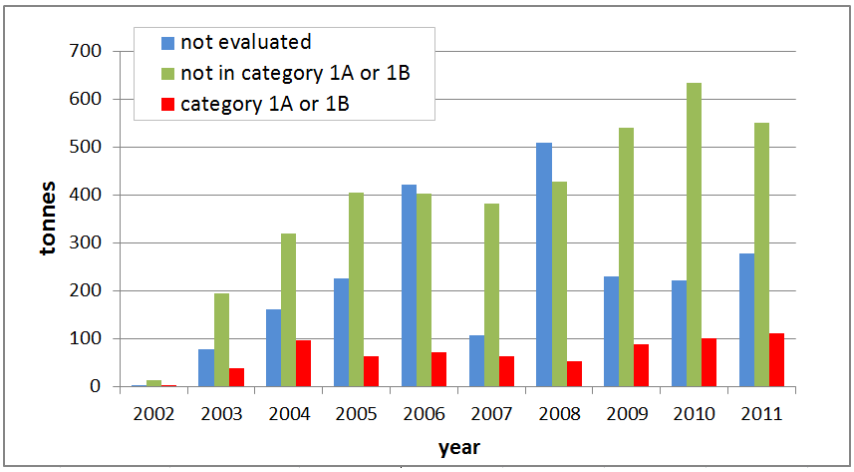

Figure 24: The annual volume of imported active ingredients per class of carcinogenic hazard in the period 2002-2011 (tonnes).

In Table 2.2 in Annex 2 the carcinogenic active ingredients that were imported in Mozambique are summarised. Carcinogenic active ingredients of primary concern (>5% in two years or more) are diuron (trade names: Diuron, Acticide, Rocima, Volcano) and mancozeb (>10 formulated products and trade names, see Annex 5 for the complete list). One carcinogenic active ingredient constituted >1% of the imports in one year, dichlorvos. This a.i. is of secondary concern.

3.4.2 Mutagenicity

The annual number of active ingredients per class of mutagenic hazard is shown in Figure 25. Only very few mutagenic active ingredients are imported in Mozambique. The majority of imported a.i. is non-mutagenic and for some substances there is no information.

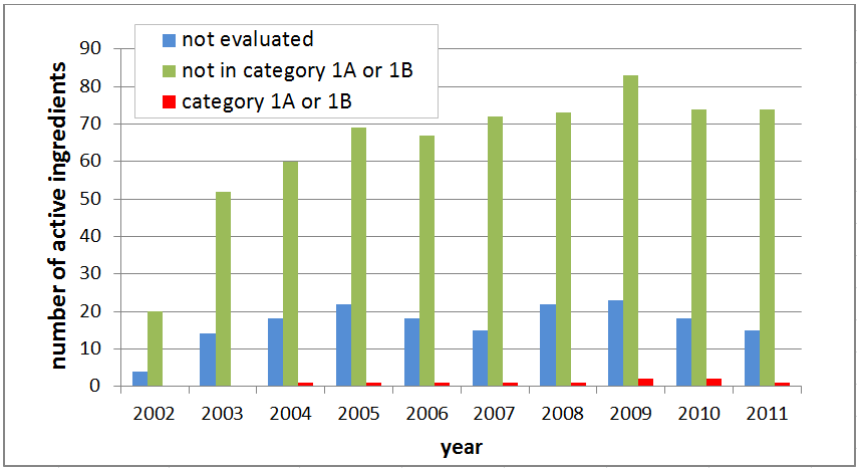

Figure 25: The annual number of imported active ingredients per class of mutagenic hazard in the period 2002-2011.

The annual imported volume of active ingredients per class of mutagenic hazard is shown in Figure 26. In terms of imported quantities, mutagenic active ingredients are almost negligible. As for the carcinogens, in 2006 and 2008 relative large volumes of active ingredients imported for which there is no information on their mutagenicity.

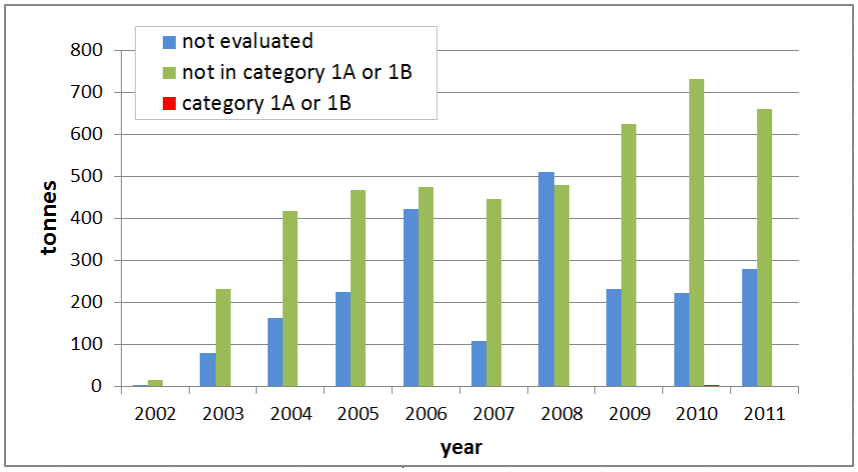

Figure 26: The annual volume of imported active ingredients per class of mutagenic hazard in the period 2002-2011 (tonnes).

In Table 2.3 in Annex 2 the mutagenic active ingredients that were imported in Mozambique are summarised. Only two active ingredients occur in this table, benomyl and carbendazim. They are not imported in Mozambique in large quantities (0.3% of total yearly imported volume or less) and are not compounds of primary or secondary concern according to the criteria used.

3.4.3 Toxicity to reproduction

The annual number of active ingredients per hazard class of reproductive toxicity is shown in Figure 27. Only very few a.i. that are toxic to reproduction are imported.

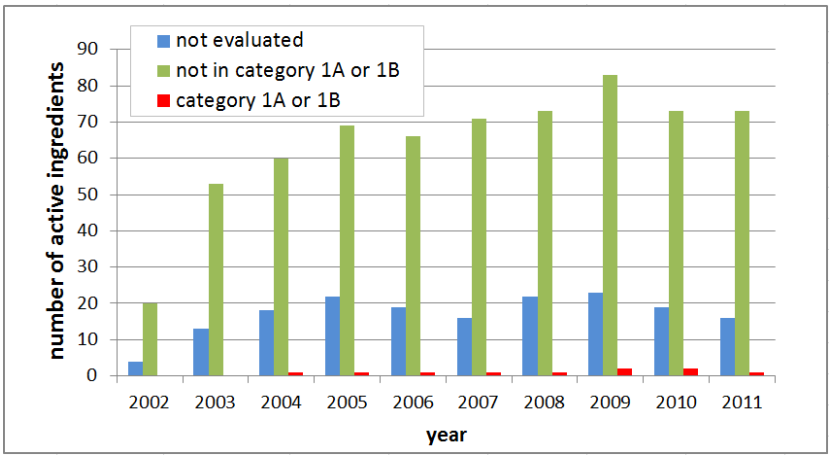

Figure 27: The annual number of imported active ingredients per hazard class of reproductive toxicity in the period 2002-2011.

The annual volume of active ingredients per hazard class of reproductive toxicity is shown in Figure 28. Again, almost no reproductively toxic a.i. are imported in Mozambique, but in 2006 and 2008 relative large volumes of active ingredients imported for which there is no information on reproductive toxicity.

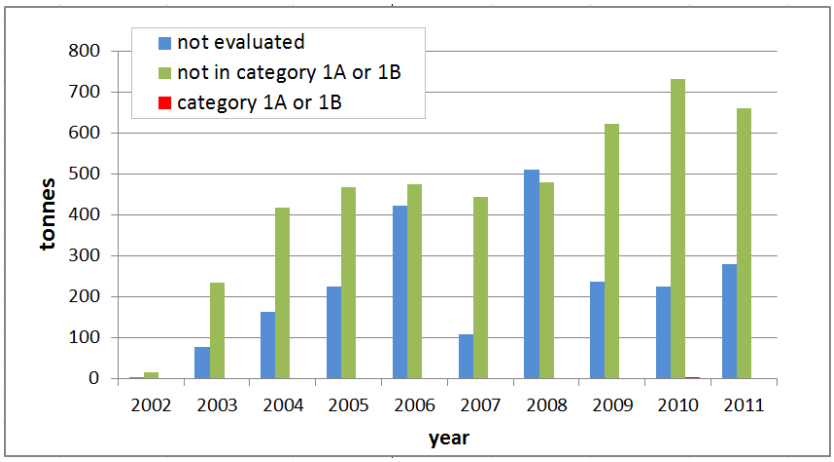

Figure 28: The annual volume of imported active ingredients per hazard class of reproductive toxicity in the period 2002-2011 (tonnes).

Table 2.4 in Annex 2 summarises the active ingredients that were imported in Mozambique and that are toxic to reproduction. The compounds in this table are the same as the mutagenic compounds (Table 2.3 in Annex 2): benomyl and carbendazim. These are not of primary or secondary concern (see §3.4.2).

3.5 Acute environmental hazard

The numbers and volumes per environmental hazard class are presented on active ingredient basis.

3.5.1 Fish

The annual number of imported active ingredients per fish toxicity class is shown in Figure 29. The graph shows that the active ingredients imported in Mozambique are relatively toxic to fish. More than half of the a.i. is moderately to highly toxic to fish and the relative numbers change little from 2002 to 2011.

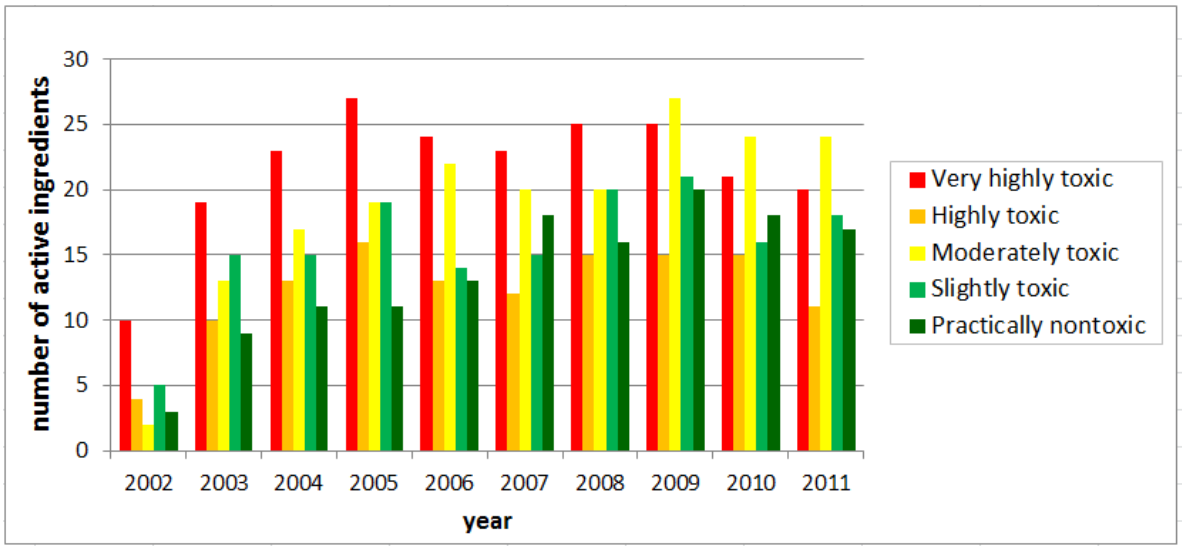

Figure 29: The annual number of imported active ingredients per fish toxicity class in the period 2002-2011.

The annual volume of active ingredients per fish toxicity class is shown in Figure 30. This image is different from Figure 29. Here, it can clearly be seen that imported volume of active ingredients that is only slightly or practically non-toxic to fish increases over the years. In 2011 more than half of the imported volume of a.i. belongs to these two classes. In 2005, 2006 and 2008 peaks can be observed for the imported volumes of a.i. that are moderately toxic to fish. These are caused by the relatively high amounts of DDT imported in Mozambique in those years.

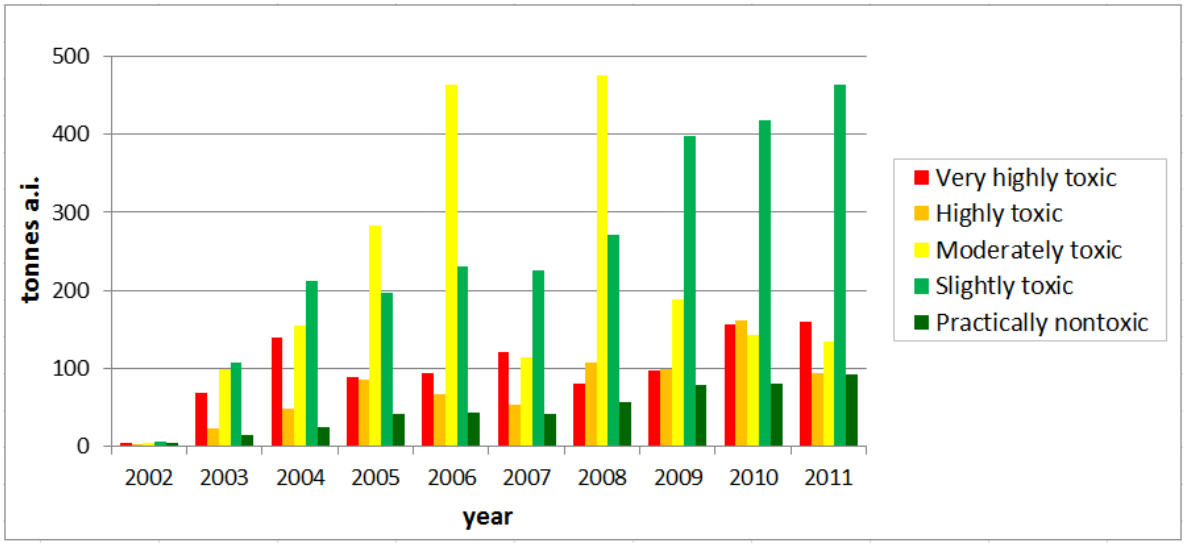

Figure 30: The annual volume of imported active ingredients per fish toxicity class in the period 2002-2011 (tonnes).

3.5.2 Aquatic invertebrates

The annual number of active ingredients per *Daphnia* toxicity class is shown in Figure 31. Many imported active ingredients are toxic to *Daphnia* and thus to aquatic invertebrates. The relative numbers of imported that are toxic change little over time.

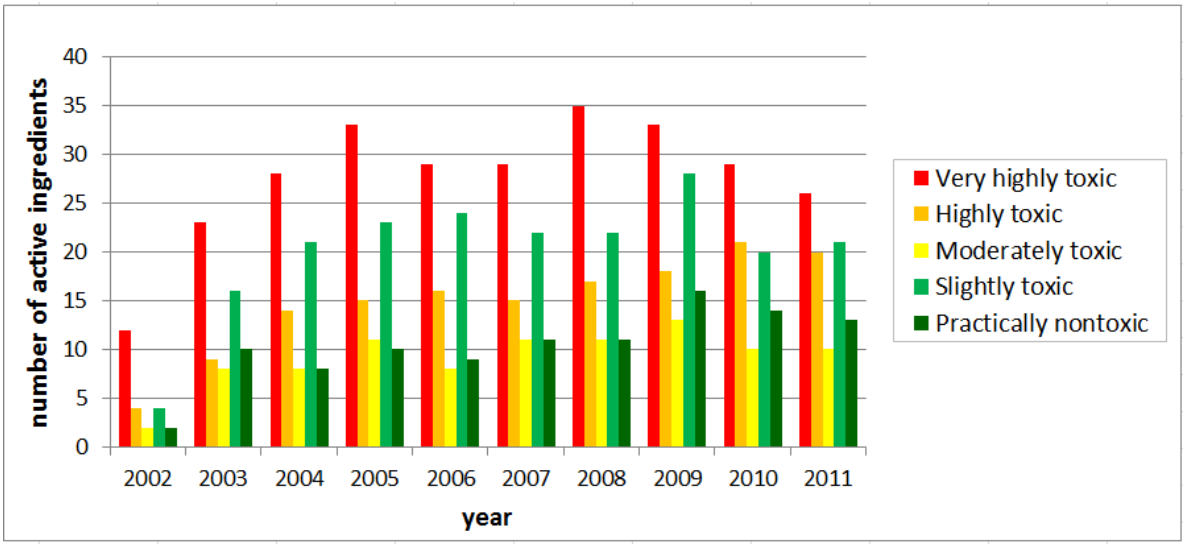

Figure 31: The annual number of imported active ingredients per *Daphnia* toxicity class in the period 2002-2011.

The annual volume of active ingredients per *Daphnia* toxicity class is shown in Figure 32. Expressed as imported volumes of a.i., the fractions highly and very highly toxic a.i. are lower, with the exception of the two familiar peaks in 2005, 2006 and 2008 (DDT). Over the years the relative imported volume of compounds that are slightly or practically non-toxic increases.

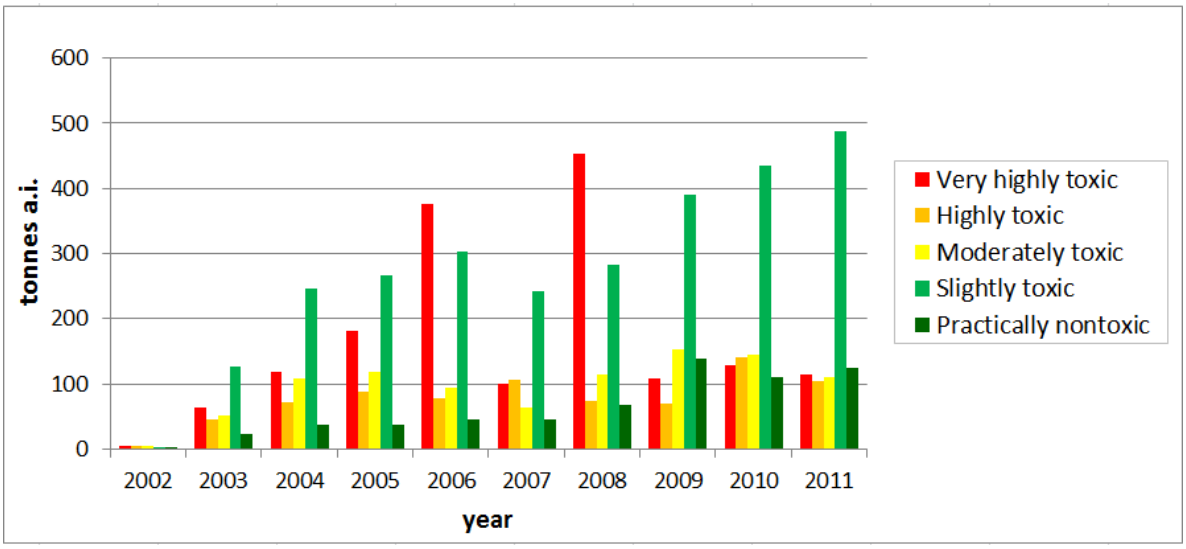

Figure 32: The annual volume of imported active ingredients per *Daphnia* toxicity class in the period 2002-2011 (tonnes).

3.5.3 Algae

The annual imported number of active ingredients per algae toxicity class is shown in Figure 33. More than half of the active ingredients imported in Mozambique are moderately, highly or very highly toxic to algae and relative numbers change little over time.

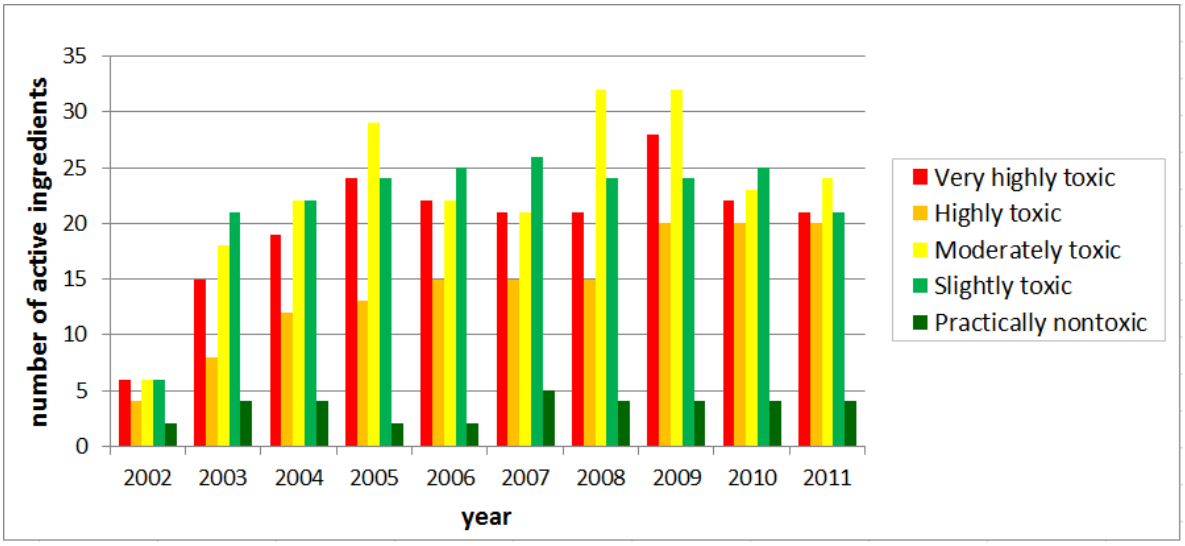

Figure 33: The annual number of imported active ingredients per algae toxicity class in the period 2002-2011.

The annual volume of active ingredients per algae toxicity class is shown in Figure 34. From 2004 to 2011 the imported volumes a.i. per class change little. The exceptions are the peaks for slightly toxic a.i. in 2005, 2008 and 2009, caused by the relatively high imports of DDT.

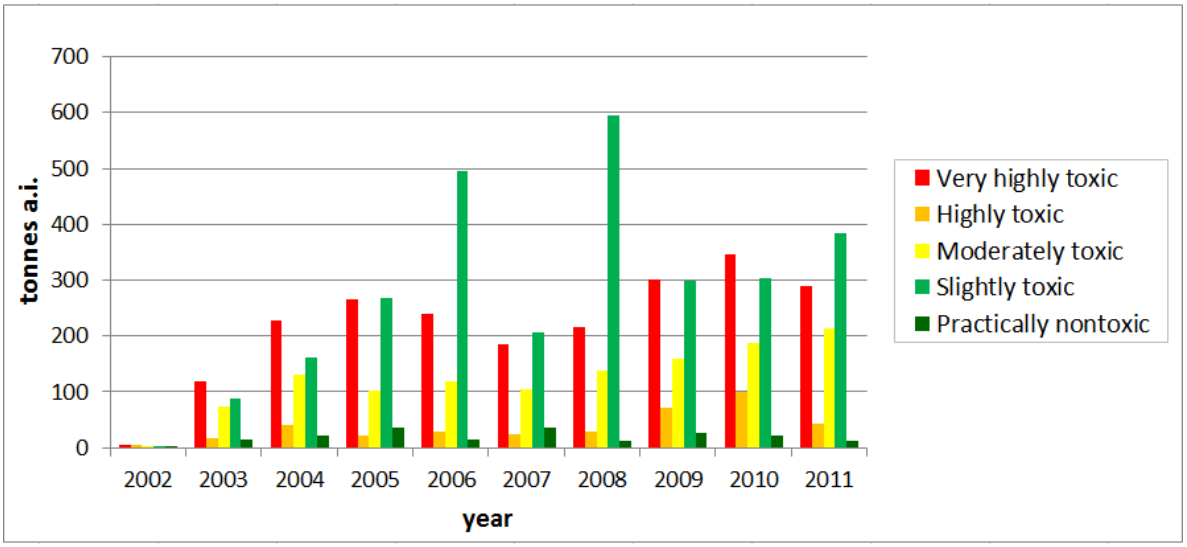

Figure 34: The annual volume of imported active ingredients per algae toxicity class in the period 2002-2011 (tonnes).

3.5.4 Bees

The annual number of active ingredients per bee toxicity class is shown in Figure 35. The relative imported numbers of a.i. that are slightly or very slightly toxic to bees is higher than for the aquatic organisms in the previous paragraphs, i.e., these two classes represent more than half of the imported a.i.

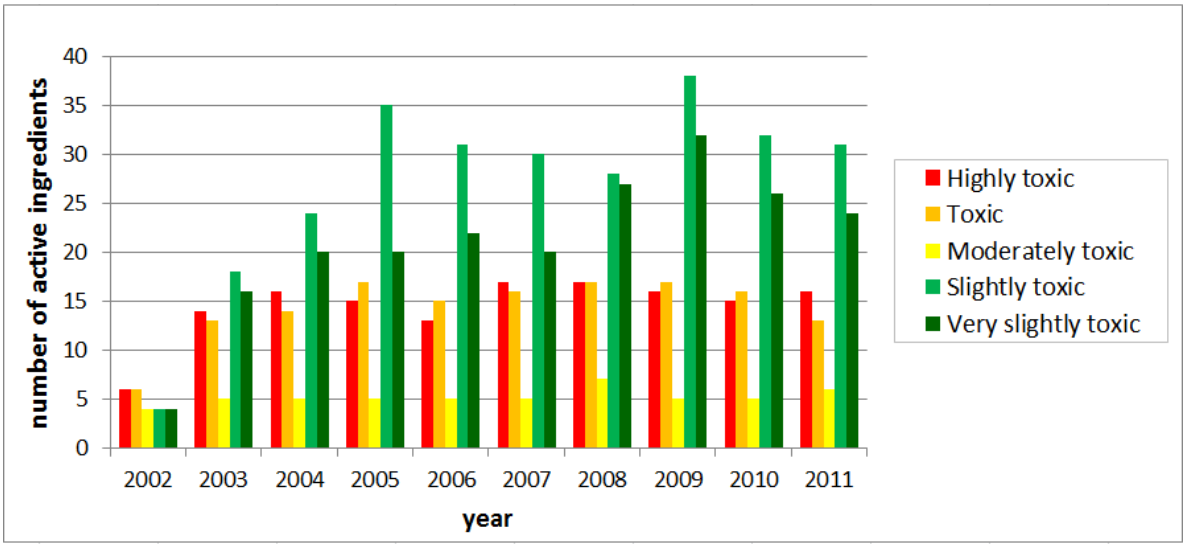

Figure 35: The annual number of imported active ingredients per bee toxicity class in the period 2002-2011.

The annual volume of active ingredients per bee toxicity class is shown in Figure 36. In terms of imported volume the a.i. that are slightly to very slightly toxic are even more represented, more than 75% in most years and increasing.

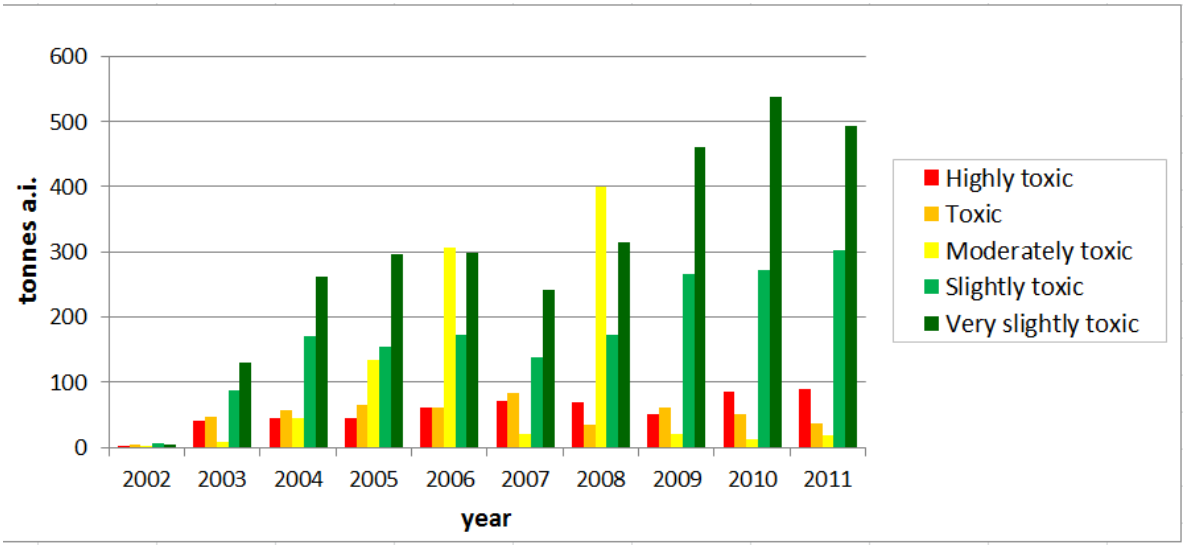

Figure 36: The annual volume of imported active ingredients per bee toxicity class in the period 2002-2011 (tonnes).

3.6 Environmental Toxic Load

The Environmental Toxic Load (ETL) indicators are calculated according to Equation 3 and presented in figures as the annual sum of all active ingredients imported. Compounds with the major contribution to the ETL are mentioned in the text. Annex 3 contains tables with the relative contributions of the 175 active ingredients to the total indicator values.

3.6.1 Fish

The annual Environmental Toxic Load for fish is shown in Figure 37. This indicator shows more changes over time than can be seen in the classification of imported numbers (Figure 29) and volumes (Figure 30) of active ingredients. The ETL for fish increases from 2002 to 2004 and peaks in 2010. In 2011 the ETL value is more than halved compared to 2010.

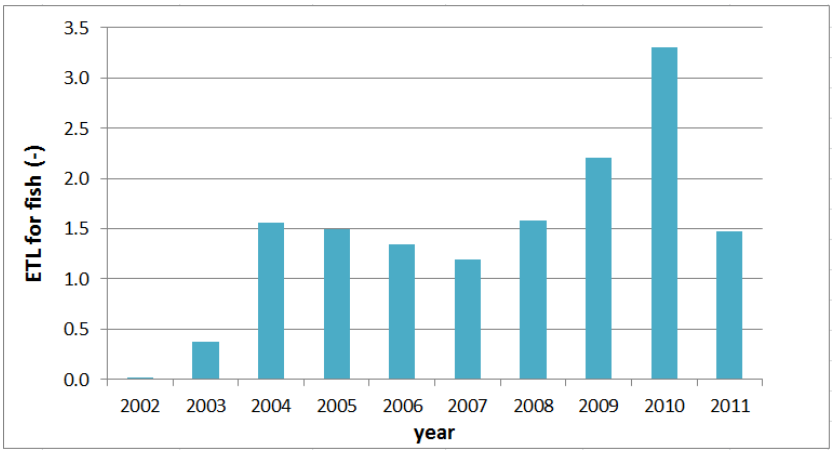

Figure 37: The annual Environmental Toxic Load for fish of active ingredients imported in Mozambique in the period 2002-2011.

Over the years one compound explains 50% or more of the total ETL for fish in more than two years (Table 3.1, Annex 3), lambda-cyhalothrin (trade names: Cyclon, Demand, Duduthrin Fortis, Icon, Iconet, Karate, Moz Lambda-cyhalothrin, Revival, Zakaka, Zakanaka, see Annex 5). It is therefore of primary concern. From 2005 to 2011 lambda-cyhalothrin was solely responsible for more than 80% of the ETL value (with the exception of 2007: 67%). The ETL peak value in 2010 is also explained by lambda-cyhalothrin. Active ingredients of secondary concern for fish are aluminium phosphide, chlorpyrifos, cyfluthrin, cypermethrin and endosulfan.

3.6.2 Aquatic invertebrates

The annual Environmental Toxic Load for the water flea *Daphnia* is shown in Figure 38. The ETL for *Daphnia* also increases initially, but from 2004 to 2011 it fluctuates between 3.0 and 7.0. It is considerably reduced in 2011 compared to 2010.

Over the years ETL values are determined by a limited number of active ingredients (Table 3.2 in Annex 3). They are mainly organophosphate compounds and synthetic pyrethroids: chlorpyrifos, cypermethrin, DDT (DDT, again, only in 2005, 2006 and 2008), dichlorvos, ethion, fenvalerate, lambda-cyhalothrin and pirimiphos-methyl. These active ingredients did not explain more than 50% of the ETL value in 2 years or more, but only >10% in one year or more. They are therefore categorised as of secondary concern for aquatic invertebrates according to the criteria set out in §2.4.

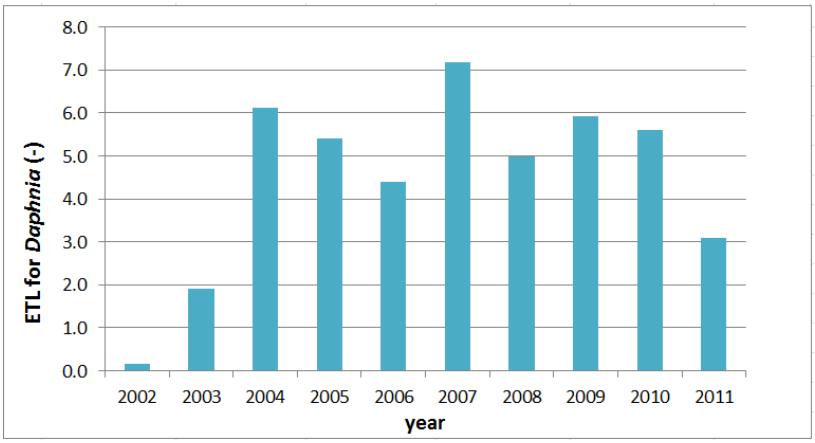

Figure 38: The annual Environmental Toxic Load for *Daphnia* of active ingredients imported in Mozambique in the period 2002-2011.

3.6.3 Algae

The annual Environmental Toxic Load for algae is shown in Figure 39. The toxic load of the imported active ingredients to algae increases from 2002 to 2005, decreases in 2006 and 2007 and increases again the following years. The pattern closely resembles the pattern observed for the total volume of pesticide products imported in Mozambique over the same period (Figure 7).

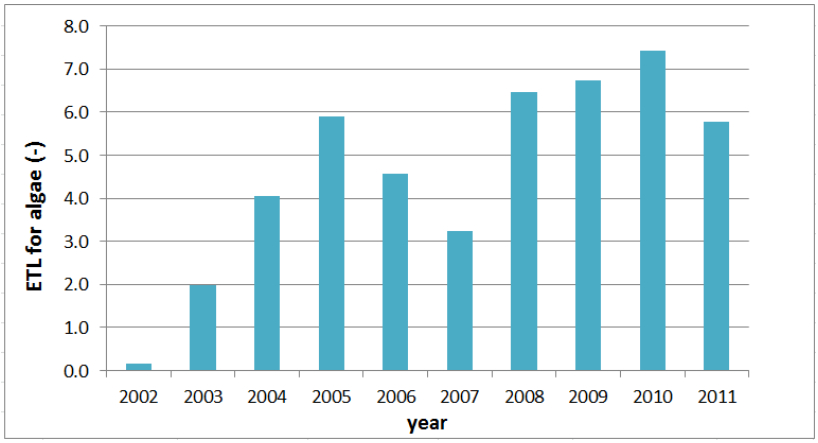

Figure 39: The annual Environmental Toxic Load for algae of active ingredients imported in Mozambique `in the period 2002-2011.

In all years, except 2002, 69% to 85% of the ETL value for algae is caused by the import of the a.i. acetochlor (Table 3.3, Annex 3). This is the only active ingredient of primary concern to algae. Trade names are Acetochlor, Bullet, Villa and Volcano (Annex 5). Paraquat contributes 5%-21% from 2003 to 2011 and 99% in 2002. The third a.i. that causes a potential hazard for algae is ametryn, which explains 4%-12% of the ETL yearly from 2003 to 2011. Both compounds represent > 10% of the ETL in more than one year and are therefore classified as of secondary concern.

3.6.4 Bees

The annual Environmental Toxic Load for bee is shown in Figure 40. The ETL increases considerably from 2002 to 2008 and then drops again. From 2009 to 2011 it remains at almost the same level of 0.07-0.08.

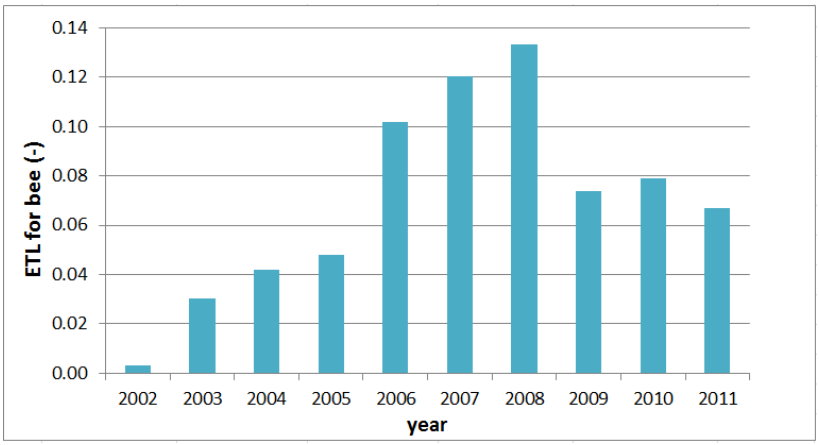

Figure 40: The annual Environmental Toxic Load for bees of active ingredients imported in Mozambique in the period 2002-2011.

The active ingredients that together determine most of the ETL values for bees vary considerably from year to year without any consistent trends in time (Table 3.4, Annex 3). One active ingredient constitutes >50% of the ETL value in more than 2 years and is of primary concern for bees, imidacloprid (trade names: Bandit, Condifor, Courag, Gaucho, Imidabiogel, Imidacel, Imidagold, Maxforce Quantum, Midaclordan, Monceren, Moz Imidacloprid, Premise, Protect, Quick Bait Spray Fly Bait, Seed Plus and Thunder, see Annex). The a.i. that are of secondary concern are bendiocarb, chlorpyrifos, cyfluthrin, cypermethrin, deltamethrin, lambda-cyhalothrin, profenofos and thiamethoxam.

3.7 Groundwater leaching potential

The calculated GUS indicator and the groundwater leaching potential class of the active ingredients in the imported products is listed Table 4.1 in Annex 4. The annual number of active ingredients per groundwater leaching potential class is shown in Figure 41. Over the whole period most imported a.i. have a low to very low leaching potential. Relative numbers in the different classes change little over time.

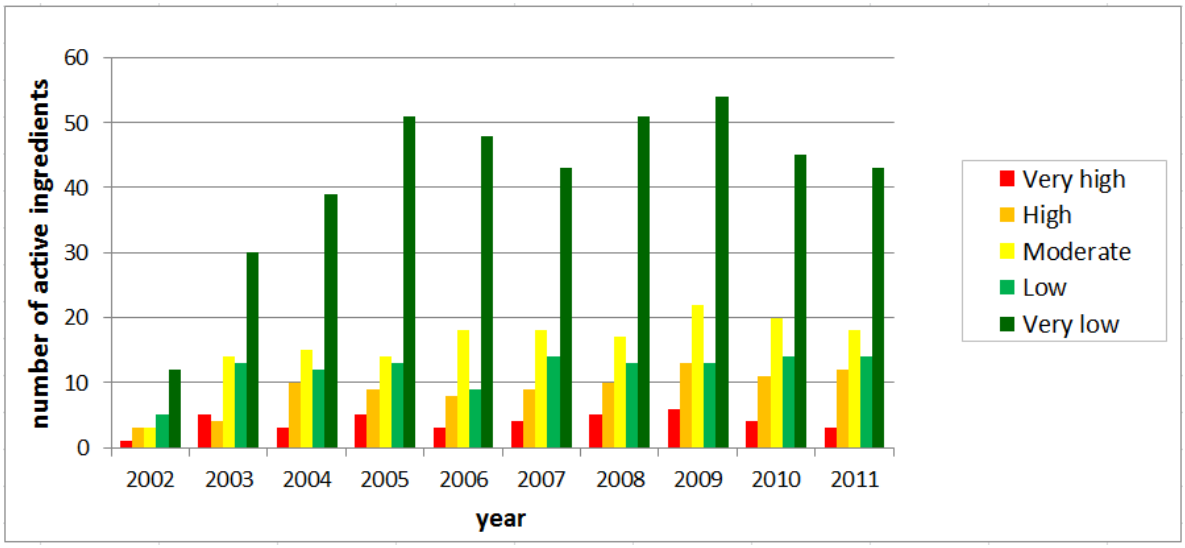

Figure 41: The annual number of imported active ingredients per groundwater leaching potential class in the period 2002-2011.

The annual volume of active ingredients per groundwater leaching potential class is shown in Figure 42. In terms of imported volume the a.i. with a moderate leaching potential are more important than in terms of imported numbers of a.i. (Figure 41), but the volumes of a.i. with a high or very high leaching potential are small. The two peaks of imported pesticides with a very low leaching potential in 2006 and 2008 are caused by DDT that strongly absorbs to particles and organic matter (GUS: -4.5).

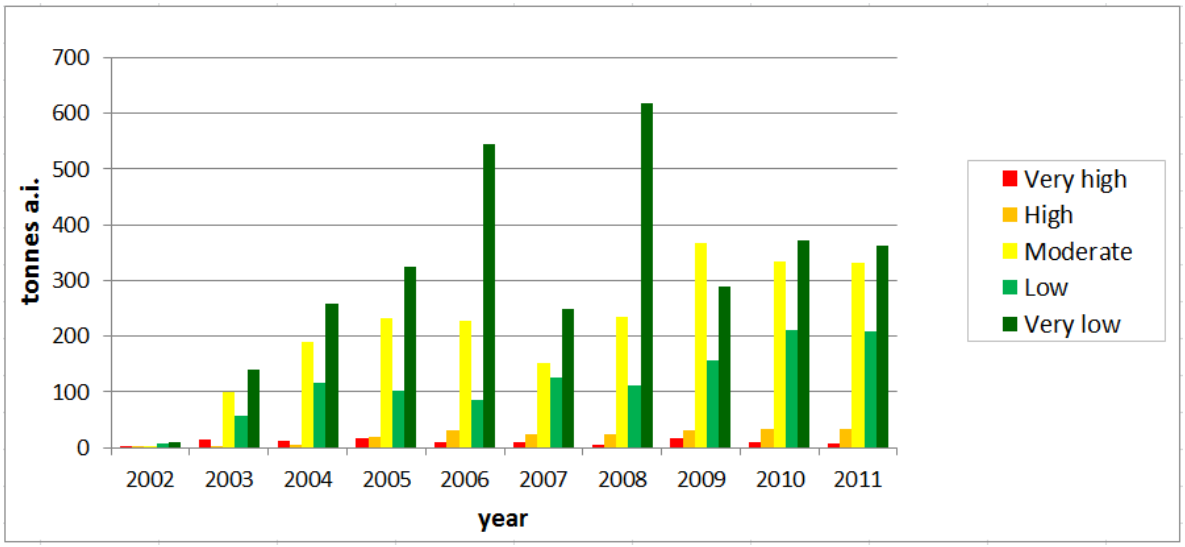

Figure 42: The annual volume of imported active ingredients per groundwater leaching potential class in the period 2002-2011 (tonnes).

The percentage of the total yearly imported volumes of active ingredients with a very high (Class 5) or high (Class 4) potential to leach to the groundwater are listed in Table 4.2 in Annex 4. Compounds of primary concern, i.e., Class 5 a.i. that constitute more than 1% of the total imported volume in two years or more, are methyl bromide (trade name: Volcano) and tebuthiuron (Volcano, Volcano Bundu). Of secondary concern are Atrazine (Class 4), Clomazone (Class 4), Hexazione (Class 5), Imidacloprid (Class 4) and Propoxur (Class 4).

4 Discussion

This chapter summarizes and discusses the main findings of the study. First the limitations of the methods are discussed. Secondly the trends in time of pesticide use, hazards and the Environmental Toxic Loads (ETLs) are analysed.[2]

4.1 Limitations and advantages of the methods

4.1.1 Use of import data

The analyses, trends and calculated indicators reported in this report are entirely based on import data. It is implicitly assumed that import data can be used as a surrogate for actual usage data when the potential hazards of formulated products and active ingredients are assessed. The assumption in that case would be that imported compounds are applied in the field in the same year that they are imported. It must be well understood that this is not the case in reality. Imported pesticide products may not be sold immediately, and if they are sold they may not be applied instantly. The actual hazards and risks of the use of the imported pesticides may well occur later and will depend on the actual use pattern, i.e., all applied within a short period or applied in portions over larger periods. We do, however, know that all imported pesticides are actually used in Mozambique and are not further exported.

There was no background information available to interpret several conspicuous observations such as the limited number of import events in the years 2002 and 2003, and for particular products, the large fluctuations of the volumes imported in subsequent years. An example is the imported volume of products based on DDT which alternately showed high import peaks in some years and absence of imported volumes in others.

Because import data were used in this report as a proxy for data on actual national use, care must be taken when interpreting and communicating the findings of the study.

4.1.2 Hazard assessments

The hazard assessments for aquatic organisms, groundwater and bees that were done during this study rank pesticides relative to each other from high to low hazard. The hazard assessments do not provide information on the actual risks in the field posed by these pesticides. Real risks to aquatic organisms, bees and groundwater depend on both the toxicity of the pesticide and the actual exposure of organisms to the pesticide. Exposure is, among other things, determined by pesticide formulation, soil properties, climate, application regimes, conditions during application, persistence of pesticides in the ecosystem, the presence and distance to surface water bodies, presence of fish and bees, buffer strips and other mitigation techniques employed, etc. These factors were not taken into account. Hazard assessments such as these, however, can be used to decide whether follow-up risk assessments are required.

The risk of judging pesticides on the basis of hazard assessment only is that farmers may be encouraged to base their choice of pesticide on only one parameter — low toxicity — without due consideration being taken into account of the overall risk, which requires the total exposure to also be considered. While, for pesticides with a low toxicity, repeated use may lead to increased exposure and therefore pose a higher risk than pesticides with a high toxicity but low rates of exposure. Therefore

[2] Parts of this discussion, especially about the methods, is the same as for the exercise that was done for pesticides used in cotton (De Blécourt et al., 2010). In these cases we have copied parts of this report and only slightly modified them (§4.1.2, §4.1.3).

drawing conclusions on hazard indicators only is not advised and it is recommended to use a simplified risk assessment method, for example PRIMET (Peeters et al., 2008).

The hazard assessments for aquatic organisms do not take into account the persistence of the compound. Highly toxic pesticides with a low persistence in the ecosystem can pose a lower risk to aquatic organisms than persistent compounds with lower toxicity. The approach could in the future be improved by including persistence and use patterns in the equation.

The hazard assessments for groundwater take into account mobility and degradation in soil, but not toxicity of the pesticides. Whether the use of a specific compound is a risk to groundwater depends on the toxicity of the compound, the distance to groundwater and the use of the groundwater. The hazard assessment for groundwater can be improved by including toxicity in the indicator.

4.1.3 Environmental Toxic Load

Environmental Toxic Load (ETL) indicators were used to evaluate the consequences of changes in pesticide use on average toxic loads to the environment. The ETL was calculated separately for fish, aquatic invertebrates (*Daphnia*), algae and bees. The ETL gives an indication of the average amount of toxic pressure applied on one (1) hectare of agricultural land in one (1) year. The ETL indicator combines the average amount of pesticides applied in the total agricultural area of the country with the toxicity of the active ingredients used. The actual exposure to the pesticide is not included in the ETL because this would require modelling. The ETL, therefore, is not an indicator of the risk associated with the use of a pesticide, or the actual impact on organisms in the field, but rather the ETL is a composed indicator for the relative hazard based on pesticide imports. For example, the active ingredient of an imported pesticide may be toxic to bees and increase the ETL value. But when it is a granular formulation and the pesticide is non-systemic, bees may never be exposed.

The ETL is used to compare average toxic loads to the environment (1) between pesticides, (2) between years and (3) in the case of the aquatic toxicity also between different groups of aquatic species (fish, water fleas and algae). As the ETL is averaged over the whole agricultural area, the ETL does not account for differences between regions where relatively high or low amounts of toxic substances are used. So even when the ETL is relatively low for a country in a given year, there could still be environmental risks in a particular area where a highly toxic active ingredient is used extensively.

4.1.4 GUS index

The GUS index has limited data needs and should be considered as a simple indicator of the groundwater leaching potential. It takes into account the persistence (degradation half-life) and mobility (sorption coefficient to soil organic carbon) of active ingredients. The leaching potential of metabolites is not considered, although some of these compounds pose greater hazards than their precursor. In addition, pH dependent sorption is not considered in the GUS. Using a combined sorption coefficient for calculating the GUS for soils with different pH, would result in a shift to a higher groundwater leaching potential class. For these reasons, the results of the analysis of the groundwater leaching potential of the imported active ingredients should be interpreted with some care.

4.1.5 Advantages of hazard analysis

In the previous paragraphs especially the limitations of the methods and indicators were discussed. However, the hazard-based method and the ETL also have certain advantages over more complex risk-based indicators. The amount of parameters needed for the analyses is limited. This is an advantage in developing countries where adequate data on pesticide use and exposure may often be very difficult to obtain. Furthermore, the methods are very suitable for trend analysis because data are analysed in a uniform way. Finally, these analyses are relatively cheap and fast. When time and budget are limiting factors their use will quickly provide some general insights which allows for a more focussed risk assessment as a follow-up.

4.2 Trends in pesticide imports

In this study trends in pesticide imports and hazards were assessed over a ten year period, from 2002 to 2011. During these years the total agricultural area of Mozambique, as reported by FAOSTAT, only very slightly increased (1.4%). Agricultural production, i.e., harvests that were reported for the various crops grown in the country, increased 40%, from 10 million tonnes in 2002 to 14 million tonnes in 2011. Because the total agricultural area only changed little during the same period, it must be concluded that on the whole agriculture in the country must have intensified.

This assumed intensification is reflected in the trend of the total volume of pesticides imported in the country. Imports were lowest in 2002, but it is not clear if the import data that were compiled for this year are complete. However, from 2003 to 2011 the imported total volume of formulated pesticides also increased considerably, from some 670 tonnes in 2003 to more than 2,500 tonnes in 2010 and 2011 (there was a temporary decrease in 2007). The number of active pesticide importers also increased over the study period, from a mere 5 in 2002 to more than 15 in 2011. The number of active importers temporarily declines around 2007, which could perhaps explain part of the reduced pesticide imports observed around the same time. Over the 10 year period one importer, Agrifocus Lda, is responsible for almost two thirds of the total imported volume of pesticide products.

The type of pesticides imported in Mozambique is very consistent over time. The majority of products consists of insecticides, followed by the herbicides and fungicides. The imported amounts of other type of pesticides such as rodenticides, nematicides, molluscicides and growth regulators is relatively small.

The trends in the imported volumes of active ingredients will be discussed in terms of their potential hazards in the following paragraphs. In general it could be observed that some older and very noxious active ingredients like methyl bromide may have been phased out already because they are not imported in later years. Other compounds keep on being used. The import data for 2005, 2006 and 2008 for example show some conspicuous peaks for DDT (Figure 13) which are repeatedly reflected by some of the human health and environmental indicators.

4.3 Human health hazard

The acute human health hazard of the pesticides imported in Mozambique was evaluated using the WHO classification for formulated pesticide products. Whereas the total volume of imported pesticides increased from 2002 to 2011, the fraction of highly hazardous products of the imported volume decreased and the fraction of products with a (very) low hazard increased. Over the period 9 active ingredients of primary concern (in Class 1b products) were imported, but mostly in rather limited quantities. Pesticide products containing aluminium phosphide were the most consistently imported Class Ib products over the 10-year period. However, some Class II products were imported in larger volumes and therefore of secondary concern. These contained active ingredients of secondary concern such as ametryn, DDT and more recently lambda-cyhalothrin.

Only few pesticide products with a known chronic hazard were imported in the country although imported volumes may still range from several tens to several hundred tonnes of the active ingredients. Compounds of primary concern are mancozeb and diuron (both carcinogenic), dichlorvos (also carcinogenic) is of secondary concern.

4.4 Environmental hazard

A considerable number of the pesticides imported into Mozambique are acutely toxic to fish, aquatic invertebrates, algae and to bees. However, the less hazardous pesticides represent a much higher volume of imports. For all four groups of species, the volume of slightly toxic or very slightly toxic active ingredients is highest. There are no clearly observable trends in time in environmental hazard of the imported products. Numbers and imported volumes for all toxicity classes increase as a

consequence of increasing imports, but there are no clear trends towards the import of more hazardous or less hazardous active ingredients in time.

The picture is somewhat different when the environmental toxic load is evaluated. This indicator corrects for the total agricultural area and cumulates the relative hazards of all imported active ingredients. All calculated ETL values increase during the first three or four years of the 10-yr. period. In other words, because more pesticides are imported per hectare of arable land, the potential environmental hazard increases (assuming that these pesticides are actually used). After this initial period the trends are slightly different.

The ETL for fish fluctuates around 1.5 from 2004 to 2008 and then suddenly increases in 2009 and 2010. In 2011 the ETL is back at c. 1.5 (Figure 37). During the first years many active ingredients that are well known to be very toxic to fish contribute to the ETL value (endosulfan, chlorpyriphos etc.). In the later years the ETL is for a very large part the result of the import of lambda-cyhalothrin (only compound classified as of primary concern). This pesticide is also responsible for the ETL peak values.

The relative hazard for aquatic invertebrates (*Daphnia*) also fluctuates but decreases in 2011 (Figure 38). The ETL usually depends on a combination of several organophosphate and synthetic pyrethroid compounds, but in changing combinations. Over the last four years, chlorpyrifos and lambda-cyhalothrin are major contributors to the hazard. DDT hazard to *Daphnia* peaks in 2006 and 2008.

The relative hazard to algae follows a trend that is similar as for *Daphnia*: an initial increase followed by a dip in 2007, an increase again and a slight decrease in 2011 (Figure 39). Acetochlor is responsible for a major part of the ETL value (of primary concern), followed by paraquat and ametryn (of secondary concern).

Because the indicators are based on a similar kind of data, The ETL values for fish, *Daphnia* and algae can be compared among each other. The ETL values for *Daphnia* and algae are of the same order of magnitude, i.e., 3-7 from 2004 to 2011. The value for fish is more than two times lower, c. 1-3 in the same years. These observations may be explained by the fact that more insecticides than herbicides are imported in Mozambique and that in general insecticides are more toxic to aquatic invertebrates than to fish, and that herbicides are more toxic to algae than to aquatic invertebrates or fish.

The ETL for bees, and thus the relative hazard of the imported pesticides, increases steadily from 2002 to 2006 before dropping to half the peak value in 2009. From 2009 to 2011 it stays at the same level (Figure 40). The ETL is the result of a suite of different insecticides, among which imidacloprid figures most prominently (of primary concern).

The groundwater leaching potential of the active ingredients imported in Mozambique is not very high. The hazard of the majority of the imported a.i. is classified as moderate to very low. The a.i. with the highest leaching potential are methyl bromide and tebuthiuron (of primary concern).

5 Conclusions

The most significant observations according to this study are:

- The volume of pesticides imported increased almost threefold, from 670 tonnes in 2003 to 2592 tons in 2011. Agricultural production increased by 40 % from 9.9 million tonnes in 2002 to 13,9 million tonnes in 2011, whereas the agricultural area increased only by 1.4%;
- The types of pesticides imported in the country are very consistent over time. The majority of products consists of insecticides, followed by the herbicides and fungicides;
- The volume of highly hazardous products imported over time decreased and the volume of products with a (very) low hazard increased;
- Only few pesticide products with a known chronic hazard to human health were imported in the country, although carcinogenic products were imported at the rate of 100 tons per year;
- A considerable number of the pesticides imported into the country are acutely toxic to fish, aquatic invertebrates, algae and bees. However, the less hazardous pesticides represent a much higher volume of imports;
- The Environmental Toxic Load (ETL) (relative hazard corrected for surface of agricultural area) to aquatic organisms (fish, aquatic invertebrates and algae) increases from 2002 to 2010, but decreases for all three groups of species in 2011;
- Overall, the hazard of the imported pesticides is more than two times higher to aquatic invertebrates and algae than to fish;
- The ETL to bees also increases from 2002 to 2008, but is considerably lower from 2009 to 2011;
- Only few active ingredients with a very high or high leaching potential are imported in the country.

The pesticides that contributed most to the overall human health hazards and environmental hazards are given in Table 6. Active ingredients of primary or secondary concern were identified the criteria set out in §2.4. These criteria combine both potential hazard of the pesticides and imported quantities in Mozambique. Annex 5 provides the volumes of the all formulated pesticides imported in Mozambique that contain active ingredients of primary concern for all years of the period 2002-2011. These tables may be used for specific hazard reducing measures. Such tables may also be generated for pesticides of secondary concern or for any other pesticide of interest using the pivot table that is provided with the revised spreadsheet containing the Pesticide Import data.

Three things must be noted in respect to this Table: 1) pesticides with a low toxicity and a high environmental persistence are not considered. Such pesticides may even represent a bigger threat to the environment than highly toxic pesticides with a low environmental persistence; 2) the Environmental Toxic Loads are based on import data and do not account for any regional variations in use, e.g. extensive use of highly toxic pesticides in a particular area; 3) none of the classifications of pesticide active ingredients as of primary or secondary concern was based on estimated properties (see §2.1.2).

One final and general recommendation is that records of pesticide import volumes and relevant properties, including the active ingredients, can be analysed much more efficiently when the data are organised in a database environment. A database structure is needed in order to define the relations between products and compounds, and to maintain the integrity of the data that will be entered. If similar exercises are planned for Mozambique or other countries in the future, designing and setting up such a database would proof a very fruitful investment.

Table 6: Pesticides imported in Mozambique from 2002 to 2011 that are of concern in terms of potential human health and environmental hazard and annually imported quantity (for criteria, see §2.4).

Type of hazard	Pesticide active ingredient of primary concern	Pesticide active ingredient of secondary concern
Human health		
Acute (WHO classification)	Class I pesticide products containing: Abamectin Aldicarb Aluminium phoshide Fenamiphos Methomyl Mevinphos Monocrotophos Oxamyl Terbufos	Class II pesticide products containing: Ametryn DDT Lambda-cyhalothrin
Chronic	Diuron (carcinogenic) Mancozeb (carcinogenic)	Dichlorvos (carcinogenic)
Environment		
Fish	Lambda-cyhalothrin	Aluminium phoshide Chlorpyrifos Cyfluthrin Cypermethrin Endosulfan
Aquatic invertebrates	-	Chlorpyrifos Cypermethrin DDT Dichlorvos Ethion Fenvalerate Lambda-cyhalothrin Pirimiphos-methyl
Algae	Acetochlor	Ametryn Paraquat
Bees	Imidacloprid	Bendiocarb Chlorpyrifos Cyfluthrin Cypermethrin Deltamethrin Lambda-cyhalothrin Profenofos Thiamethoxam
Leaching to groundwater	Methyl bromide Tebuthiuron	Atrazine Clomazone Hexazione Imidacloprid Propoxur

References & sources

Gustafson, D. I., 1989. Groundwater Ubiquity Score: a simple method for assessing pesticide leachability. *Environmental Toxicology and Chemistry* 8: 339-357.

De Blécourt, M., J. Lahr & P.J. van den Brink, 2010. Pesticide use in cotton in Australia, Brazil, India, Turkey and USA. SEEP documents, ICAC, 144 pp. Available from: http://www.icac.org/seep/documents/reports/2010_alterra_report.pdf

FAO, FAOSTAT, http://faostat3.fao.org/; accessed on July 1, 2013.

GHS, 2008. Globally Harmonized System of Classification and labelling of chemicals; Part 3 Health Hazards. United Nations. Retrieved, October 2009, from: http://www.unece.org/trans/danger/publi/ghs/ghs_rev02/02files_e.html

Kruijne, R., J. Deneer, J. Lahr & J. Vlaming, 2011. HAIR2010 Documentation. Calculating risk indicators related to agricultural use of pesticides within the European Union. Report nr. 2113.1, Alterra, Wageningen UR, Wageningen, 202 pp. Available from: http://www.hair.pesticidemodels.eu/documentation/HAIR2010%20Documentation.pdf

Mensink B.J.W.G., M. Montforts, L. Wijkhuizen-Maslankiewicz, H. Tibosch & J.B.H.J. Linders. 1995. Manual for summarizing and evaluating the environmental aspects of plant protection products. Report no. 679101022. RIVM, Bilthoven, The Netherlands.

Peeters, F.M., P.J. van den Brink, J. Vlaming, J.G. Groenwold, W.H.J. Beltman & J.J.T.I. Boesten, 2008. PRIMET version 2.0, technical description and manual. A decision support system for assessing Pesticide RIsks in the tropics to Man, Environment and Trade. Alterra report no. 1648, Alterra, Wageningen UR, Wageningen. Available from: http://www.primet.wur.nl/documentation.shtml.

PPDB, 2009. The Pesticide Properties Database (PPDB) developed by the Agriculture & Environment Research Unit (AERU), University of Hertfordshire, funded by UK national sources and the EU-funded FOOTPRINT project (FP6-SSP-022704). Retrieved June, 2009 from http://www.eu-footprint.org/ppdb.html.

US-EPA. The ECOTOX (ECOTOXicology) database provides single chemical toxicity information for aquatic and terrestrial life. Retrieved June, 2009, from http://cfpub.epa.gov/ecotox/.

US-EPA. Technical Overview of Ecological Risk Assessment: Ecotoxicity Categories for Terrestrial and Aquatic Organisms. Retrieved July, 2009, from http://www.epa.gov/oppefed1/ecorisk_ders/toera_analysis_eco.htm.

WHO, 2010. The WHO Recommended Classification of Pesticides by Hazard and Guidelines to Classification 2009, World Health Organization, Geneva, 81 pp.

Annexes

1. Compound properties
2. Hazard to human health
3. Environmental toxic load
4. Groundwater leaching

Annex 1: Compound properties

Compound properties
Tables with the properties of the active ingredients in the imported products, 2002-2011;

1. Sources
2. Fate
3. Toxicity

Table 1.1: Source of fate and toxicity properties of the 175 active ingredients in the imported products, 2002-2011.

Source	Code (Table 2, 3)	DegT50	Koc	EC50 algae	EC50 Daphnia	EC50 fish	LD50 bee	LD50 rat
FootPrint	FP	54	138	131	145	143	135	55
FAO HHP	HHP	33						95
NMI 3	NMI	57						
Alterra ERA	ERA		1	1		1		
Mean value chemical class	CC	13	11	21	19	13	16	15
Mean value product group	PG	18	25	22	11	18	24	10

Table 1.2: Fate properties of the 175 active ingredients in the imported products, 2002-2011.

Nr.	Cas-Nr.	CompoundName	Chemical class	Product group	DegT50 (d)	source	Koc (L/kg)	source
1	94-75-7	2,4-D	aryloxyalkanoic acid	herbicide	16	NMI	88.4	FP
2	2008-39-1	2,4-D dimethylamine	aryloxyalkanoic acid	herbicide	19	CC	81.2	CC
3	71751-41-2	Abamectin	avermectin	insecticide	29	NMI	14000	FP
4	30560-19-1	Acephate	organophosphate	insecticide	3	HHP	302	FP
5	135410-20-7	Acetamiprid	neonicotinoid	insecticide	3	FP	200	FP
6	-999	Acetic acid + ammonia	organic acid	herbicide	160	PG	24379	PG
7	34256-82-1	Acetochlor	chloroacetamide	herbicide	14	FP	156	FP
8	15972-60-8	Alachlor	chloroacetamide	herbicide	14	FP	335	FP
9	116-06-3	Aldicarb	carbamate	insecticide	5	NMI	36	FP
10	67375-30-8	Alpha-cypermethrin	pyrethroid	insecticide	35	FP	57889	FP
11	20859-73-9	Aluminium phosphide	inorganic compound	insecticide	0	FP	2701	CC
12	834-12-8	Ametryn	triazine	herbicide	37	HHP	316	FP
13	129909-90-6	Amicarbazone	triazolinone	herbicide	21	FP	51.7	FP
14	33089-61-1	Amitraz	amidine	insecticide	0	HHP	1000	FP
15	1912-24-9	Atrazine	triazine	herbicide	58	NMI	100	FP
16	131860-33-8	Azoxystrobin	strobilurin	fungicide	94	NMI	589	FP
18	68038-71-1	Bacillus thuringiensis	biopesticide	insecticide	19	CC	191989	PG
19	22781-23-3	Bendiocarb	carbamate	insecticide	4	FP	385	FP
20	17804-35-2	Benomyl	benzimidazole	fungicide	0	NMI	1900	FP
21	83055-99-6	Bensulfuron-methyl	sulfonylurea	herbicide	24	FP	370	FP
22	25057-89-0	Bentazone	benzothiazinone	herbicide	37	NMI	55.3	FP
23	68359-37-5	Beta-cyfluthrin	pyrethroid	insecticide	13	FP	64300	FP
24	56073-10-0	Brodifacoum	hydrocoumarin	other	157	HHP	86200	FP
25	314-40-9	Bromacil	uracil	herbicide	60	FP	32	FP
26	1689-99-2	Bromoxynil octanoate	hydroxybenzonitrile	herbicide	1	FP	639	FP
27	41483-43-6	Bupirimate	pyrimidinol	fungicide	151	NMI	767	FP

28	33629-47-9	Butralin	dinitroaniline	herbicide	22	FP	46391	FP
29	133-06-2	Captan	phthalimide	fungicide	1	NMI	200	FP
30	63-25-2	Carbaryl	carbamate	insecticide	16	FP	300	FP
31	10605-21-7	Carbendazim	benzimidazole	fungicide	71	NMI	400	FP
32	1563-66-2	Carbofuran	carbamate	insecticide	17	NMI	22	FP
33	55285-14-8	Carbosulfan	carbamate	insecticide	21	FP	9489	FP
34	5234-68-4	Carboxin	oxathiin	fungicide	0	FP	99.4	FP
35	470-90-6	Chlorfenvinphos	organophosphate	insecticide	62	NMI	680	FP
36	99283-00-8	Chlorimuron	sulfonylurea	herbicide	17	CC	205	CC
37	1897-45-6	Chlorothalonil	chloronitrile	fungicide	14	NMI	850	FP
38	2921-88-2	Chlorpyrifos	organophosphate	insecticide	50	FP	8151	FP
39	5598-13-0	Chlorpyrifos-methyl	organophosphate	insecticide	81	NMI	4645	FP
40	8000-29-1	Citronella oil	unclassified	other	136	PG	7721846	PG
41	81777-89-1	Clomazone	isoxazolidinone	herbicide	111	NMI	300	FP
42	13822-80-5	Copper ammonium acetate	inorganic compound	fungicide	4402	CC	4657	CC
43	20427-59-2	Copper hydroxide	inorganic compound	fungicide	10000	HHP	12000	FP
44	1317-39-1	Copper oxide	inorganic compound	fungicide	10000	HHP	2701	CC
45	1332-40-7	Copper oxychloride	inorganic compound	fungicide	10000	HHP	4657	CC
46	101205-02-1	Cycloxydim	cyclohexanedione oxime	herbicide	1	NMI	59	FP
47	68359-37-5	Cyfluthrin	pyrethroid	insecticide	0	NMI	123930	FP
48	57966-95-7	cymoxanil	cyanoacetamide oxime	fungicide	1	NMI	145	FP
49	52315-07-8	Cypermethrin	pyrethroid	insecticide	60	FP	156250	FP
50	66215-27-8	Cyromazine	triazine	insecticide	32	NMI	765	FP
51	584-79-2	D-allethrin	pyrethroid	insecticide	60	HHP	2414	FP
52	533-74-4	Dazomet	dithiocarbamate	other	0	NMI	10	FP
53	50-29-3	DDT	organochlorine	insecticide	6200	FP	260324	FP
54	11-30-1	Decanol	organic alcohol	other	136	PG	7721846	PG
55	52918-63-5	Deltamethrin	pyrethroid	insecticide	30	HHP	1.0E+07	FP
56	333-41-5	Diazinon	organophosphate	insecticide	49	NMI	609	FP
57	62-73-7	Dichlorvos	organophosphate	insecticide	2	NMI	50	FP

58	7173-51-5	Didecyldimethylammonium chloride	quaternary ammonium compound	fungicide	1495	PG	1469081	ERA
59	134-62-3	Diethyltoluamide	benzamide	other	136	PG	478	FP
60	119446-68-3	Difenoconazole	triazole	insecticide	109	NMI	3760	FP
61	104653-34-1	Difethialone	coumarin anticoagulant	other	635	FP	54000000	FP
62	35367-38-5	Diflubenzuron	benzoylurea	insecticide	12	NMI	10000	FP
63	60-51-5	Dimethoate	organophosphate	insecticide	8	NMI	30.1	FP
64	330-54-1	Diuron	urea	herbicide	81	NMI	813	FP
65	115-29-7	Endosulfan	organochlorine	insecticide	50	FP	11500	FP
66	106325-08-0/133855-98-8	Epoxiconazole	triazole	fungicide	314	NMI	1802	FP
67	16672-87-0	Ethephon	ethylene generator	other	16	FP	2540	FP
68	563-12-2	Ethion	organophosphate	insecticide	90	FP	17240	FP
69	52304-36-6	Ethylbutylacetylaminopropionate	organic ester	other	136	PG	7721846	PG
70	106-93-4	Ethylene dibromide	brominated alkene	other	136	PG	7721846	PG
71	75-21-8	Ethylene oxide	organic epoxide	other	136	PG	7721846	PG
72	22224-92-6	Fenamiphos	organophosphate	insecticide	1	FP	100	FP
73	13356-08-6	Fenbutatin oxide	organotin	insecticide	95	HHP	183550	FP
74	122-14-5	Fenitrothion	organophosphate	insecticide	21	NMI	2000	FP
75	39515-41-8/64257-84-7	Fenpropathrin	pyrethroid	insecticide	28	HHP	5000	FP
76	55-38-9	Fenthion	organophosphate	insecticide	34	HHP	1500	FP
77	51630-58-1	Fenvalerate	pyrethroid	insecticide	35	HHP	5273	FP
78	120068-37-3	Fipronil	phenylpyrazole	insecticide	142	FP	577	FP
80	79241-46-6	Fluazifop-P-butyl	aryloxyphenoxypropionate	herbicide	3	NMI	3394	FP
81	69770-45-2	Flumethrin	pyrethroid	insecticide	26	CC	853297	CC
82	2164-17-2	Fluometuron	unclassified	herbicide	160	PG	24379	PG
83	69377-81-7	fluroxypyr	pyridine compound	herbicide	111	NMI	24600	FP
84	50-00-0	Formaldehyde	organic aldehyde	other	6	FP	37	FP
85	98-01-1	Furfural	heterocyclic aldehyde	other	1	FP	94.82	FP
86	1071-83-6	Glyphosate	glycine derivative	herbicide	17	NMI	1435	FP
87	135397-30-7	Halosulfuron	pyrimidinylsulfonylurea	herbicide	247	HHP	14141	PG
88	100784-20-1	Halosulfuron-methyl	pyrimidinylsulfonylurea	herbicide	14	HHP	109	FP

89	79983-71-4	Hexaconazole	triazole	fungicide	225	HHP	1040	FP
90	51235-04-2	Hexazinone	triazinone	herbicide	105	FP	54	FP
91	67485-29-4	Hydramethylnon	trifluoromethyl aminohydrazone	insecticide	7	HHP	730000	FP
92	104098-48-8	Imazapic	imidazolinone	herbicide	120	FP	137	FP
93	81334-34-1	Imazapyr	imidazolinone	herbicide	11	FP	125	FP
94	138261-41-3	Imidacloprid	neonicotinoid	insecticide	169	NMI	189	FP
95	72963-72-5	Imiprothrin	pyrethroid	insecticide	5	FP	402	FP
96	173584-44-6	Indoxacarb	oxadiazine	insecticide	17	NMI	6450	FP
97	141112-29-0	Isoxaflutole	isoxazole	insecticide	2	NMI	145	FP
98	91465-08-6	Lambda-cyhalothrin	pyrethroid	insecticide	25	FP	157000	FP
99	330-55-2	Linuron	urea	herbicide	47	NMI	739	FP
100	103055-07-8	Lufenuron	benzoylurea	insecticide	16	FP	41182	FP
101	121-75-5	Malathion	organophosphate	insecticide	1	HHP	1800	FP
102	8018-01-7	Mancozeb	dithiocarbamate	fungicide	18	HHP	998	FP
103	94-74-6	MCPA	aryloxyalkanoic acid	herbicide	22	NMI	74	FP
104	104206-82-8	Mesotrione	triketone	herbicide	16	NMI	122	FP
105	57837-19-1	Metalaxyl	phenylamide	fungicide	70	HHP	165	FP
106	70630-17-0	Metalaxyl-M	phenylamide	fungicide	216	NMI	660	FP
107	108-62-3	Metaldehyde	cyclo-octane	insecticide	8	NMI	240	FP
109	10265-92-6	Methamidophos	organophosphate	insecticide	2	NMI	1	FP
110	2032-65-7	Methiocarb	carbamate	insecticide	35	HHP	660	FP
111	16752-77-5	Methomyl	carbamate	insecticide	30	HHP	72	FP
112	74-83-9	Methyl bromide	inorganic compound	insecticide	55	FP	22	FP
113	2682-20-4	Methyl isothiazolin one	isothiozolinones	other	136	PG	7721846	PG
114	26172-55-4	Methylchoroisothiazolinone	isothiozolinones	other	136	PG	7721846	PG
115	51218-45-2	Metolachlor	chloroacetamide	herbicide	32	NMI	120	FP
116	21087-64-9	Metribuzin	triazinone	herbicide	12	FP	37.9	FP
117	74223-64-6	Metsulfuron-methyl	sulfonylurea	herbicide	10	FP	39.5	FP
118	7786-34-7	Mevinphos	organophosphate	insecticide	0	NMI	44	FP
119	-999	Mineral oil	unclassified	insecticide	132	PG	191989	PG

120	2212-67-1	Molinate	thiocarbamate	herbicide	12	HHP	190	FP
121	6923-22-4	Monocrotophos	organophosphate	insecticide	7	FP	32.8	FP
122	2163-80-6	Monosodium methyl arsenate	arsenate	herbicide	200	HHP	24379	PG
123	25154-52-3	Nonylphenol	alkylphenol	other	136	PG	7721846	PG
124	1003-07-2	Octylisothiazolinone	isothiozolinones	other	136	PG	7721846	PG
125	19666-30-9	Oxadiazon	oxidiazole	herbicide	502	FP	3200	FP
126	23135-22-0	Oxamyl	carbamate	insecticide	12	NMI	16.6	FP
127	42874-03-3	Oxyfluorfen	diphenyl ether	herbicide	35	FP	17636	FP
128	4685-14-7	Paraquat	bipyridylium	herbicide	2800	HHP	1000000	FP
129	66063-05-6	pencycuron	phenylurea	insecticide	32	HHP	6207	FP
130	40487-42-1	Pendimethalin	dinitroaniline	herbicide	90	FP	17581	FP
131	52645-53-1	Permethrin	pyrethroid	insecticide	42	HHP	100000	FP
132	26002-80-2	phenothrin	pyrethroid	insecticide	1	FP	310320	FP
133	13598-36-2	Phosphoric acid	inorganic compound	other	4402	CC	4657	CC
134	1918-02-1	Picloram	pyridine compound	herbicide	83	FP	13	FP
135	8002-09-3	Pine oil	biopesticide	herbicide	19	CC	24379	PG
136	51-03-6	Piperonyl butoxide	unclassified	insecticide	13	HHP	89125	FP
137	29232-93-7	Pirimiphos methyl	organophosphate	insecticide	22	NMI	1100	FP
138	23031-36-9	Prallethrin	pyrethroid	insecticide	26	CC	853297.5	CC
139	41198-08-7	Profenofos	organophosphate	insecticide	7	HHP	3476	FP
140	7287-19-6	Prometryn	triazine	herbicide	60	HHP	400	FP
141	709-98-8	Propanil	anilide	herbicide	0	FP	152	FP
142	2312-35-8	Propargite	sulfite ester	insecticide	56	FP	56500	FP
143	12071-83-9/9016-72-2	Propineb	dithiocarbamate	fungicide	3	FP	18	FP
144	114-26-1	Propoxur	carbamate	insecticide	35	NMI	51.72	FP
145	8003-34-7	Pyrethrins	unclassified	insecticide	132	PG	191989	PG
146	84087-01-4	Quinclorac	quinolinecarboxylic acid	herbicide	450	FP	50	FP
147	119738-06-6	Quizalofop-P-tefuryl	aryloxyphenoxypropionate	herbicide	0	FP	477	FP
150	87392-12-9/178961-20-1	S-Metolachlor	chloroacetamide	herbicide	20	NMI	2261	FP
151	168316-95-8	Spinosad	biopesticide	insecticide	31	NMI	34600	FP

152	99105-77-8	Sulcotrione	triketone	herbicide	12	NMI	36	FP
153	122836-35-5	Sulfentrazone	aryl triazolinone	herbicide	541	FP	43	FP
154	7704-34-9	Sulphur	inorganic compound	fungicide	30	FP	1950	FP
155	107534-96-3	Tebuconazole	triazole	herbicide	95	NMI	1554	FP
156	34014-18-1	Tebuthiuron	urea	herbicide	1300	HHP	80	FP
157	13071-79-9	Terbufos	organophosphate	insecticide	12	HHP	500	FP
158	5915-41-3	terbuthylazine	triazine	herbicide	105	NMI	220	FP
159	886-50-0	Terbutryn	triazine	herbicide	43	NMI	2432	FP
160	116-29-0	Tetradifon	bridged diphenyl	insecticide	112	FP	100	FP
161	7696-12-0	Tetramethrin	pyrethroid	insecticide	3	HHP	1423	FP
162	153719-23-4	Thiamethoxam	neonicotinoid	insecticide	53	NMI	56.2	FP
163	137-26-8	Thiram	dimethyldithiocarbamate	insecticide	6	NMI	670	FP
164	118712-89-3	Transfluthrin	unclassified	insecticide	132	PG	111362	PG
165	43121-43-3	Triadimefon	triazole	fungicide	26	FP	300	FP
166	55219-65-3	Triadimenol	triazole	fungicide	159	NMI	750	FP
167	52-68-6	Trichlorfon	organophosphate	insecticide	1	NMI	10	FP
170	55335-06-3	Triclopyr	pyridine compound	herbicide	35	NMI	27	FP
171	-999	Tricozene	unclassified	other	136	PG	7721846	PG
172	141517-21-7	Trifloxystrobin	strobilurin	fungicide	1	NMI	2377	FP
173	1582-09-8	Trifluralin	dinitroaniline	herbicide	181	FP	15800	FP
174	-999	Trifluthrin	pyrethroid	insecticide	26	CC	853297	CC
175	-999	Violeta Genciana	unclassified	insecticide	132	PG	191989	PG

Table 1.3: Toxicity of the 175 active ingredients in the imported products, 2002-2011.

Nr.	Compound Name	LD50 rat (mg)	source	LC50 fish (mg/L)	source	EC50 daphnia (mg/L)	source	EC50 algae (mg/L)	source	LD50 bee (µg/bee)	source
1	2,4-D	469	FP	63.4	FP	100	FP	24.2	FP	94	FP
2	2,4-D dimethylamine	585	CC	56.7	CC	145	CC	52	CC	147	CC
3	Abamectin	8.7	HHP	0.0036	FP	0.0001	FP	1.59	FP	0.0022	FP
4	Acephate	945	HHP	110	FP	67.2	FP	980	FP	1.2	FP
5	Acetamiprid	213	HHP	100	FP	49.8	FP	98.3	FP	8.09	FP
6	Acetic acid + ammonia	2782	PG	51.8	PG	92.4	PG	14.0	PG	88.6	PG
7	Acetochlor	2950	HHP	0.36	FP	8.6	FP	0.00027	FP	100	FP
8	Alachlor	930	HHP	1.8	FP	10	FP	0.966	FP	16	FP
9	Aldicarb	0.93	HHP	0.56	FP	0.42	FP	50	FP	0.09	FP
10	Alpha-cypermethrin	79	HHP	0.0028	FP	0.0003	FP	0.1	FP	0.033	FP
11	Aluminium phosphide	8.7	HHP	0.0097	FP	0.37	FP	0.058	FP	0.24	FP
12	Ametryn	110	HHP	5	FP	28	FP	0.0036	FP	100	FP
13	Amicarbazone	1015	HHP	120	FP	119	FP	14.0	PG	24.8	FP
14	Amitraz	800	HHP	0.74	FP	0.035	FP	12	FP	50	FP
15	Atrazine	2000	HHP	4.5	FP	85	FP	0.059	FP	100	FP
16	Azoxystrobin	5000	FP	0.47	FP	0.23	FP	0.36	FP	25	FP
18	Bacillus thuringiensis	3579	CC	171	PG	57	CC	45.09	PG	50	CC
19	Bendiocarb	55	HHP	1.55	FP	0.03	FP	1.71	FP	0.1	FP
20	Benomyl	10000	FP	0.17	FP	0.28	FP	2	FP	10	FP
21	Bensulfuron-methyl	5000	FP	66	FP	130	FP	0.02	FP	51.4	FP
22	Bentazone	1100	HHP	100	FP	64	FP	10.1	FP	200	FP
23	Beta-cyfluthrin	11	HHP	0.000068	FP	0.00029	FP	10	FP	0.001	FP
24	Brodifacoum	0.3	HHP	0.051	FP	0.98	FP	5.53	PG	62	PG
25	Bromacil	5200	HHP	36	FP	119	FP	0.013	FP	100	FP
26	Bromoxynil octanoate	238	FP	0.041	FP	0.046	FP	0.043	FP	100	FP

27	Bupirimate	4000	FP	1	FP	3.41	FP	1.6	FP	50	FP
28	Butralin	1049	HHP	0.37	FP	0.12	FP	0.12	FP	95.7	FP
29	Captan	2000	FP	0.186	FP	7.1	FP	1.18	FP	100	FP
30	Carbaryl	300	HHP	2.6	FP	0.0064	FP	0.6	FP	0.14	FP
31	Carbendazim	10000	FP	0.19	FP	0.15	FP	7.7	FP	50	FP
32	Carbofuran	8	HHP	0.18	FP	0.0094	FP	6.5	FP	0.036	FP
33	Carbosulfan	250	HHP	0.015	FP	0.0015	FP	47	FP	0.18	FP
34	Carboxin	2588	FP	2.3	FP	57	FP	0.48	FP	100	FP
35	Chlorfenvinphos	31	HHP	1.1	FP	0.00025	FP	1.36	FP	0.55	FP
36	Chlorimuron	4102	HHP	108	CC	140	CC	0.033	CC	38.2	CC
37	Chlorothalonil	5000	FP	0.038	FP	0.084	FP	0.21	FP	40	FP
38	Chlorpyrifos	135	HHP	0.0013	FP	0.0001	FP	0.48	FP	0.059	FP
39	Chlorpyrifos-methyl	2814	FP	0.41	FP	0.0006	FP	0.57	FP	0.11	FP
40	Citronella oil	4323	CC	2.65	CC	0.256	CC	0.17	CC	62	PG
41	Clomazone	1369	HHP	15.5	FP	12.7	FP	0.136	FP	85.3	FP
42	Copper ammonium acetate	1298	CC	1667	CC	167	CC	73.9	CC	62.1	CC
43	Copper hydroxide	1000	HHP	0.017	FP	0.038	FP	0.009	FP	44.5	FP
44	Copper oxide	300	FP	0.207	FP	0.45	FP	0.147	FP	116	FP
45	Copper oxychloride	1298	CC	1667	CC	167	CC	73.9	CC	62.1	CC
46	Cycloxydim	3900	HHP	220	FP	70.8	FP	74.9	FP	100	FP
47	Cyfluthrin	15	HHP	0.00047	FP	0.00016	FP	10	FP	0.001	FP
48	cymoxanil	1196	HHP	29	FP	27	FP	0.254	FP	85.3	FP
49	Cypermethrin	250	HHP	0.0028	FP	0.0003	FP	0.1	FP	0.02	FP
50	Cyromazine	3300	HHP	100	FP	100	FP	124	FP	186	FP
51	D-allethrin	685	HHP	19	FP	0.021	FP	8.5	CC	3.4	FP
52	Dazomet	415	FP	0.3	FP	19	FP	0.16	FP	24	FP
53	DDT	113	FP	7	FP	0.005	FP	45.1	PG	5	FP
54	Decanol	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
55	Deltamethrin	135	HHP	0.00026	FP	0.00056	FP	9.1	FP	0.0015	FP
56	Diazinon	300	HHP	3.1	FP	0.001	FP	6.4	FP	0.09	FP

57	Dichlorvos	56	HHP	0.55	FP	0.00019	FP	52.8	FP	0.29	FP
58	Didecyldimethylammonium chloride	150	HHP	1.16	FP	0.094	FP	0.66	ERA	88.3	PG
59	Diethyltoluamide	2000	HHP	71.3	FP	75	FP	5.53	PG	62	PG
60	Difenoconazole	1453	HHP	1.1	FP	0.77	FP	0.032	FP	100	FP
61	Difethialone	0.56	HHP	0.051	FP	0.0044	FP	0.18	FP	62	PG
62	Diflubenzuron	4640	FP	0.13	FP	0.0026	FP	20	FP	25	FP
63	Dimethoate	150	HHP	30.2	FP	2	FP	90.4	FP	0.12	FP
64	Diuron	3400	HHP	6.7	FP	5.7	FP	0.0027	FP	100	FP
65	Endosulfan	80	HHP	0.002	FP	0.44	FP	2.15	FP	7.81	FP
66	Epoxiconazole	3160	FP	3.14	FP	8.69	FP	1.19	FP	83	FP
67	Ethephon	1564	FP	100	FP	31.7	FP	20.9	FP	100	FP
68	Ethion	208	HHP	0.5	FP	0.000056	FP	88.3	CC	20.6	FP
69	Ethylbutylacetylaminopropionate	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
70	Ethylene dibromide	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
71	Ethylene oxide	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
72	Fenamiphos	15	HHP	0.0093	FP	0.0019	FP	3.8	FP	0.28	FP
73	Fenbutatin oxide	2630	HHP	0.00114	FP	0.048	FP	0.0036	FP	200	FP
74	Fenitrothion	503	FP	1.3	FP	0.0086	FP	1.3	FP	0.16	FP
75	Fenpropathrin	66	HHP	0.0023	FP	0.00053	FP	2	FP	0.05	FP
76	Fenthion	586	HHP	0.8	FP	0.0057	FP	1.79	FP	0.308	FP
77	Fenvalerate	450	HHP	0.0036	FP	0.00003	FP	50	FP	0.23	FP
78	Fipronil	92	HHP	0.248	FP	0.19	FP	0.068	FP	0.0042	FP
80	Fluazifop-P-butyl	2451	HHP	1.41	FP	0.62	FP	0.67	FP	200	FP
81	Flumethrin	972	CC	1.36	CC	0.0093	CC	8.47	CC	0.33	CC
82	Fluometuron	4323	CC	2.65	CC	0.26	CC	0.17	CC	88.6	PG
83	fluroxypyr	2000	FP	14.3	FP	100	FP	49.8	FP	100	FP
84	Formaldehyde	550	HHP	1.84	FP	0.43	FP	0.88	FP	62	PG
85	Furfural	65	HHP	3.06	FP	20.4	FP	5.53	PG	62	PG
86	Glyphosate	4230	HHP	38	FP	40	FP	4.4	FP	100	FP
87	Halosulfuron	8866	HHP	51.8	PG	92.4	PG	98	FP	88.6	PG

88	Halosulfuron-methyl	7758	FP	131	FP	107	FP	0.0053	FP	100	FP
89	Hexaconazole	2180	HHP	3.4	FP	2.9	FP	1.7	FP	0.1	FP
90	Hexazinone	1690	HHP	320	FP	85	FP	0.0145	FP	60	FP
91	Hydramethylnon	1200	HHP	0.16	FP	1.14	FP	0.018	FP	30	FP
92	Imazapic	5000	FP	100	FP	100	FP	0.051	FP	100	FP
93	Imazapyr	2000	FP	100	FP	100	FP	71	FP	25	FP
94	Imidacloprid	450	HHP	211	FP	85	FP	10	FP	0.0037	FP
95	Imiprothrin	900	HHP	0.038	FP	0.051	FP	3.1	FP	0.33	CC
96	Indoxacarb	286	HHP	0.65	FP	0.6	FP	0.11	FP	0.094	FP
97	Isoxaflutole	5000	FP	1.7	FP	1.5	FP	0.12	FP	100	FP
98	Lambda-cyhalothrin	56	HHP	0.00021	FP	0.00036	FP	0.3	FP	0.038	FP
99	Linuron	1146	FP	3.15	FP	0.31	FP	0.016	FP	160	FP
100	Lufenuron	2000	FP	29	FP	0.0013	FP	8.8	FP	197	FP
101	Malathion	2100	HHP	0.018	FP	0.0007	FP	13	FP	0.16	FP
102	Mancozeb	5000	FP	0.074	FP	0.073	FP	0.044	FP	141	FP
103	MCPA	700	HHP	50	FP	190	FP	79.8	FP	200	FP
104	Mesotrione	5000	FP	120	FP	900	FP	3.5	FP	11	FP
105	Metalaxyl	670	HHP	100	FP	28	FP	33	FP	200	FP
106	Metalaxyl-M	375	HHP	100	FP	100	FP	36	FP	127	FP
107	Metaldehyde	227	HHP	75	FP	78.4	FP	75.9	FP	87.5	FP
109	Methamidophos	30	HHP	25	FP	0.27	FP	178	FP	0.22	FP
110	Methiocarb	20	HHP	0.65	FP	0.008	FP	2.2	FP	0.23	FP
111	Methomyl	17	HHP	0.63	FP	0.0076	FP	100	FP	0.16	FP
112	Methyl bromide	214	FP	3.9	FP	2.6	FP	3.2	FP	50	FP
113	Methyl isothiazolin one	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
114	Methylchoroisothiazolinone	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
115	Metolachlor	2780	HHP	3.9	FP	23.5	FP	57.1	FP	110	FP
116	Metribuzin	322	HHP	74.6	FP	49	FP	0.02	FP	53	FP
117	Metsulfuron-methyl	5000	FP	150	FP	150	FP	0.045	FP	25	FP
118	Mevinphos	3.5	FP	0.012	FP	0.00016	FP	71	FP	0.027	FP

119	Mineral oil	4323	CC	2.65	CC	0.256	CC	0.17	CC	26.3	PG
120	Molinate	720	HHP	16	FP	14.9	FP	0.5	FP	11	FP
121	Monocrotophos	14	HHP	7	FP	0.023	FP	88.3	CC	0.02	FP
122	Monosodium methyl arsenate	2782	PG	51.8	PG	92.4	PG	14.0	PG	88.6	PG
123	Nonylphenol	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
124	Octylisothiazolinone	631	PG	25.2	PG	21.1	PG	5.53	PG	62	PG
125	Oxadiazon	5000	FP	1.2	FP	2.4	FP	0.004	FP	100	FP
126	Oxamyl	6	HHP	3.13	FP	0.319	FP	0.93	FP	0.38	FP
127	Oxyfluorfen	5000	FP	0.25	FP	0.72	FP	2	FP	100	FP
128	Paraquat	150	HHP	19	FP	4.4	FP	0.00023	FP	9.06	FP
129	pencycuron	5000	FP	0.3	FP	0.3	FP	0.3	FP	98.5	FP
130	Pendimethalin	1050	HHP	0.138	FP	0.28	FP	0.006	FP	100	FP
131	Permethrin	500	FP	0.0125	FP	0.0006	FP	0.0125	FP	0.029	FP
132	phenothrin	5000	FP	0.0027	FP	0.0043	FP	8.5	CC	0.33	CC
133	Phosphoric acid	454	FP	1667	CC	167	CC	73.9	CC	62.1	CC
134	Picloram	8200	HHP	8.8	FP	44.2	FP	60.2	FP	74	FP
135	Pine oil	3579	CC	51.8	PG	57	CC	14.0	PG	50.0	CC
136	Piperonyl butoxide	7220	FP	5.3	FP	0.51	FP	0.24	FP	294	FP
137	Pirimiphos methyl	1667	HHP	0.404	FP	0.00021	FP	1	FP	0.22	FP
138	Prallethrin	460	HHP	0.012	FP	0.0062	FP	8.47	CC	0.026	FP
139	Profenofos	358	HHP	0.08	FP	0.5	FP	88.3	CC	0.095	FP
140	Prometryn	3150	HHP	5.5	FP	12.66	FP	0.002	FP	99	FP
141	Propanil	1400	HHP	5.4	FP	2.39	FP	0.11	FP	94.3	FP
142	Propargite	2639	FP	0.043	FP	0.014	FP	1.08	FP	47.9	FP
143	Propineb	8500	HHP	0.4	FP	4.7	FP	2.68	FP	70	FP
144	Propoxur	50	FP	6.2	FP	0.15	FP	26.1	CC	1.35	FP
145	Pyrethrins	750	HHP	2.65	CC	0.26	CC	0.17	CC	26.3	PG
146	Quinclorac	2680	HHP	100	FP	29.8	FP	6.53	FP	181	FP
147	Quizalofop-P-tefuryl	1012	HHP	0.23	FP	1.51	FP	1.9	FP	100	FP
150	S-Metolachlor	2577	HHP	1.23	FP	26	FP	0.008	FP	85	FP

151	Spinosad	3738	HHP	30	FP	14	FP	0.09	FP	0.0029	FP
152	Sulcotrione	5000	FP	227	FP	848	FP	1.2	FP	50	FP
153	Sulfentrazone	2855	FP	93.8	FP	60.4	FP	32.8	FP	25.1	FP
154	Sulphur	2000	FP	0.063	FP	0.063	FP	0.063	FP	100	FP
155	Tebuconazole	1700	HHP	4.4	FP	2.79	FP	1.96	FP	83.05	FP
156	Tebuthiuron	644	HHP	87	FP	225	FP	0.05	FP	30	FP
157	Terbufos	2	HHP	0.004	FP	0.00031	FP	1.4	FP	4.1	FP
158	terbuthylazine	2160	HHP	2.2	FP	21.2	FP	0.012	FP	22.6	FP
159	Terbutryn	2500	FP	1.1	FP	2.66	FP	0.0024	FP	225	FP
160	Tetradifon	14700	FP	880	FP	2	FP	100	FP	11	FP
161	Tetramethrin	5000	FP	0.016	FP	0.045	FP	8.5	FP	0.16	FP
162	Thiamethoxam	1563	FP	125	FP	100	FP	100	FP	0.005	FP
163	Thiram	1800	FP	0.046	FP	0.011	FP	0.065	FP	100	FP
164	Transfluthrin	5000	FP	0.0007	FP	0.0017	FP	0.1	FP	26.3	PG
165	Triadimefon	300	FP	4.08	FP	7.16	FP	2.01	FP	25	FP
166	Triadimenol	900	HHP	21.3	FP	51	FP	9.6	FP	200	FP
167	Trichlorfon	212	FP	0.7	FP	0.00096	FP	10	FP	0.4	FP
170	Triclopyr	710	HHP	117	FP	131	FP	75.8	FP	100	FP
171	Tricozene	4323	CC	2.65	CC	0.256	CC	0.17	CC	62	PG
172	Trifloxystrobin	5000	FP	0.015	FP	0.011	FP	0.0053	FP	200	FP
173	Trifluralin	5000	FP	0.088	FP	0.245	FP	0.0122	FP	100	FP
174	Trifluthrin	972	CC	1.36	CC	0.0093	CC	8.5	CC	0.33	CC
175	Violeta Genciana	4323	CC	2.65	CC	0.256	CC	0.17	CC	26.3	PG

Annex 2 Human hazard

Tables;

1. Products with major contribution to the acute human hazard
2. Carcinogenic active ingredients
3. Mutagenic active ingredients
4. Active ingredients toxic to reproduction

Table 2.1: Products with major contribution to the acute human hazard: i.e. all Highly hazardous products (WHO class Ib) and the Moderately hazardous products (WHO class II) with a contribution > 1% of the annual volume of all products imported.

Year	Product ID	Product name	(kg)	(%)	WHO class
2002	1904	Phosgard 56% FT	1512	1.61	Ib
2002	1779	Nemacur 40% EC	500	0.53	Ib
2002	1406	Gramoxone 20% SL	8000	8.50	II
2002	2363	Tamaron 58% SL	2500	2.66	II
2002	2622	Villa Politrin 20% EC	2200	2.34	II
2002	818	Copper Oxychloride 85% WP	1500	1.59	II
2002	2535	Universal Metamidofos 58,5% SL	1500	1.59	II
2002	1827	Otrthene 75% SP	1200	1.28	II
2002	2501	Universal Cooper Oxychloride 85% WP	1000	1.06	II
2002	2563	Universal Skoffel 14.5% SL	1000	1.06	II
2002	2595	Villa MCPA 20% EC	1000	1.06	II
2003	1340	Fumaphos 56% FT	7015	1.05	Ib
2003	95	Aldicarb 15% GR	3800	0.57	Ib
2003	2376	Temik 15% GR	3200	0.48	Ib
2003	2866	Volcano Aldicarb 15% GR	2400	0.36	Ib
2003	97	Aluminium Phosphide 57% FT	2214	0.33	Ib
2003	1904	Phosgard 56% FT	2016	0.30	Ib
2003	2536	Universal Mevinfos 15% EC	1000	0.15	Ib
2003	1779	Nemacur 40% EC	750	0.11	Ib
2003	2634	Volamiphos 40% EC	750	0.11	Ib
2003	2537	Universal Monocrotofos 40% SL	500	0.07	Ib
2003	3011	Volcano Ametrin 50% EC	39920	5.96	II
2003	3172	Volcano cipermetrina 20% EC	35500	5.30	II
2003	1516	Karate 5% EC	27360	4.09	II
2003	1377	Gesapax 50% SC	25600	3.82	II
2003	883	Cipercal P 72% SL	25126	3.75	II
2003	1238	Ficam VC 80% WP	25038	3.74	II
2003	1406	Gramoxone 20% SL	21800	3.26	II
2003	98	Ametrin 50% SC	20600	3.08	II
2003	1322	Fortis Ultra 4.75% EC	14980	2.24	II
2003	3722	Volcano Methyl Bromide 100 %GA	10500	1.57	II
2003	1620	MCPA 400 SL	10100	1.51	II
2003	914	Cyperpro 72% EC	10000	1.49	II
2003	3668	Volcano MCPA 40% SL	9560	1.43	II
2003	3716	Volcamo Methamidophos 58.5% SL	9000	1.34	II
2003	2746	Volcano 90 SL	7340	1.10	II
2003	2535	Universal Metamidofos 58,5% SL	7000	1.05	II
2004	1198	Falfume 57% FT	8000	0.61	Ib
2004	1957	Quickphos 56% FD	2880	0.22	Ib
2004	1904	Phosgard 56% FT	1512	0.11	Ib
2004	2878	Volcano Alluminium Phosphide 57% FT	1000	0.08	Ib
2004	2376	Temik 15% GR	600	0.05	Ib
2004	2866	Volcano Aldicarb 15% GR	560	0.04	Ib

2004	1906	Phoskill 40% SC	500	0.04	Ib
2004	1340	Fumaphos 56% FT	346	0.03	Ib
2004	2616	Villa Platoon 31% SL	250	0.02	Ib
2004	3011	Volcano Ametrin 50% EC	118820	9.00	II
2004	3286	Volcano Endosulfan 47.5% SC	71574	5.42	II
2004	1516	Karate 5% EC	41576	3.15	II
2004	3668	Volcano MCPA 40% SL	40180	3.04	II
2004	1406	Gramoxone 20% SL	36000	2.73	II
2004	1327	Fortis Xtra 8.8% EC	31250	2.37	II
2004	1321	Fortis K 5% EC	30750	2.33	II
2004	3716	Volcamo Methamidophos 58.5% SL	30600	2.32	II
2004	4245	Zipper 20% EC	30240	2.29	II
2004	732	Ciclor 72% Ec	28050	2.12	II
2004	1455	Icon 10% WP	23345	1.77	II
2004	1377	Gesapax 50% SC	22400	1.70	II
2004	1238	Ficam VC 80% WP	17500	1.33	II
2004	3131	Volcano Cooper Oxychloride 85% WP	15500	1.17	II
2004	2746	Volcano 90 SL	15424	1.17	II
2005	2866	Volcano Aldicarb 15% GR	11400	0.71	Ib
2005	2878	Volcano Alluminium Phosphide 57% FT	3315	0.21	Ib
2005	2634	Volamiphos 40% EC	2000	0.12	Ib
2005	1340	Fumaphos 56% FT	378	0.02	Ib
2005	1904	Phosgard 56% FT	210	0.01	Ib
2005	4171	Vydate 31% SL	160	0.01	Ib
2005	139	Avi-DDT 75% WP	136000	8.49	II
2005	3011	Volcano Ametrin 50% EC	117000	7.31	II
2005	1455	Icon 10% WP	60698	3.79	II
2005	4080	Volmetra 50% SC	50800	3.17	II
2005	3716	Volcamo Methamidophos 58.5% SL	50120	3.13	II
2005	1327	Fortis Xtra 8.8% EC	43100	2.69	II
2005	1321	Fortis K 5% EC	32820	2.05	II
2005	3287	Volcano Endosulfan 50% EC	24000	1.50	II
2005	1238	Ficam VC 80% WP	20000	1.25	II
2005	3131	Volcano Cooper Oxychloride 85% WP	19500	1.22	II
2005	3172	Volcano cipermetrina 20% EC	18764	1.17	II
2005	883	Cipercal P 72% SL	18000	1.12	II
2006	1198	Falfume 57% FT	6001	0.30	Ib
2006	2878	Volcano Alluminium Phosphide 57% FT	4311	0.21	Ib
2006	2634	Volamiphos 40% EC	1025	0.05	Ib
2006	1904	Phosgard 56% FT	210	0.01	Ib
2006	1340	Fumaphos 56% FT	126	0.01	Ib
2006	1954	Provoke 75% WG	369339	18.19	II
2006	3011	Volcano Ametrin 50% EC	132880	6.54	II
2006	1321	Fortis K 5% EC	68060	3.35	II
2006	4241	Zakanaka Top 10% EC	53910	2.66	II
2006	4198	Zakanaka K 6% EC	52440	2.58	II
2006	4080	Volmetra 50% SC	41080	2.02	II
2006	1238	Ficam VC 80% WP	36200	1.78	II
2006	3668	Volcano MCPA 40% SL	31810	1.57	II
2006	3172	Volcano cipermetrina 20% EC	24500	1.21	II
2006	4219	Zakaka Pro 64,8% EC	24290	1.20	II
2006	3716	Volcamo Methamidophos 58.5% SL	23220	1.14	II
2006	3131	Volcano Cooper Oxychloride 85% WP	22750	1.12	II
2006	4134	Volquato 20% SL	20900	1.03	II
2007	1198	Falfume 57% FT	8800	0.69	Ib
2007	2878	Volcano Alluminium Phosphide 57% FT	6021	0.47	Ib
2007	2634	Volamiphos 40% EC	1500	0.12	Ib
2007	1906	Phoskill 40% SC	1200	0.09	Ib
2007	1957	Quickphos 56% FD	599	0.05	Ib
2007	1904	Phosgard 56% FT	210	0.02	Ib
2007	4171	Vydate 31% SL	120	0.01	Ib
2007	1340	Fumaphos 56% FT	42	0.00	Ib
2007	3011	Volcano Ametrin 50% EC	92140	7.21	II

2007	3668	Volcano MCPA 40% SL	54760	4.29	II
2007	3716	Volcamo Methamidophos 58.5% SL	42800	3.35	II
2007	4198	Zakanaka K 6% EC	38000	2.97	II
2007	4219	Zakaka Pro 64,8% EC	35000	2.74	II
2007	1238	Ficam VC 80% WP	32719	2.56	II
2007	1575	Lambda cyhalothrin 5% EC	30090	2.35	II
2007	882	Cyper pro 72% EC	29200	2.29	II
2007	4241	Zakanaka Top 10% EC	27880	2.18	II
2007	4134	Volquato 20% SL	21360	1.67	II
2007	3287	Volcano Endosulfan 50% EC	21000	1.64	II
2007	1321	Fortis K 5% EC	17750	1.39	II
2007	830	Courage 70% WS	17000	1.33	II
2007	4080	Volmetra 50% SC	14840	1.16	II
2007	3131	Volcano Cooper Oxychloride 85% WP	13923	1.09	II
2008	2066	Rotam Terbufos 15% GR	31000	1.53	Ib
2008	1904	Phosgard 56% FT	2079	0.10	Ib
2008	4171	Vydate 31% SL	300	0.01	Ib
2008	1954	Provoke 75% WG	513300	25.28	II
2008	1321	Fortis K 5% EC	98970	4.87	II
2008	3668	Volcano MCPA 40% SL	71100	3.50	II
2008	3011	Volcano Ametrin 50% EC	62800	3.09	II
2008	4198	Zakanaka K 6% EC	60500	2.98	II
2008	4219	Zakaka Pro 64,8% EC	45000	2.22	II
2008	3131	Volcano Cooper Oxychloride 85% WP	33010	1.63	II
2008	2746	Volcano 90 SL	27900	1.37	II
2008	4241	Zakanaka Top 10% EC	26500	1.31	II
2008	1406	Gramoxone 20% SL	21000	1.03	II
2008	3172	Volcano cipermetrina 20% EC	20500	1.01	II
2009	662	Bongo	45000	1.94	Ib
2009	2878	Volcano Alluminium Phosphide 57% FT	6510	0.28	Ib
2009	1553	Kuik	1000	0.04	Ib
2009	4171	Vydate 31% SL	480	0.02	Ib
2009	1904	Phosgard 56% FT	462	0.02	Ib
2009	3011	Volcano Ametrin 50% EC	161140	6.96	II
2009	2020	Revival 10% WP	120333	5.20	II
2009	3668	Volcano MCPA 40% SL	60360	2.61	II
2009	3131	Volcano Cooper Oxychloride 85% WP	54660	2.36	II
2009	1321	Fortis K 5% EC	42750	1.85	II
2009	4134	Volquato 20% SL	42240	1.82	II
2009	4198	Zakanaka K 6% EC	32760	1.41	II
2009	3180	Volcano D 2,4 72% SL	32000	1.38	II
2009	3716	Volcamo Methamidophos 58.5% SL	28830	1.24	II
2009	2677	Volcano 2,4 D 72% SL	28000	1.21	II
2009	4241	Zakanaka Top 10% EC	27230	1.18	II
2009	1238	Ficam VC 80% WP	26054	1.12	II
2010	2878	Volcano Alluminium Phosphide 57% FT	15519	0.58	Ib
2010	1198	Falfume 57% FT	13800	0.52	Ib
2010	1752	Moz Abamec Plus 18% EC	800	0.03	Ib
2010	1904	Phosgard 56% FT	525	0.02	Ib
2010	4171	Vydate 31% SL	500	0.02	Ib
2010	2020	Revival 10% WP	214300	8.00	II
2010	3011	Volcano Ametrin 50% EC	136060	5.08	II
2010	4241	Zakanaka Top 10% EC	63980	2.39	II
2010	3668	Volcano MCPA 40% SL	53440	2.00	II
2010	3131	Volcano Cooper Oxychloride 85% WP	52130	1.95	II
2010	2677	Volcano 2,4 D 72% SL	47000	1.76	II
2010	4219	Zakaka Pro 64,8% EC	42100	1.57	II
2010	4062	Volmet 58,5% SL	34760	1.30	II
2010	3172	Volcano cipermetrina 20% EC	32760	1.22	II
2010	1321	Fortis K 5% EC	30060	1.12	II
2011	2878	Volcano Alluminium Phosphide 57% FT	11970	0.46	Ib
2011	1904	Phosgard 56% FT	1470	0.06	Ib
2011	1756	Moz Aluminium Phosphide 56% FT	1250	0.05	Ib

2011	4171	Vydate 31% SL	300	0.01	Ib
2011	1752	Moz Abamec Plus 18% EC	240	0.01	Ib
2011	3011	Volcano Ametrin 50% EC	134900	5.20	II
2011	1203	Fendona 5% WP	75600	2.92	II
2011	3030	Volcano Copper Oxychloride 85% WP	70700	2.73	II
2011	4219	Zakaka Pro 64,8% EC	65500	2.53	II
2011	4241	Zakanaka Top 10% EC	60500	2.33	II
2011	3668	Volcano MCPA 40% SL	60200	2.32	II
2011	4198	Zakanaka K 6% EC	55300	2.13	II
2011	4134	Volquato 20% SL	35100	1.35	II
2011	1321	Fortis K 5% EC	35000	1.35	II
2011	2677	Volcano 2,4 D 72% SL	32600	1.26	II
2011	3172	Volcano cipermetrina 20% EC	30450	1.17	II

Table 2.2: Carcinogenic active ingredients with the contribution to the annual volume of active ingredients imported (in %).

Year	Compound ID	Compound name	(kg)	(%)
2002	102	Mancozeb	2000	10.7
2002	57	Dichlorvos	461	2.46
2002	131	Permethrin	24	0.13
2003	64	Diuron	20400	6.53
2003	102	Mancozeb	15248	4.88
2003	57	Dichlorvos	1641	0.53
2003	37	Chlorothalonil	400	0.13
2003	8	Alachlor	384	0.12
2003	131	Permethrin	18	0.01
2004	102	Mancozeb	44848	7.72
2004	64	Diuron	44672	7.69
2004	57	Dichlorvos	6162	1.06
2004	37	Chlorothalonil	1537	0.26
2004	8	Alachlor	384	0.07
2004	131	Permethrin	28	0.005
2005	64	Diuron	40976	5.90
2005	102	Mancozeb	20080	2.89
2005	57	Dichlorvos	1513	0.22
2005	37	Chlorothalonil	1382	0.20
2005	131	Permethrin	40	0.01
2006	64	Diuron	40312	4.49
2006	102	Mancozeb	23666	2.63
2006	57	Dichlorvos	5323	0.59
2006	8	Alachlor	1260	0.14
2006	37	Chlorothalonil	691	0.08
2006	131	Permethrin	28	0.003
2007	64	Diuron	33568	6.05
2007	102	Mancozeb	30936	5.57
2007	64	Diuron	23072	4.16
2007	102	Mancozeb	15782	2.84
2007	57	Dichlorvos	6376	1.15
2007	57	Dichlorvos	3551	0.64
2007	8	Alachlor	1800	0.32
2007	125	Oxadiazon	950	0.17
2007	37	Chlorothalonil	850	0.15
2007	131	Permethrin	246	0.04
2007	131	Permethrin	34	0.01
2007	30	Carbaryl	20	0.004
2009	64	Diuron	48899	5.69
2009	102	Mancozeb	30003	3.49
2009	125	Oxadiazon	5000	0.58
2009	57	Dichlorvos	2433	0.28
2009	37	Chlorothalonil	1000	0.12
2009	97	Isoxaflutole	750	0.09
2009	131	Permethrin	49	0.01
2009	84	Formaldehyde	13	0.00
2010	102	Mancozeb	53574	5.58
2010	64	Diuron	37889	3.95
2010	37	Chlorothalonil	5500	0.57
2010	57	Dichlorvos	2921	0.30
2010	97	Isoxaflutole	1920	0.20
2010	127	Oxyfluorfen	216	0.02
2010	131	Permethrin	114	0.01
2010	84	Formaldehyde	50	0.01
2010	30	Carbaryl	8	0.001
2011	102	Mancozeb	61075	6.48

2011	64	Diuron	43312	4.60
2011	57	Dichlorvos	5421	0.58
2011	84	Formaldehyde	1074	0.11
2011	37	Chlorothalonil	750	0.08
2011	131	Permethrin	84	0.01
2011	30	Carbaryl	84	0.01
2011	97	Isoxaflutole	15	0.002

Table 2.3: Mutagenic active ingredients with the contribution to the annual volume of active ingredients imported (in %).

Year	Compound ID	Compound name	(kg)	(%)
2004	20	Benomyl	735	0.13
2005	20	Benomyl	200	0.029
2006	20	Benomyl	200	0.022
2007	31	Carbendazim	1.3	0.0002
2008	31	Carbendazim	5	0.001
2009	20	Benomyl	500	0.058
2009	31	Carbendazim	54	0.006
2010	20	Benomyl	2800	0.29
2010	31	Carbendazim	0.4	0.00004
2011	31	Carbendazim	0.6	0.0001

Table 2.4: Active ingredients toxic to reproduction with the contribution to the annual volume of active ingredients imported (in %).

Year	Compound ID	Compound name	(kg)	(%)
2004	20	Benomyl	735	0.13
2005	20	Benomyl	200	0.029
2006	20	Benomyl	200	0.022
2007	31	Carbendazim	1.3	0.0002
2008	31	Carbendazim	5	0.001
2009	20	Benomyl	500	0.058
2009	31	Carbendazim	54	0.006
2010	20	Benomyl	2800	0.29
2010	31	Carbendazim	0.4	0.00004
2011	31	Carbendazim	0.6	0.0001

Annex 3 Environmental toxic Loads

Tables;

1. Active ingredients with the major contribution to the annual ETL for fish
2. Active ingredients with the major contribution to the annual ETL for Daphnia
3. Active ingredients with the major contribution to the annual ETL for algae
4. Active ingredients with the major contribution to the annual ETL for bees

Table 3.1: Active ingredients with the major contribution to the annual ETL for fish (i.e. > 0.5 %).

Year	RankNr	Compound Nr.	Compound name	(kg)	(%)
2002	1	38	Chlorpyrifos	240	30.1
2002	2	49	Cypermethrin	440	25.6
2002	3	11	Aluminium phosphide	847	14.2
2002	4	47	Cyfluthrin	37	12.7
2002	5	65	Endosulfan	70	5.7
2002	6	102	Mancozeb	2000	4.4
2002	7	72	Fenamiphos	200	3.5
2002	8	154	Sulphur	800	2.1
2002	9	142	Propargite	240	0.9
2003	1	98	Lambda-cyhalothrin	2158	56.8
2003	2	49	Cypermethrin	12317	24.3
2003	3	38	Chlorpyrifos	1699	7.2
2003	4	11	Aluminium phosphide	6319	3.6
2003	5	23	Beta-cyfluthrin	30	2.4
2003	6	139	Profenofos	22226	1.5
2003	7	102	Mancozeb	15248	1.1
2004	1	98	Lambda-cyhalothrin	7992	50.1
2004	2	65	Endosulfan	34103	22.4
2004	3	38	Chlorpyrifos	18078	18.3
2004	4	49	Cypermethrin	12034	5.7
2004	5	11	Aluminium phosphide	7783	1.1
2004	6	102	Mancozeb	44848	0.8
2004	7	23	Beta-cyfluthrin	40	0.8
2005	1	98	Lambda-cyhalothrin	12377	80.8
2005	2	65	Endosulfan	12140	8.3
2005	3	49	Cypermethrin	6813	3.3
2005	4	23	Beta-cyfluthrin	111	2.2
2005	5	38	Chlorpyrifos	1200	1.3
2005	6	77	Fenvalerate	3050	1.2
2005	7	73	Fenbutatin oxide	550	0.7
2006	1	98	Lambda-cyhalothrin	11698	84.4
2006	2	65	Endosulfan	7885	6.0
2006	3	49	Cypermethrin	7857	4.3
2006	4	38	Chlorpyrifos	1536	1.8
2006	5	11	Aluminium phosphide	6066	0.9
2006	6	139	Profenofos	27471	0.5
2006	7	23	Beta-cyfluthrin	23	0.5
2007	1	98	Lambda-cyhalothrin	8216	67.2
2007	2	65	Endosulfan	10588	9.1
2007	3	55	Deltamethrin	1204	7.9
2007	4	38	Chlorpyrifos	3056	4.0
2007	5	49	Cypermethrin	6174	3.8
2007	6	77	Fenvalerate	5439	2.6
2007	7	11	Aluminium phosphide	8925	1.6
2007	8	73	Fenbutatin oxide	605	0.9

2007	9	139	Profenofos	39720	0.9
2007	10	102	Mancozeb	30936	0.7
2007	11	23	Beta-cyfluthrin	23	0.6
2008	1	98	Lambda-cyhalothrin	13263	81.4
2008	2	55	Deltamethrin	1579	7.8
2008	3	38	Chlorpyrifos	3223	3.2
2008	4	49	Cypermethrin	5450	2.5
2008	5	157	Terbufos	4650	1.5
2008	6	65	Endosulfan	1050	0.7
2009	1	98	Lambda-cyhalothrin	20403	89.4
2009	2	38	Chlorpyrifos	4366	3.1
2009	3	157	Terbufos	6750	1.6
2009	4	49	Cypermethrin	4139	1.4
2009	5	77	Fenvalerate	4000	1.0
2009	6	73	Fenbutatin oxide	1164	0.9
2009	7	55	Deltamethrin	189	0.7
2010	1	98	Lambda-cyhalothrin	30610	89.4
2010	2	38	Chlorpyrifos	11772	5.6
2010	3	49	Cypermethrin	8335	1.8
2010	4	11	Aluminium phosphide	17006	1.1
2011	1	98	Lambda-cyhalothrin	12760	83.4
2011	2	38	Chlorpyrifos	4279	4.5
2011	3	49	Cypermethrin	6926	3.4
2011	4	10	Alpha-cypermethrin	3780	1.9
2011	5	65	Endosulfan	2548	1.7
2011	6	11	Aluminium phosphide	8346	1.2
2011	7	102	Mancozeb	61075	1.1
2011	8	139	Profenofos	55130	0.9
2011	9	55	Deltamethrin	145	0.8

Table 3.2: Active ingredients with the major contribution to the annual ETL for Daphnia (i.e. > 0.5 %).

Year	RankNr	Compound Nr.	Compound name	(kg)	(%)
2002	1	57	Dichlorvos	461	32.2
2002	2	38	Chlorpyrifos	240	31.8
2002	3	49	Cypermethrin	440	19.5
2002	4	137	Pirimiphos methyl	96	6.1
2002	5	39	Chlorpyrifos-methyl	200	4.4
2002	6	47	Cyfluthrin	37	3.0
2002	7	72	Fenamiphos	200	1.4
2002	8	131	Permethrin	24	0.5
2003	1	49	Cypermethrin	12317	43.9
2003	2	38	Chlorpyrifos	1699	18.2
2003	3	137	Pirimiphos methyl	3069	15.6
2003	4	57	Dichlorvos	1641	9.2
2003	5	98	Lambda-cyhalothrin	2158	6.4
2003	6	77	Fenvalerate	76	2.7
2003	7	118	Mevinphos	150	1.0
2003	8	19	Bendiocarb	20030	0.7
2003	9	33	Carbosulfan	835	0.6
2004	1	38	Chlorpyrifos	18078	60.4
2004	2	49	Cypermethrin	12034	13.4
2004	3	57	Dichlorvos	6162	10.8
2004	4	98	Lambda-cyhalothrin	7992	7.4
2004	5	137	Pirimiphos methyl	4094	6.5
2005	1	77	Fenvalerate	3050	38.6
2005	2	68	Ethion	2525	17.1
2005	3	98	Lambda-cyhalothrin	12377	13.1
2005	4	49	Cypermethrin	6813	8.6
2005	5	53	DDT	102000	7.7
2005	6	137	Pirimiphos methyl	2876	5.2
2005	7	38	Chlorpyrifos	1200	4.6
2005	8	57	Dichlorvos	1513	3.0
2005	9	35	Chlorfenvinphos	600	0.9
2006	1	53	DDT	285929	26.5
2006	2	68	Ethion	2525	20.9
2006	3	98	Lambda-cyhalothrin	11698	15.1
2006	4	57	Dichlorvos	5323	13.0
2006	5	49	Cypermethrin	7857	12.1
2006	6	38	Chlorpyrifos	1536	7.1
2006	7	77	Fenvalerate	100	1.5
2006	8	137	Pirimiphos methyl	538	1.2
2006	9	35	Chlorfenvinphos	636	1.2
2007	1	77	Fenvalerate	5439	51.5
2007	2	68	Ethion	3030	15.4
2007	3	57	Dichlorvos	6376	9.5
2007	4	38	Chlorpyrifos	3056	8.7
2007	5	98	Lambda-cyhalothrin	8216	6.5
2007	6	49	Cypermethrin	6174	5.8
2007	7	137	Pirimiphos methyl	857	1.2
2007	8	55	Deltamethrin	1204	0.6
2008	1	53	DDT	384975	31.4
2008	2	98	Lambda-cyhalothrin	13263	15.0
2008	3	38	Chlorpyrifos	3223	13.2
2008	4	77	Fenvalerate	800	10.9
2008	5	57	Dichlorvos	3551	7.6
2008	6	49	Cypermethrin	5450	7.4
2008	7	157	Terbufos	4650	6.1
2008	8	137	Pirimiphos methyl	2490	4.8
2008	9	55	Deltamethrin	1579	1.2

2008	10	35	Chlorfenvinphos	375	0.6
2009	1	77	Fenvalerate	4000	45.5
2009	2	98	Lambda-cyhalothrin	20403	19.4
2009	3	38	Chlorpyrifos	4366	14.9
2009	4	157	Terbufos	6750	7.4
2009	5	49	Cypermethrin	4139	4.7
2009	6	57	Dichlorvos	2433	4.4
2009	7	137	Pirimiphos methyl	1010	1.6
2010	1	38	Chlorpyrifos	11772	42.5
2010	2	98	Lambda-cyhalothrin	30610	30.7
2010	3	49	Cypermethrin	8335	10.0
2010	4	77	Fenvalerate	500	6.0
2010	5	57	Dichlorvos	2921	5.5
2010	6	137	Pirimiphos methyl	1966	3.4
2010	7	3	Abamectin	189	0.7
2011	1	38	Chlorpyrifos	4279	27.9
2011	2	98	Lambda-cyhalothrin	12760	23.1
2011	3	57	Dichlorvos	5421	18.6
2011	4	49	Cypermethrin	6926	15.1
2011	5	10	Alpha-cypermethrin	3780	8.2
2011	6	137	Pirimiphos methyl	1394	4.3
2011	7	3	Abamectin	115	0.8
2011	8	102	Mancozeb	61075	0.5

Table 3.3: Active ingredients with the major contribution to the annual ETL for algae (i.e. > 0.5 %).

Year	RankNr	Compound Nr.	Compound name	(kg)	(%)
2002	1	128	Paraquat	1745	98.5
2002	2	102	Mancozeb	2000	0.6
2003	1	7	Acetochlor	14652	56.5
2003	2	128	Paraquat	4721	21.4
2003	3	12	Ametryn	43060	12.5
2003	4	64	Diuron	20400	7.9
2004	1	7	Acetochlor	33768	63.0
2004	2	128	Paraquat	7418	16.3
2004	3	12	Ametryn	70610	9.9
2004	4	64	Diuron	44672	8.3
2004	5	159	Terbutryn	6203	1.3
2004	6	102	Mancozeb	44848	0.5
2005	1	7	Acetochlor	59061	76.0
2005	2	128	Paraquat	5377	8.1
2005	3	12	Ametryn	82480	8.0
2005	4	64	Diuron	40976	5.3
2005	5	140	Prometryn	5280	0.9
2005	6	130	Pendimethalin	15170	0.9
2006	1	7	Acetochlor	41454	68.7
2006	2	128	Paraquat	6604	12.8
2006	3	12	Ametryn	76710	9.5
2006	4	64	Diuron	40312	6.7
2006	5	130	Pendimethalin	14220	1.1
2007	1	7	Acetochlor	30591	71.3
2007	2	128	Paraquat	4272	11.7
2007	3	12	Ametryn	51060	8.9
2007	4	64	Diuron	23072	5.4
2007	5	130	Pendimethalin	11240	1.2
2008	1	7	Acetochlor	72239	84.3
2008	2	128	Paraquat	4600	6.3
2008	3	64	Diuron	33568	3.9
2008	4	12	Ametryn	41040	3.6
2008	5	130	Pendimethalin	26130	1.4
2009	1	7	Acetochlor	66996	74.5
2009	2	128	Paraquat	8448	11.0
2009	3	12	Ametryn	80570	6.7
2009	4	64	Diuron	48899	5.4
2009	5	130	Pendimethalin	20090	1.0
2010	1	7	Acetochlor	80856	81.8
2010	2	128	Paraquat	4540	5.4
2010	3	12	Ametryn	68030	5.2
2010	4	64	Diuron	37889	3.8
2010	5	130	Pendimethalin	61120	2.8
2011	1	7	Acetochlor	57456	74.6
2011	2	128	Paraquat	7020	10.7
2011	3	12	Ametryn	67450	6.6
2011	4	64	Diuron	43312	5.6
2011	5	130	Pendimethalin	27180	1.6

Table 3.4: Active ingredients with the major contribution to the annual ETL for bees (i.e. > 0.5 %)

Year	RankNr	Compound Nr.	Compound name	(kg)	(%)
2002	1	94	Imidacloprid	269	46.0
2002	2	47	Cyfluthrin	37	23.3
2002	3	49	Cypermethrin	440	13.9
2002	4	109	Methamidophos	2340	6.7
2002	5	38	Chlorpyrifos	240	2.6
2002	6	11	Aluminium phosphide	847	2.2
2002	7	39	Chlorpyrifos-methyl	200	1.2
2002	8	57	Dichlorvos	461	1.0
2002	9	32	Carbofuran	50	0.9
2002	10	131	Permethrin	24	0.5
2003	1	49	Cypermethrin	12317	41.6
2003	2	139	Profenofos	22226	15.8
2003	3	19	Bendiocarb	20030	13.5
2003	4	162	Thiamethoxam	521	7.0
2003	5	109	Methamidophos	12578	3.9
2003	6	98	Lambda-cyhalothrin	2158	3.8
2003	7	47	Cyfluthrin	41	2.8
2003	8	23	Beta-cyfluthrin	30	2.0
2003	9	38	Chlorpyrifos	1699	1.9
2003	10	11	Aluminium phosphide	6319	1.8
2003	11	9	Aldicarb	1410	1.1
2003	12	137	Pirimiphos methyl	3069	0.9
2003	13	3	Abamectin	23	0.7
2003	14	121	Monocrotophos	200	0.7
2004	1	49	Cypermethrin	12034	29.4
2004	2	38	Chlorpyrifos	18078	15.0
2004	3	162	Thiamethoxam	1488	14.5
2004	4	98	Lambda-cyhalothrin	7992	10.3
2004	5	19	Bendiocarb	14000	6.8
2004	6	94	Imidacloprid	332	4.4
2004	7	109	Methamidophos	19656	4.4
2004	8	139	Profenofos	5150	2.6
2004	9	47	Cyfluthrin	54	2.6
2004	10	23	Beta-cyfluthrin	40	2.0
2004	11	11	Aluminium phosphide	7783	1.6
2004	12	3	Abamectin	58	1.3
2004	13	57	Dichlorvos	6162	1.0
2004	14	137	Pirimiphos methyl	4094	0.9
2004	15	63	Dimethoate	1440	0.6
2004	16	89	Hexaconazole	1147	0.6
2005	1	94	Imidacloprid	2161	25.0
2005	2	49	Cypermethrin	6813	14.6
2005	3	98	Lambda-cyhalothrin	12377	13.9
2005	4	139	Profenofos	19977	9.0
2005	5	162	Thiamethoxam	910	7.8
2005	6	19	Bendiocarb	16000	6.8
2005	7	109	Methamidophos	35024	6.8
2005	8	23	Beta-cyfluthrin	111	4.8
2005	9	47	Cyfluthrin	90	3.9
2005	10	78	Fipronil	120	1.2
2005	11	53	DDT	102000	0.9
2005	12	38	Chlorpyrifos	1200	0.9
2005	13	9	Aldicarb	1710	0.8
2005	14	89	Hexaconazole	1733	0.7

2005	15	77	Fenvalerate	3050	0.6
2005	16	137	Pirimiphos methyl	2876	0.6
2006	1	94	Imidacloprid	12367	66.9
2006	2	49	Cypermethrin	7857	7.9
2006	3	98	Lambda-cyhalothrin	11698	6.2
2006	4	19	Bendiocarb	28960	5.8
2006	5	139	Profenofos	27471	5.8
2006	6	109	Methamidophos	14110	1.3
2006	7	53	DDT	285929	1.1
2006	8	47	Cyfluthrin	46	0.9
2006	9	89	Hexaconazole	3464	0.7
2006	10	78	Fipronil	120	0.6
2006	11	38	Chlorpyrifos	1536	0.5
2006	12	11	Aluminium phosphide	6066	0.5
2007	1	94	Imidacloprid	12924	59.1
2007	2	55	Deltamethrin	1204	13.6
2007	3	139	Profenofos	39720	7.1
2007	4	49	Cypermethrin	6174	5.2
2007	5	19	Bendiocarb	26175	4.4
2007	6	98	Lambda-cyhalothrin	8216	3.7
2007	7	109	Methamidophos	33521	2.6
2007	8	38	Chlorpyrifos	3056	0.9
2007	9	11	Aluminium phosphide	8925	0.6
2008	1	94	Imidacloprid	14802	61.3
2008	2	55	Deltamethrin	1579	16.1
2008	3	98	Lambda-cyhalothrin	13263	5.3
2008	4	139	Profenofos	29802	4.8
2008	5	49	Cypermethrin	5450	4.2
2008	6	19	Bendiocarb	10816	1.7
2008	7	53	DDT	384975	1.2
2008	8	109	Methamidophos	12969	0.9
2008	9	38	Chlorpyrifos	3223	0.8
2008	10	47	Cyfluthrin	47	0.7
2008	11	3	Abamectin	79	0.6
2009	1	94	Imidacloprid	5955	44.1
2009	2	98	Lambda-cyhalothrin	20403	14.7
2009	3	19	Bendiocarb	21243	5.8
2009	4	49	Cypermethrin	4139	5.7
2009	5	78	Fipronil	840	5.5
2009	6	47	Cyfluthrin	188	5.2
2009	7	139	Profenofos	14256	4.1
2009	8	55	Deltamethrin	189	3.4
2009	9	109	Methamidophos	23886	3.0
2009	10	162	Thiamethoxam	465	2.5
2009	11	38	Chlorpyrifos	4366	2.0
2009	12	3	Abamectin	82	1.0
2010	1	94	Imidacloprid	3781	26.2
2010	2	98	Lambda-cyhalothrin	30610	20.6
2010	3	49	Cypermethrin	8335	10.7
2010	4	78	Fipronil	1586	9.7
2010	5	139	Profenofos	27170	7.3
2010	6	38	Chlorpyrifos	11772	5.1
2010	7	162	Thiamethoxam	950	4.9
2010	8	47	Cyfluthrin	166	4.3
2010	9	109	Methamidophos	20335	2.4
2010	10	3	Abamectin	189	2.2
2010	11	55	Deltamethrin	120	2.1
2010	12	11	Aluminium phosphide	17006	1.8
2010	13	19	Bendiocarb	4648	1.2
2011	1	94	Imidacloprid	3553	29.1
2011	2	139	Profenofos	55130	17.6
2011	3	162	Thiamethoxam	1917	11.6
2011	4	49	Cypermethrin	6926	10.5

2011	5	98	Lambda-cyhalothrin	12760	10.2
2011	6	19	Bendiocarb	11648	3.5
2011	7	10	Alpha-cypermethrin	3780	3.5
2011	8	47	Cyfluthrin	101	3.1
2011	9	55	Deltamethrin	145	2.9
2011	10	38	Chlorpyrifos	4279	2.2
2011	11	3	Abamectin	115	1.6
2011	12	11	Aluminium phosphide	8346	1.1
2011	13	109	Methamidophos	7634	1.1
2011	14	57	Dichlorvos	5421	0.6
2011	15	151	Spinosad	52	0.5

Annex 4: Groundwater leaching

Tables;

1. GUS and groundwater leaching potential class of the active ingredients
2. Active ingredients with the Very high and High groundwater leaching potential class.

Table 4.1: The GUS and groundwater leaching potential class of the active ingredients in the imported products.

Nr.	Compound Name	GUS	Class
1	2,4-D	2.5	3
2	2,4-D dimethylamine	3.0	3
3	Abamectin	-0.2	1
4	Acephate	0.73	1
5	Acetamiprid	0.81	1
6	Acetic acid + ammonia	-0.3	1
7	Acetochlor	2.1	3
8	Alachlor	1.7	2
9	Aldicarb	1.7	2
10	Alpha-cypermethrin	-1.2	1
11	Aluminium phosphide	-2.8	1
12	Ametryn	2.4	3
13	Amicarbazone	3.3	4
14	Amitraz	-5	1
15	Atrazine	3.5	4
16	Azoxystrobin	2.4	3
18	Bacillus thuringiensis	-1.3	1
19	Bendiocarb	0.85	1
20	Benomyl	-3.6	1
21	Bensulfuron-methyl	2.0	2
22	Bentazone	3.5	4
23	Beta-cyfluthrin	-0.9	1
24	Brodifacoum	-1.5	1
25	Bromacil	4.4	5
26	Bromoxynil octanoate	0	1
27	Bupirimate	2.4	3
28	Butralin	-0.9	1
29	Captan	0	1
30	Carbaryl	1.8	2
31	Carbendazim	2.6	3
32	Carbofuran	3.3	4
33	Carbosulfan	0.030	1
34	Carboxin	-10.0	1
35	Chlorfenvinphos	2.1	3
36	Chlorimuron	2.4	3
37	Chlorothalonil	1.2	2
38	Chlorpyrifos	0.15	1
39	Chlorpyrifos-methyl	0.64	1

40	Citronella oil	-5.7	1
41	Clomazone	3.1	4
42	Copper ammonium acetate	2.1	3
43	Copper hydroxide	-0.3	1
44	Copper oxide	2.3	3
45	Copper oxychloride	2.3	3
46	Cycloxydim	0	1
47	Cyfluthrin	0.33	1
48	cymoxanil	0	1
49	Cypermethrin	-2.1	1
50	Cyromazine	1.7	2
51	D-allethrin	1.5	2
52	Dazomet	-15	1
53	DDT	-4.5	1
54	Decanol	-5.7	1
55	Deltamethrin	-4.4	1
56	Diazinon	2.1	3
57	Dichlorvos	0.69	1
58	Didecyldimethylammonium chloride	-6.9	1
59	Diethyltoluamide	3.3	4
60	Difenoconazole	0.87	1
61	Difethialone	-10.5	1
62	Diflubenzuron	0	1
63	Dimethoate	2.3	3
64	Diuron	2.1	3
65	Endosulfan	-0.1	1
66	Epoxiconazole	1.9	2
67	Ethephon	0.72	1
68	Ethion	0	1
69	Ethylbutylacetylaminopropionate	-5.7	1
70	Ethylene dibromide	-5.7	1
71	Ethylene oxide	-5.7	1
72	Fenamiphos	0	1
73	Fenbutatin oxide	-2.5	1
74	Fenitrothion	0.92	1
75	Fenpropathrin	0.44	1
76	Fenthion	1.3	2
77	Fenvalerate	0.43	1
78	Fipronil	2.7	3
80	Fluazifop-P-butyl	0.22	1
81	Flumethrin	-2.4	1
82	Fluometuron	-0.3	1
83	fluroxypyr	-0.8	1
84	Formaldehyde	1.9	2
85	Furfural	0	1
86	Glyphosate	1.0	2
87	Halosulfuron	-0.4	1
88	Halosulfuron-methyl	2.2	3
89	Hexaconazole	2.3	3
90	Hexazinone	4.6	5
91	Hydramethylnon	-1.6	1

92	Imazapic	3.9	4
93	Imazapyr	2.0	2
94	Imidacloprid	3.8	4
95	Imiprothrin	0.98	1
96	Indoxacarb	0.23	1
97	Isoxaflutole	0.55	1
98	Lambda-cyhalothrin	-1.7	1
99	Linuron	1.9	2
100	Lufenuron	-0.7	1
101	Malathion	0	1
102	Mancozeb	1.3	2
103	MCPA	2.9	3
104	Mesotrione	2.3	3
105	Metalaxyl	3.3	4
106	Metalaxyl-M	2.8	3
107	Metaldehyde	1.5	2
109	Methamidophos	1.2	2
110	Methiocarb	1.8	2
111	Methomyl	3.2	4
112	Methyl bromide	4.6	5
113	Methyl isothiazolin one	-5.7	1
114	Methylchoroisothiazolinone	-5.7	1
115	Metolachlor	2.9	3
116	Metribuzin	2.6	3
117	Metsulfuron-methyl	2.4	3
118	Mevinphos	-11.8	1
119	Mineral oil	-2.2	1
120	Molinate	1.9	2
121	Monocrotophos	2.3	3
122	Monosodium methyl arsenate	-0.3	1
123	Nonylphenol	-5.7	1
124	Octylisothiazolinone	-5.7	1
125	Oxadiazon	1.3	2
126	Oxamyl	3.0	4
127	Oxyfluorfen	-0.4	1
128	Paraquat	-6.9	1
129	pencycuron	0.31	1
130	Pendimethalin	-0.5	1
131	Permethrin	-1.6	1
132	phenothrin	0	1
133	Phosphoric acid	2.1	3
134	Picloram	5.5	5
135	Pine oil	-0.2	1
136	Piperonyl butoxide	-1.1	1
137	Pirimiphos methyl	1.3	2
138	Prallethrin	-2.4	1
139	Profenofos	0.59	1
140	Prometryn	2.5	3
141	Propanil	-9.1	1
142	Propargite	-1.3	1
143	Propineb	1.3	2

144	Propoxur	3.9	4
145	Pyrethrins	-2.2	1
146	Quinclorac	6.1	5
147	Quizalofop-P-tefuryl	-6.6	1
150	S-Metolachlor	0.84	1
151	Spinosad	-0.8	1
152	Sulcotrione	2.6	3
153	Sulfentrazone	6.5	5
154	Sulphur	1.0	2
155	Tebuconazole	1.6	2
156	Tebuthiuron	6.5	5
157	Terbufos	1.4	2
158	terbuthylazine	3.4	4
159	Terbutryn	1.0	2
160	Tetradifon	4.1	5
161	Tetramethrin	0.40	1
162	Thiamethoxam	3.9	4
163	Thiram	0.91	1
164	Transfluthrin	-2.2	1
165	Triadimefon	2.2	3
166	Triadimenol	2.5	3
167	Trichlorfon	0	1
170	Triclopyr	4.0	4
171	Tricozene	-5.7	1
172	Trifloxystrobin	0	1
173	Trifluralin	-0.4	1
174	Trifluthrin	-2.4	1
175	Violeta Genciana	-2.2	1

Table 4.2: Active ingredients in the Very high (5) and High (4) groundwater leaching potential class with a contribution to the annual volume of Active ingredients imported > 0.01 %.

Year	Compound number	Compound name	Class number	Volume (kg ai)	(%)
2002	144	Propoxur	4	461	2.46
	94	Imidacloprid		269	1.44
	32	Carbofuran		50	0.27
2003	112	Methyl bromide	5	10290	3.29
	156	Tebuthiuron		2840	0.91
	25	Bromacil		1000	0.32
	90	Hexazinone		360	0.12
	144	Propoxur	4	641	0.21
	162	Thiamethoxam		521	0.17
	170	Triclopyr		96	0.03
2004	112	Methyl bromide	5	12740	2.19
	162	Thiamethoxam	4	1488	0.26
	144	Propoxur		1162	0.20
	15	Atrazine		713	0.12
	94	Imidacloprid		332	0.06
	126	Oxamyl		78	0.01
	158	terbuthylazine		75	0.01
2005	112	Methyl bromide	5	10290	1.48
	90	Hexazinone		3418	0.49
	156	Tebuthiuron		2950	0.42
	25	Bromacil		110	0.02
	15	Atrazine	4	13268	1.91
	94	Imidacloprid		2161	0.31
	170	Triclopyr		1795	0.26
	144	Propoxur		1513	0.22
	162	Thiamethoxam		910	0.13
	41	Clomazone		336	0.05
	158	terbuthylazine		175	0.03
2006	156	Tebuthiuron	5	5450	0.61
	90	Hexazinone		4046	0.45
	94	Imidacloprid	4	12367	1.38
	15	Atrazine		11020	1.23
	170	Triclopyr		2563	0.29
	144	Propoxur		1833	0.20
	105	Metalaxyl		332	0.04
	158	terbuthylazine		150	0.02
2007	156	Tebuthiuron	5	5590	1.01
	90	Hexazinone		3110	0.56
	94	Imidacloprid	4	12924	2.33
	15	Atrazine		3823	0.69
	170	Triclopyr		2678	0.48
	22	Bentazone		2208	0.40
	105	Metalaxyl		646	0.12
	144	Propoxur		364	0.07
2008	156	Tebuthiuron	5	3935	0.40
	90	Hexazinone		154	0.02
	94	Imidacloprid	4	14802	1.49
	41	Clomazone		4704	0.47
	170	Triclopyr		3754	0.38
	144	Propoxur		367	0.04
	15	Atrazine		113	0.01
2009	156	Tebuthiuron	5	10855	1.26
	90	Hexazinone		5674	0.66
	134	Picloram		480	0.06
	146	Quinclorac		315	0.04
	25	Bromacil		215	0.02
	41	Clomazone	4	13056	1.52
	94	Imidacloprid		5955	0.69

	170	Triclopyr		3955	0.46
	144	Propoxur		1869	0.22
	92	Imazapic		1050	0.12
	111	Methomyl		900	0.10
	13	Amicarbazone		875	0.10
	22	Bentazone		864	0.10
	105	Metalaxyl		696	0.08
	162	Thiamethoxam		465	0.05
	15	Atrazine		409	0.05
	126	Oxamyl		149	0.02
2010	90	Hexazinone	5	8227	0.86
	156	Tebuthiuron		2130	0.22
	41	Clomazone	4	19680	2.05
	94	Imidacloprid		3781	0.39
	170	Triclopyr		2640	0.28
	144	Propoxur		2394	0.25
	15	Atrazine		1450	0.15
	162	Thiamethoxam		950	0.10
	105	Metalaxyl		904	0.09
	92	Imazapic		378	0.04
	126	Oxamyl		155	0.02
	22	Bentazone		96	0.01
2011	90	Hexazinone	5	4560	0.48
	156	Tebuthiuron		1550	0.16
	41	Clomazone	4	11933	1.27
	170	Triclopyr		6163	0.65
	94	Imidacloprid		3553	0.38
	144	Propoxur		2376	0.25
	162	Thiamethoxam		1917	0.20
	15	Atrazine		1500	0.16
	92	Imazapic		1092	0.12
	13	Amicarbazone		700	0.07
	22	Bentazone		624	0.07
	105	Metalaxyl		550	0.06

Annex 5: Imported formulated products containing active ingredients of primary concern

Human health

CompoundName	Abamectin

Sum of Volume_ai_kg	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Agrometic 1.8% EC	23	40	16	41	45	79	82	45	72	444
Moz Abamec Plus 18% EC								144	43	187
Volcano Agromectin 1.8% EC		18								18
Grand Total	**23**	**58**	**16**	**41**	**45**	**79**	**82**	**189**	**115**	**649**

CompoundName	Aldicarb

Sum of Volume_ai_kg	2003	2004	2005	Grand Total
Aldicarb 15% GR	570			570
Temik 15% GR	480	90		570
Volcano Aldicarb 15% GR	360	84	1710	2154
Grand Total	**1410**	**174**	**1710**	**3294**

CompoundName	Aluminium phosphide

Sum of Volume_ai_kg	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Aluminium Phosphide 57% FT		1262									1262
Falfume 57% FT			4560		3421	5016			7866		20863
Fumaphos 56% FT		3929	194	212	71	24					4428
Moz Aluminium Phosphide 56% FT										700	700
Phosgard 56% FT	847	1129	847	118	118	118	1164	259	294	823	5715
Quickphos 56% FD			1613			335					1948
Volcano Alluminium Phosphide 57% FT			570	1890	2457	3432		3711	8846	6823	27728
Grand Total	**847**	**6319**	**7783**	**2219**	**6066**	**8925**	**1164**	**3969**	**17006**	**8346**	**62645**

CompoundName	Fenamiphos

Sum of Volume_ai_kg	2002	2003	2005	2006	2007	Grand Total
Nemacur 10% GR		50				50
Nemacur 40% EC	200	300				500
Volamiphos 40% EC		300	800	410	600	2110
Grand Total	**200**	**650**	**800**	**410**	**600**	**2660**

CompoundName	Methomyl

Sum of Volume_ai_kg	2009	Grand Total
Kuik	900	900
Grand Total	**900**	**900**

CompoundName	Mevinphos

Sum of Volume_ai_kg	2003	Grand Total
Universal Mevinfos 15% EC	150	150
Grand Total	**150**	**150**

CompoundName	Monocrotophos

Sum of Volume_ai_kg	2003	2004	2007	Grand Total
Phoskill 40% SC		200	480	680
Universal Monocrotofos 40% SL	200			200
Grand Total	**200**	**200**	**480**	**880**

CompoundName	Oxamyl

Sum of Volume_ai_kg	2004	2005	2007	2008	2009	2010	2011	Grand Total
Villa Platoon 31% SL	78							78
Vydate 31% SL		50	37	93	149	155	93	577
Grand Total	**78**	**50**	**37**	**93**	**149**	**155**	**93**	**654**

CompoundName	Terbufos

Sum of Volume_ai_kg	2008	2009	Grand Total
Bongo		6750	6750
Rotam Terbufos 15% GR	4650		4650
Grand Total	**4650**	**6750**	**11400**

CompoundName	Diuron

Sum of Volume_ai_kg	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Acticide EPW							2			2
Diuron 80% SC	7200	1600			2592	4800				16192
Rocima 363 N							1	1		2
Volcano Diuron 800 SC	13200	43072	40976	40312	20480	28768	48896	37888	43312	316904
Grand Total	**20400**	**44672**	**40976**	**40312**	**23072**	**33568**	**48899**	**37889**	**43312**	**333100**

CompoundName	Mancozeb

Sum of Volume_ai_kg	2002	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Dithan M 45 800 WP		800	4000	1600							6400
Dithane M 60 OS									390		390
Dithane NT 80% WP										800	800
Mancozeb 80% WP	1200	3440									4640
Metamin Fae Pm 72% WP										627	627
Milor								2624			2624
Milthane Super 80% WP									16000		16000
Policar MZ 80% WP										1408	1408
Ridomil Gold MZ 68 WG		1088	2304		346	576	1382			64	5760
Sunstar Super 72% WP									3200		3200
Unilax 72% WP			144			40					184
Unizeb 80% WP	800	3200	3600								7600
Uthane 80% WP			6400		4000	1600					12000
Volcano Crater MX 72% WP					2560	5120		2568	2432	3776	16456
Volcano Mancozeb 80% WP		6720	28400	18480	16760	23600	14400	24811	31552	54400	219123
Grand Total	**2000**	**15248**	**44848**	**20080**	**23666**	**30936**	**15782**	**30003**	**53574**	**61075**	**297212**

Environment

CompoundName	Lambda-cyhalothrin

Sum of Volume_ai_kg	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Cyclon 10 EC						2				2
Demand 2.5 CS		15								15
Duduthrin 5% EC								250		250
Fortis K 5% EC		1538	1641	3403	888	4949	2138	1503	1750	17808
Fortis Ultra 4.75% EC	375									375
Fortis Xtra 8.8% EC	2	1500	2069							3571
Icon 10 CS						45				45
Icon 10% WP	317	2334	6070	67	98	50			133	9069
Icon 2,5% EC	63	12	38	24	60	72				268
Iconet 2.5% CS	33	427	68	6						535
Karate 5% CS			18	651	33					702
Karate 5% EC	1368	2079	720				18			4185
Karate Zeon 5% CS						17			29	45
Lambda cyhalothrin 5% EC		88	53		1505					1645
Moz Lambda-Cyhalothrin 5% EC									6	6
Revival 10% WP							12033	21430		33463
Revival 25% EC						750	1595		750	3095
Zakaka Pro 64,8% EC			260	1166	1680	2160	1020	2021	3144	11451
Zakanaka Top 10% EC			510	3235	1673	1590	1634	3839	3630	16110
Zakanaka K 6% EC			300	3146	2280	3630	1966	1567	3318	16207
Zakanaka Topro 68,8% EC			630							630
Grand Total	**2158**	**7992**	**12377**	**11698**	**8216**	**13263**	**20403**	**30610**	**12760**	**119476**

CompoundName	Acetochlor

Sum of Volume_ai_kg	2003	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Acetochlor 90% EC	2700					3105				5805
Bullet 70% SC		126	75		126	126				453
Villa Acetochlor 90% EC			13320	3204						16524
Volcano Acetochlor 90% EC	11952	33642	45666	38250	30465	69008	66996	80856	57456	434291
Grand Total	**14652**	**33768**	**59061**	**41454**	**30591**	**72239**	**66996**	**80856**	**57456**	**457073**

CompoundName	Imidacloprid

Sum of Volume_ai_kg	2002	2004	2005	2006	2007	2008	2009	2010	2011	Grand Total
Bandit 35% SC					316	4756	3290	1629	1925	11916
Bandit 70% WG								2013		2013
Confidor 20% SL	129		162		104	140				535
Courage 60% FS			936							936
Courage 70% WS				12187	11900	9660	2013			35760
Gaucho 70% WS	140		1							141
Imidabiogel 2,15% PC					2		161	62	86	312
Imidacel 20% SL								77	300	377
Imidagold 20% SL					160	40	10			210
Maxforce Quantum RB									0	0
Midaclordan									500	500
Monceren GT 390 FS			140							140
Moz Imidacloprid 35% SC									42	42
Premise 35% SC							1			1
Protect 20% SL		332	730	180	400	202	480		700	3024
Quick Bait Spray Fly Bait									0	0
Seed Plus 30% WS					1	5				6
Thunder 145 O-TEQ			192		40					232
Grand Total	**269**	**332**	**2161**	**12367**	**12924**	**14802**	**5955**	**3781**	**3553**	**56144**

CompoundName	Methyl bromide

Sum of Volume_ai_kg	2003	2004	2005	Grand Total
Volcano Methyl Bromide 100 %GA	10290	12740	10290	33320
Grand Total	**10290**	**12740**	**10290**	**33320**

CompoundName	Tebuthiuron

Sum of Volume_ai_kg	2003	2005	2006	2007	2008	2009	2010	2011	Grand Total
Tebuthiuron 50% SC	2200				1400				3600
Volcano Bundu 50% SC		110			35	215			360
Volcano Tebuthiuron 500 SC	640	2840	5450	5590	2500	10640	2130	1550	31340
Grand Total	**2840**	**2950**	**5450**	**5590**	**3935**	**10855**	**2130**	**1550**	**35300**

Alterra Wageningen UR
P.O. Box 47
6700 AB Wageningen
The Netherlands
T +31 (0)317 48 07 00
www.wageningenUR.nl/en/alterra

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The mission of Wageningen UR (University & Research centre) is 'To explore the potential of nature to improve the quality of life'. Within Wageningen UR, nine specialised research institutes of the DLO Foundation have joined forces with Wageningen University to help answer the most important questions in the domain of healthy food and living environment. With approximately 30 locations, 6,000 members of staff and 9,000 students, Wageningen UR is one of the leading organisations in its domain worldwide. The integral approach to problems and the cooperation between the various disciplines are at the heart of the unique Wageningen Approach.

Terbufos (Ref: AC 92100)

(Also known as: sebuphos; terbuphos)

Last updated: 27/11/2019

PPDB

GENERAL INFORMATION

Description	An insecticide and nematicide used to control soil and other pests
Example pests controlled	Wireworms; Maggots; Rootworm larvae; White grubs; Black maize beetles; Nematodes; Aphids
Example applications	Corn; Sugarbeet; Sorghum; Sunflower; Citrus; Potatoes; Peanuts
Efficacy & activity	-
Availability status	Current
Introduction & key dates	First registered in US in 1974

UK regulatory status

UK approval status	Not approved

EC Regulation 1107/2009 (repealing 91/414)

EC Directive 91/414 Status	Not approved
Dossier rapporteur/co-rapporteur	Not applicable
Date inclusion expires	Expired
EU Candidate for substitution (CfS)	-
Listed in EU database	Yes
Approved for use (✓) or known to be used (#) in the following EU-27 Member States	

AT	BE	BG	CY	CZ	DE	DK	EE	EL
ES	**FI**	**FR**	**HR**	**HU**	**IE**	**IT**	**LT**	**LU**
LV	**MT**	**NL**	**PL**	**PT**	**RO**	**SE**	**SI**	**SK**

Also used in

Also used in	Australia, USA

Chemical structure

Isomerism	-
Chemical formula	$C_9H_{21}O_2PS_3$
Canonical SMILES	CCOP(=S)(OCC)SCSC(C)(C)C
Isomeric SMILES	No data
International Chemical Identifier key (InChIKey)	XLNZEKHULJKQBA-UHFFFAOYSA-N
International Chemical Identifier (InChI)	InChI=1S/C9H21O2PS3/c1-6-10-12(13,11-7-2)15-8-14-9(3,4)5/h6-8H2,1-5H3

2D structure diagram/image available?	Yes

General status

Pesticide type	Insecticide, Nematicide
Substance group	Organophosphate
Minimum active substance purity	-
Known relevant impurities	-
Substance origin	Synthetic
Mode of action	Systemic. Cholinesterase inhibitor.
CAS RN	13071-79-9
EC number	235-963-8
CIPAC number	459
US EPA chemical code	105001
PubChem CID	25670
Molecular mass	288.4
PIN (Preferred Identification Name)	S-[(tert-butylsulfanyl)methyl] O,O-diethyl phosphorodithioate
IUPAC name	S-tert-butylthiomethyl O,O-diethyl phosphorodithioate
CAS name	S-[[(1,1-dimethylethyl)thio]methyl] O,O-diethyl phosphorodithioate
Other status information	Severe Marine Pollutant; Chemical subject to PIC regulations; Found infrequently in drinkwater supplies
Relevant Environmental Water Quality Standards	-
Herbicide Resistance Classification (HRAC)	Not applicable
Herbicide Resistance Classification (WSSA)	Not applicable
Insecticide Resistance Classification (IRAC)	1B
Fungicide Resistance Classification (FRAC)	Not applicable
Examples of recorded resistance	*Diabrotica undecimpunctata*, *Schizaphis graminum*
Physical state	Pale yellow liquid

Formulations

Property	Value
Example manufacturers & suppliers of products using this active now or historically	• Counter • Contraven • Aragran

Property	Value
Example products using this active	• Amvac • BASF • American Cyanamid
UK LERAP status	No UK approval for use as a pesticide under EC Regulation 1107/2009
Formulation and application details	Usually formulated as granules

ENVIRONMENTAL FATE

Property		Value	Source; quality score; and other information	Interpretation
Solubility - In water at 20 °C (mg l^{-1})		4.5	K4	Low
Solubility - In organic solvents at 20 °C (mg l^{-1})		300000	L2 Acetone	-
Melting point (°C)		-29.2	L3	-
Boiling point (°C)		-	-	-
Degradation point (°C)		-	-	-
Flashpoint (°C)		88	L3 (open cup)	-
Octanol-water partition coefficient at pH 7, 20 °C	P	3.24 X 10^{04}	Calculated	-
	Log P	4.51	G4	High
Bulk density (g ml^{-1})		1.11	L3	-
Dissociation constant pKa) at 25 °C		-	-	-
		-		
Vapour pressure at 20 °C (mPa)		34.6	G4	Highly volatile
Henry's law constant at 25 °C (Pa m^3 mol^{-1})		2.70	H4	Moderately volatile
GUS leaching potential index		1.25	Calculated	Low leachability
SCI-GROW groundwater index (µg l^{-1}) for a 1 kg ha^{-1} or 1 l ha^{-1} application rate	Value	2.01 X 10^{-02}	Calculated	-
	Note	-		
Potential for particle bound transport index		Low	Calculated	-
Maximum UV-vis absorption L mol^{-1} cm^{-1}		-	-	-
Surface tension (mN m^{-1})		-	-	-

Degradation

Property	Value	Source; quality score; and other information	Interpretation

Property		Value	Source; quality score; and other information	Interpretation
General biodegradability		-		
Soil degradation (days) (aerobic)	DT_{50} (typical)	8	K4	Non-persistent
	DT_{50} (lab at 20 °C)	5	H4	Non-persistent
	DT_{50} (field)	12	H4	Non-persistent
	DT_{90} (lab at 20 °C)	-	-	-
	DT_{90} (field)	-	-	-
	DT_{50} modelling endpoint	-	-	-
	Note	Best available data		
Dissipation rate RL_{50} on plant matrix	Value	-	-	-
	Note	-		
Dissipation rate RL_{50} on and in plant matrix	Value	-	-	-
	Note	-		
Aqueous photolysis DT_{50} (days) at pH 7	Value	4.5	K4	Moderately fast
	Note	-		
Aqueous hydrolysis DT_{50} (days) at 20 °C and pH 7	Value	6.5	K4	Non-persistent
	Note	Not sensitive to pH		
Water-sediment DT_{50} (days)		-	-	-
Water phase only DT_{50} (days)		-	-	-

Soil adsorption and mobility

Property		Value	Source; quality score; and other information	Interpretation
Linear	K_d	-	G3	Slightly mobile
	K_{oc}	500		
	Notes and range	-		
Freundlich	K_f	24.4	R3	Slightly mobile
	K_{foc}	700		
	$^1/_n$	1.09		
	Notes and range	Soil characteristics - New Zealand Tokomaru soil with OC 3.2%		
pH sensitivity		-		

Other known metabolites

Metabolite name and reference	Aliases	Formation medium / Rate	Estimated maximum occurrence fraction	Metabolising enzymes
terbufos sulfoxide	-	Soil; Plant; Animal	-	-
terbufos sulfone	-	Soil; Plant; Animal	-	-
terbufos oxon sulfoxide	-	a = Soil; b= Plant; c = Animal	a=0.05	-
terbufos oxon sulfone	-	Plant	-	-
terbufos oxon	-	Animal	-	-
O,O-diethyl phosphorothioate	-	Rats (Urinary)	-	-
diethyl phosphate	-	Rats (Urinary)	-	-
O,O-diethyl phosphorodithioate	-	Rats (Urinary)	-	-

ECOTOXICOLOGY

Property		Value	Source; quality score; and other information	Interpretation
Bio-concentration factor	BCF (l kg^{-1})	286	F4	Threshold for concern
	CT_{50} (days)	Not available		-
Mammals - Acute oral LD_{50} (mg kg^{-1})		1.3	G4 Rat	High
Mammals - Short term dietary NOEL	(mg kg^{-1})	-	L2 Rat 2 year	-
	(ppm diet)	1		-
Birds - Acute LD_{50} (mg kg^{-1})		> 185	L3 *Anas platyrhynchos*	Moderate
Birds - Short term dietary (LC_{50}/LD_{50})		-	-	-
Fish - Acute 96 hour LC_{50} (mg l^{-1})		> 0.004	L3 *Lepomis macrochirus*	High
Fish - Chronic 21 day NOEC (mg l^{-1})		0.0006	P3 *Oncorhynchus mykiss* growth	High
Aquatic invertebrates - Acute 48 hour EC_{50} (mg l^{-1})		0.00031	K3 *Daphnia magna*	High
Aquatic invertebrates - Chronic 21 day NOEC (mg l^{-1})		-	-	-
Aquatic crustaceans - Acute 96 hour LC_{50} (mg l^{-1})		0.00022	F3 *Americamysis bahia*	High
Sediment dwelling organisms - Acute 96 hour LC_{50} (mg l^{-1})		-	-	-
Sediment dwelling organisms - Chronic 28 day NOEC, static, water (mg l^{-1})		-	-	-
Sediment dwelling organisms - Chronic 28 day NOEC, sediment (mg kg^{-1})		-	-	-

Property		Value	Source; quality score; and other information	Interpretation
Aquatic plants - Acute 7 day EC_{50}, biomass (mg l^{-1})		-	-	-
Non-target plants		-	-	-
		-	-	-
Algae - Acute 72 hour EC_{50}, growth (mg l^{-1})		1.4	K3 Unknown species	Moderate
Algae - Chronic 96 hour NOEC, growth (mg l^{-1})		-	-	-
Honeybees (*Apis* spp.)	Contact acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	4.1	F4	Moderate
	Oral acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	-	-	-
	Unknown mode acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	-	-	-
Bumblebees (*Bombus* spp.)	Contact acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	-	-	-
		-		
	Oral acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	-	-	-
		-		
Mason bees (*Osmia* spp.)	Contact acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	-	-	-
	Oral acute LD_{50} (worst case from 24, 48 and 72 hour values - µg bee^{-1})	-	-	-
Other pollinators (1)	Acute LD_{50} (worst case from 24, 48 and 72 hour values - µg $insect^{-1}$)	-	-	-

Property		Value	Source; quality score; and other information	Interpretation
	Mode of exposure	-		
Other pollinators (2)	Acute LD_{50} (worst case from 24, 48 and 72 hour values - µg insect^{-1})	-	-	-
	Mode of exposure	-		
Earthworms - Acute 14 day LC_{50} (mg kg^{-1})		4	Q3	High
Earthworms - Chronic NOEC, reproduction (mg kg^{-1})		-	-	-
Other soil macro-organisms	Acute LC_{50} (mg kg^{-1})	-	-	-
	Chronic NOEC (mg kg^{-1})	-	-	-
Other arthropod (1)	LR_{50} g ha^{-1}	-	-	-
	% Effect	-	-	-
Other arthropod (2)	LR_{50} g ha^{-1}	-	-	-
	% Effect	-	-	-
Soil micro-organisms		-	-	-
Mesocosm study data	NOEAEC mg l^{-1}	-	-	-
	NOEAEC mg l^{-1}	-	-	-

HUMAN HEALTH AND PROTECTION

General

Property	Value	Source; quality score; and other information	Interpretation
Threshold of Toxicological Concern (Cramer Class)	High (class III)	-	-
Mammals - Acute oral LD_{50} (mg kg^{-1})	1.3	G4 Rat	High
Mammals - Dermal LD_{50} (mg kg^{-1} body weight)	1.0	L3 Rabbit	-
Mammals - Inhalation LC_{50} (mg l^{-1})	0.0061	L3 Rat	-
Other Mammal toxicity endpoints	-	-	-
ADI - Acceptable Daily Intake (mg kg^{-1} bw day^{-1})	0.0006	F5 JMPR 2003	-
ARfD - Acute Reference Dose (mg kg^{-1} bw day^{-1})	0.002	F5 JMPR 2003	-

Property		Value	Source; quality score; and other information	Interpretation
AAOEL - Acute Acceptable Operator Exposure Level (mg kg^{-1} bw day^{-1})		-	-	-
AOEL - Acceptable Operator Exposure Level - Systemic (mg kg^{-1} bw day^{-1})		-	-	-
Dermal penetration studies (%)		-	-	-
Dangerous Substances Directive 76/464		List I; List II	-	-
Exposure Routes	Public	-		
	Occupational	-		
European MRLs		EU MRL pesticide database		
Drinking Water Standards		-	-	-
Drinking Water MAC (µg l^{-1})		-	-	-

Health issues

Specific human health issues			
	Carcinogen	Genotoxic	Endocrine disruptor
	X	A3; B0; C0; D0; E3	No data found
	Reproduction / development effects	Acetyl cholinesterase inhibitor	Neurotoxicant
	No data found	✓	✓
	Respiratory tract irritant	Skin irritant	Skin sensitiser
	No data found	✓	No data found
	Eye irritant	Phototoxicant	
	✓	No data found	
General human health issues	Highly toxic		

Handling issues

Property	Value and interpretation
General	No information available
CLP classification 2013	Health: H300, H310 Environment: H400, H410
EC Risk Classification	T+ - Very toxic: R27/28 N - Dangerous for the environment: R50, R53
EC Safety Classification	S1/2, S36/37, S45, S60, S61
WHO Classification	Ia (Extremely hazardous)
UN Number	3018
Waste disposal & packaging	-

TRANSLATIONS

Language	Name
English	terbufos
French	terbuphos
German	Terbufos
Danish	terbufos
Italian	terbufos
Spanish	terbufos
Greek	terbufos
Polish	terbufos
Swedish	-
Hungarian	-
Dutch	terbufos

Record last updated: 27/11/2019

Contact: aeru@herts.ac.uk

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TERBUFOS (167)

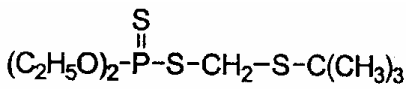
First draft prepared by Dr Salwa Dogheim, Central Laboratory of Residue Analysis of Pesticides and Heavy Metals in Food, Agriculture Research Centre, Ministry of Agriculture, Cairo, Egypt.

EXPLANATION

Terbufos was evaluated for the first time by JMPR in 1989. A further residue review was undertaken in 1990. At the 36th Session of the CCPR, the compound was scheduled for residues periodic review in 2005. The toxicological review was conducted in 2003, which established an ADI of 0.0006 mg/kg bw/day and an acute RfD of 0.002 mg/kg bw/day.

The manufacturer provided information on the latest GAP, residue data on a number of crops: including banana, coffee beans, sugar beets, maize, sorghum, and sweet corn. Metabolism, analytical methods, and relevant storage stability studies were also provided. Australia submitted information on the use pattern, national MRLs and residue definition.

IDENTITY

ISO common name:	Terbufos
IUPAC Name	*S-tert*-butylthiomethyl *0,0*-diethyl phosphorodithioate
CAS No.	13071-79-9
Synonyms and trade names	Counter, CL 92100, AC 92100, Hunter
Structural formula	
Molecular Formula	$C_9H_{21}O_2PS_3$
Molecular Weight	288.43 g/mole

Physical and Chemical Properties

The physical and chemical properties of terbufos are summarized in Table 1.

Table 1. Physical and chemical properties of terbufos

Property	Characteristics	Test Substance	Reference
Physical state	Liquid at ambient temperature	TGAI	TE-301-007
Colour	Colourless to pale yellow	TGAI	TE-301-007
Odour	Mercaptan-like	TGAI	TE-301-007
Purity	86% - 89%	TGAI	TE-301-007
Melting point	Product is liquid at room temperature	TGAI	TE-301-007
Boiling Point	55 °C at 0.02 mm Hg	TGAI	TE-301-007
Relative density	1.11 g/mL at 20 °C	TGAI	TE-301-007
pH	4.12 average in H_2O/dioxane mixture	TGAI	TE-301-007
Storage stability	Stable for more than two years at room temperature. Decomposes upon prolonged heating at temperatures above 120°C. Subject to alkaline hydrolysis in presence of strong bases.	TGAI	TE-301-007
Solubility in organic solvents, g/100 g at 20°C	Solubility was ≥100 g/100mL solvent for each of the following solvents at 20 ºC: Acetone, acetonitrile, benzene, chloroform, dichloroethane, ethanol, n-heptane, dichloromethane, and toluene	TGAI	TE-301-007

Property	Characteristics	Test Substance	Reference
Solubility in water	5.4 mg/L water at 25°C; pH 4, 7, 10 buffers: 5.6, 4.9, 4.5 mg/L, respectively, at 25°C	PAI	TE-301-007
	Solubility of two important metabolites: terbufos sulfoxide, 2936 mg/L; terbufos sulfone, 240 mg/L (each in water at 27°C)	PAI	TE-311-003
Vapour pressure	3.16×10^{-4} mm Hg at 25°C 6.98×10^{-4} mm Hg at 35°C 12.4×10^{-4} mm Hg at 45°C	PAI	TE-301-007
Dissociation constant	Not applicable; compound does not dissociate	---	---
Octanol/water partition coefficient	Log Kow = 4.71	PAI	TE-301-007
Hydrolysis	At pH 5 and 20-25°C, half-life 4.5 days At pH 7 and 25°C, half-life 5.5 days At pH 9 and 25°C, half-life 8.5 days At the conclusion of a four-week study, 75.1, 72.4, and 68.3% of the radioactivity at pH 5, 7, and 9, respectively, was hydrophilic, with formaldehyde constituting the principal degradation product. Organophilic products consisted of the phosphorylated series of oxidative metabolites.	PAI QUES	TE-630-001
Photolysis	Less than 1% of the applied dose (4 ppm) of terbufos remained after 1-day exposure to natural sunlight in pond water, with the sulfoxide CL 94301 accounting for 45.2%. Formaldehyde appeared to be the principal water-soluble reaction product. Organophilic radioactivity was due mainly to the phosphorylated oxidative metabolites and a minor amount of the methylated mercaptan series.	PAI	TE-630-001

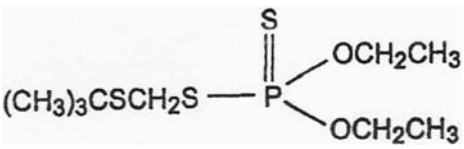
TGAI= Technical grade active ingredient.
PAI = Pure active ingredient.

Formulations

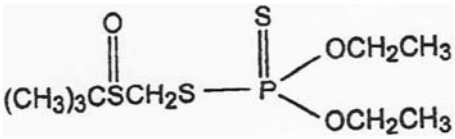
Terbufos is available in granular formulations with active ingredient content of 5%, 10%, 15%, or 20%.

METABOLISM AND ENVIRONMENTAL FATE

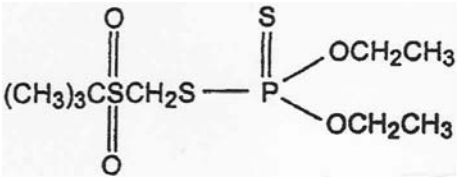
The metabolism of terbufos was investigated in animals (goat and poultry) and plants (soybean, sugar beets, sweet corn, cabbage and rape) using [methylene-^{14}C]terbufos. In some studies, [^{13}C]-terbufos labelled at the same methylene carbon was used as mass marker to facilitate the identification of metabolites by mass spectrometry. The list of metabolites and major breakdown products of terbufos, together with the code names and common names and chemical structures are presented in Figure 1. The chemical structure of terbufos, showing the positions of the carbon-13 and carbon-14 label is shown in Figure 2.



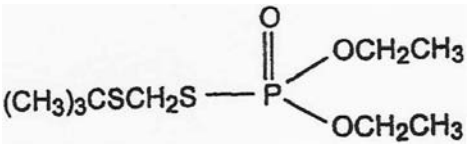
Terbufos (CL 92,100)
Phosphorodithioic Acid, *S*-(*tert*-butylthio) methyl *O,O*-diethyl ester



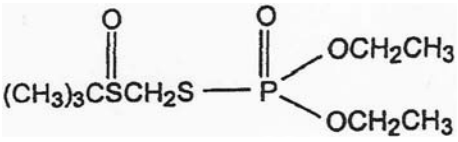
Terbufos sulfoxide (CL 94,301)
Phosphorodithioic acid. *S-(tert*-butylsulfinyl) methyl *O,O*-diethyl ester



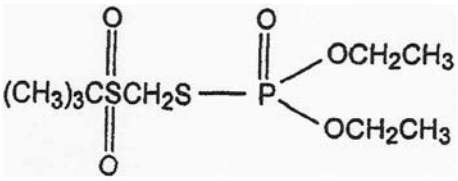
Terbufos sulfone (CL 94,320)
Phosphorodithioic acid, *S*-(*tert* -butylsulfonyl) methyl *O,O*-diethyl ester



Terbufoxon (CL 94,221)
Phosphorothioic acid, *S*-(*tert*-butylthio) methyl, *O,O* -diethyl ester



Terbufoxon sulfoxide (CL 94,365)
Phosphorothioic acid, .*S*-(*tert* -butylsulfinyl) methyl,*O,O* -diethyl ester



Terbufoxon sulfone (CL 94,302)
Phosphorothioic acid, *S-(tert*-butylsulfonyl) methyl, *O,O*-diethyl ester

Figure 1. Terbufos and its metabolites.

```
(CH3)3C-S-CH2-S-P-(OC2H5)2
          *      ||
                 S
```

*Denotes the position of carbon-14 label

```
(CH3)3C-S-CH2-S-P-(OC2H5)2
          *      ||
                 S
```

*Denotes the position of carbon-13 label

Figure 2. Chemical structure of terbufos showing positions of 13C and 14C-labels.

Animal Metabolism

Data was submitted to the meeting by the manufacturer on a study conducted to determine the absorption, distribution, metabolism and elimination of terbufos in rats, study no. (TE-440-004) by Cheng, T. (1992).

Metabolism in goat

In goat metabolism studies (TE 440-002 and TE-440-005) by Zulalian J. (1990) and Zulalian J. (1992) respectively, [^{14}C]terbufos was administered via capsule to two lactating goats. Each goat was dosed, once daily for seven consecutive days at dosages equivalent to 0.281 and 2.53 mg/kg in the diet calculated on the basis of dose administered and actual feed consumption. A third goat served as a control. The three experimental goats were females with average weight (45-65 kg) and aged over two years.

The total recoveries of radioactivity in the urine, faeces, cage wipes, cage washes, milk and tissues from the low and high dosed animals were 98.9 and 98.0%, respectively. The major route of excretion was via the urine, which accounted for 96.0 and 86.9% of the administered radioactivity, respectively.

The total radioactive residue (TRR) in daily milk samples was < 0.01 mg/kg (low dose) and 0.02-0.03 mg/kg (high dose, day 7). Residues in the liver, kidney, muscle, fat and blood of the low dose animal were all < 0.01 mg/kg. In the high dose animal, residues were 0.08, 0.04, < 0.01, < 0.01 and 0.03 mg/kg, respectively. The radioassay was validated at a detection limit equal to 0.01 mg/kg equivalents of [^{14}C]terbufos. The percentage of administered radioactivity and TRR in goat milk, blood and tissues are summarized in Tables 2 and 3.

Table 2. Radioactivity in milk of goats dosed with [^{14}C]terbufos for 7 consecutive days.

Collection Time	Group A (Control)	Group B (0.28 mg/kg in diet)	Group C (2.53 mg/kg in diet)
Percent Total Radioactivity			
Pre-dose	NA	NA	NA
Day 1	NA	ND	0.12
Day 2	NA	0.06	0.12
Day 3	NA	0.08	0.13
Day 4	NA	0.08	0.12
Day 5	NA	0.09	0.11
Day 6	NA	0.09	0.13
Day 7	NA	0.09	0.14
Total	NA	0.49	0.87
µg Equivalents ^{14}C-labeled CL 92100/g			
Pre-dose	NA	NA	NA
Day 1	NA	ND	0.02
Day 2	NA	< 0.01	0.02
Day 3	NA	< 0.01	0.02
Day 4	NA	< 0.01	0.02
Day 5	NA	< 0.01	0.02
Day 6	NA	< 0.01	0.02
Day 7	NA	< 0.01	0.03

NA = not applicable, ND = not detectable (< 0.01 mg/kg)

Table 3. Radioactivity in blood and tissues of goats dosed with [^{14}C]terbufos for 7 consecutive days.

Tissue	Group A (Control)	Group B (0.28 mg/kg in diet)	Group C (2.53 mg/kg in diet)
Percent of Radioactivity			
Blood	NA	< 0.01	< 0.01
Fat (omental)	NA	0.02	0.02
Kidneys	NA	0.02	0.03
Liver	NA	0.20	0.35
Muscle (leg and loin)	NA	0.08	0.02
Total	NA	0.32	0.42
µg Equivalents ^{14}C-Labeled CL 92100/g			
Blood	NA	< 0.01	0.03
Fat (omental)	NA	< 0.01	< 0.01
Kidneys	NA	< 0.01	0.04
Liver	NA	< 0.01	0.08
Muscle (leg and loin)	NA	< 0.01	< 0.01

Of the TRR in milk (high dose), 32.7% (< 0.01 mg/kg) was organosoluble, 34.8% (0.01 mg/kg) was water soluble and 29.3% (< 0.01 mg/kg) remained in the post-extracted solid (PES). HPLC and two-dimensional TLC analysis of the organosoluble milk residue showed two unknowns each in concentrations of < 0.01 mg/kg and accounting for 25.5% and 3.6% of the TRR. Three metabolites of the non-phosphorylated series, CL 202474, CL 99843, and CL 99875, were detected by TLC. The concentration of each of these components was < 0.01 mg/kg. Significantly, terbufos or its phosphorylated metabolites were not detected in milk.

Of the TRR in liver (high dose), 13.9% (0.01 mg/kg) was organosoluble, 27.5% (0.02 mg/kg) was water soluble, and 55.6% (0.04 mg/kg) remained in the PES. HPLC and TLC analyses of the organosoluble liver residue showed several unknowns accounting for 1 to 5% of the TRR (all < 0.01 mg/kg) and trace amounts of terbufos (2.1%, < 0.01 mg/kg) and the non-phosphorylated metabolite CL 99875 (1.9%, < 0.01 mg/kg). HPLC analysis of the water soluble residue showed several components each accounting for < 0.01 mg/kg of the TRR. Characterization of the PES liver residue (0.04 mg/kg) by enzyme hydrolysis with protease released 5.9% (0.01 mg/kg) of the radioactivity as organosoluble and 27.6% (< 0.01 mg/kg) as water soluble. Chemical (base) hydrolysis (6N NaOH) released 5.7% (< 0.01 mg/kg) as organosoluble, 67.9% (0.03 mg/kg) as water soluble and 5.1% (< 0.01 mg/kg) remained in the PES.

Of the TRR in kidney (high dose), 11.9% (< 0.01 mg/kg) was organosoluble, 46.5% (0.02 mg/kg) was water soluble, and 32.3% (0.01 mg/kg) remained in the PES. HPLC analysis of the water soluble radioactivity showed multiple components, each accounting for < 0.01 ppm. Terbufos was also observed (< 0.01 mg/kg). The concentration of metabolites found in goat tissues, milk and urine are summarized in Table 4.

Table 4. Metabolites detected in tissues, milk, and urine from goats treated with [^{14}C]terbufos.

Compound	Kidney[a]	Liver[b]	Milk[a]	Urine
Percent of TRR (mg/kg) HPLC Method I				
Unknown A[c]	30.3 (0.01)	16.9 (0.01)	24.5 (< 0.01)	79.1 (1.21)
CL 99843	ND	ND	2.9 (< 0.01)	11.3 (0.17)
CL 99875	ND	1.90 (< 0.01)	ND	ND
Terbufos (CL 92100)	9.50 (< 0.01)	2.10 (< 0.01)	ND	ND
Percent of TRR (mg/kg) HPLC Method II				
Unknown B	3.1 (< 0.01)	ND	ND	17.48 (0.22)
Unknown C	18.7 (< 0.01)	2.36 (< 0.01)	25.5 (< 0.01)	58.4 (0.75)
Unknown D	ND	17.3 (0.014)[d]	ND	14 (0.20)
Unknown E	ND	5.39 (< 0.01)	3.6 (< 0.01)	4.66 (0.07)
Unknown F	ND	0.88	ND	

Data are from a goat treated with [^{14}C]terbufos at 3.41 mg/day (2.53 ppm in the diet Group C) for 7 consecutive Days

[a] From organic extract.

[b] From aqueous extracts.

[c] Unknown A contained several components based on HPLC Method II.

[d] More than one peak in this area.

The metabolism study indicated that when terbufos is administered to lactating goats, it is absorbed, detoxified and eliminated (see 2003 JMPR Toxicological Evaluation on rat metabolism) predominantly in the urine. Neither terbufos nor any of the phosphorylated oxidative metabolites were observed in milk. None of the phosphorylated oxidative metabolites were detected in tissues, however, terbufos was observed at low concentrations in liver (< 0.01 mg/kg) and in kidney (< 0.01 mg/kg).

Small amounts (< 0.01 mg/kg) of unchanged terbufos, and the non-phosphorylated metabolites (CL 202474, CL 99843, CL 99875), were detected. The presence of terbufos, and possibly free and/or protein-bound non-phosphorylated metabolites (CL 99843, CL 99875, CL 202474), indicated terbufos was extensively metabolized. Hydrolysis of the thiolophosphorus bond (P-S) followed by enzymatic S-methylation, desulfuration, and sulfoxidation occurred in the metabolism of terbufos in goats. The proposed metabolic pathway of terbufos in goats is presented in Figure 3.

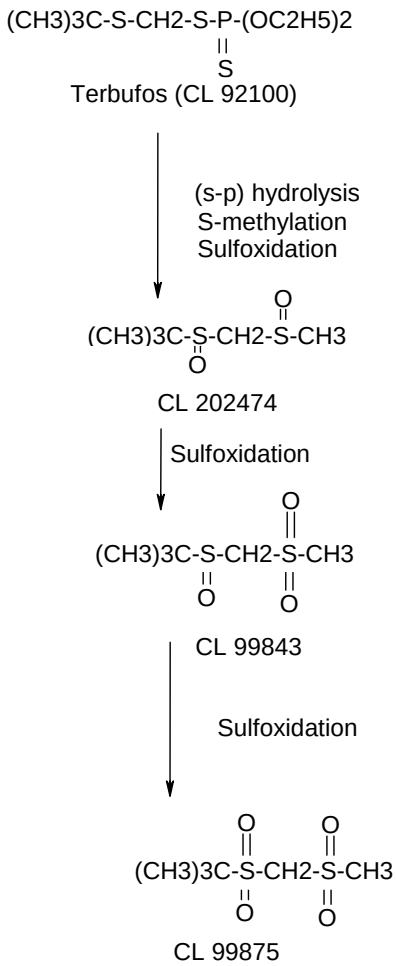


Figure 3. Proposed metabolic pathway of terbufos in lactating goat.

Metabolism in hens

A hen metabolism study (TE-440-003) was conducted by Brindle, P. (1990) to determine the residue levels as well as the nature of terbufos (CL 92100)-derived residues in the eggs, blood and edible tissues of laying hens following administration of highly exaggerated levels of [^{14}C]terbufos.

Five groups of DeKalb XL White Leghorn hens, each hen about 46 weeks old and weighing approximately 1.5 kg, were used as test animals. Three groups of five hens, A, B and C, were dosed via capsule for five consecutive days with the feed equivalent of 0 mg/kg (control), 0.35 mg/kg, and 1.05 mg/kg [^{14}C]terbufos, respectively. Two groups of ten hens, D and E, both dosed at 1.05 mg/kg with high specific activity of [^{14}C]terbufos were included in the study for use in metabolite identification and residue method validation work, in the event that the total residues exceeded the validated detection limit of the radioassay. The specific activity of the test substance used for the preparation of capsules for Groups B and C was 0.9 µCi/mg, and 30.2 µCi/mg (containing the ^{13}C-mass marker) for Groups D and E, respectively.

Recovery of [^{14}C]residues in excreta over the 5-day treatment period averaged 91.4% of the total administered dose for Group B, and 88.9% for Group C, respectively. For both dose levels, residues in eggs (days 1 through 5, both white and yolk), blood, skin with adhering fat, muscle, liver or kidney tissues were all less than the validated detection limit of the radioassay (< 0.05 mg/kg). Since the number of eggs collected from Groups B and C on the last day of the study were limited, the eggs produced on days 4 and 5 of treatment from Groups D and E were analyzed and the results provided additional evidence that total residues were < 0.05 mg/kg in both egg white and yolk.

Plant Metabolism

The metabolic fate of [^{14}C]terbufos in plants was studied in soybeans, sugar beet, sweet corn, cabbage and rape.

Metabolism in soybeans

In the soybean metabolism study (TE-640-001), by Chiu, T. (1981), plants were grown under field conditions from seed treated in the furrow at a rate of 1.1 kg ai/ha with [methylene-^{14}C]terbufos (specific activity of 18.4 µCi/mg, radiopurity of 98.6%). The [^{14}C]terbufos was diluted two-fold with non-radioactive standard compound (99% purity) resulting in a specific activity of 9.2 µCi/mg. This material was then formulated as 15G by dissolving 103 mg of the compound in 1 mL of dichloromethane and mixing with 585 mg of the formulation reagent consisting of 27.5 mg of Deactivator A mixed with 557.5 mg of Creek-O-Nite granules.

A 1.22 x 1.22 metres plot fenced with the chicken wire and set up with two furrows, each 1.22 metres in length and spaced 0.76 metres apart, was used for planting soybeans. The furrows were about 1.3 to 2.6 cm. in depth and were evenly treated with the formulated material. The seeds were planted about 1 inch apart in the furrow and covered with the top soil. The soybean plants of Adelphi variety were grown in Princeton sandy loam soil under the natural field conditions at the Agricultural Centre in Princeton, New Jersey.

The total radioactive residues (TRR) found in the plant, expressed as mg/kg equivalents of terbufos, were 13.3 mg/kg and 1.5 mg/kg in plants at one and two months after the treatment, respectively. At harvest, residue levels were 1.8 mg/kg in fodder, 1.6 mg/kg in hulls and 1.3 mg/kg in seeds (Table 5).

Table 5. TRR in soybeans grown in soil treated with [^{14}C]terbufos at 1.1 kg ai/ha.

Sample	Post treatment Interval (Months)	Residue (mg/kg)[a]
Control Plant	1	< 0.01
Treated Plant		13.3
Control Plant	2	< 0.01
Treated Plant		1.5

Sample	Post treatment Interval (Months)	Residue (mg/kg)[a]
Control Fodder	4[b]	< 0.01
Treated Fodder		1.8
Control Hull		< 0.01
Treated Hull		1.6
Control Seeds		< 0.01
Treated Seeds		1.3

[a] Expressed as terbufos equivalents.
[b]Harvest (normal maturity).

In the early stages of growth, 75% of the radioactivity was extractable from the plants. At the one-month sampling, 43% of the total extractable residue was identified as the phosphorylated metabolites CL 94,301 (sulfoxide), CL 94,302 (oxygen analog sulfone), CL 94,320 (sulfone) and CL 94,365 (oxygen analog sulfoxide).

Accounting for 11% of the residue were the non-phosphorylated metabolites CL 99,875 and CL 9,843. The remaining residue was comprised of five unknown metabolites (4%) and origin-bound compounds (17%). At harvest the only identifiable metabolite was CL 99,875, which was found in all three commodities, hulls (5%), fodder (2%) and seed (7%). The remaining residue was either shown to be very polar extractable materials or proven to have the carbon-14 incorporated into the cellulose and lignin of the hulls and fodder, and into the protein and oil of the seed.

The extractable radioactive residues from soybean fodder, hull and seed treated with [^{14}C]terbufos at 1.1 kg ai/ha and collected at 4-months post-treatment are summarized in Table 6 and Table 7. At harvest, the only identifiable metabolite in soybean seeds was CL 99,875 (Table 8).

Table 6. Extractability of radioactivity from soybean fodder and hull treated with [^{14}C]terbufos.

Fractions From Sequential Extraction	Percent Radioactivity	
	Fodder	Hull
1. Methanol	21.0	25.9
2. 2% Conc. HCl in 80% Methanol:H2O	13.3	32.5
3. 10% NaOH Reflux	37.7	30.9
a. Acid-Soluble at pH 1.0 [(a)]	(22.9)	(24.6)
b. Crude Lignin [(b)]	(7.8)	(6.3)
4. Crude Cellulose [(c)]	28.0	10.7
Total	100.0	100.0

[a] The filtrates of PES refluxed with 10% NaOH for 24 hours, followed by adjusting the filtrates to pH 1.0.
[b] The pellets were centrifuged after adjusting the 10% NaOH-soluble fractions of PES to pH 1.0.
[c] The filtered cake obtained from the 10% NaOH refluxed mixture, followed by washing with l0% NaOH solution and water.

Table 7. Extractability of radioactivity from soybean seed treated with [^{14}C]terbufos.

Fractions of Isolation	Percent Distribution in Various Fractions
1. Methanol: Dichloromethane (10:90; 300 mL x 2)	35.1
2. Methanol: Acetone (1:1; 300 mL x 2)	5.2
3. Concentrated HCl: Methanol (2:98; 300 mL x 2)	20.4
4. Soybean Seed PES [(a)]	39.3
Total	100.0

[a] The filtered cake obtained from the extraction with 2% concentrated HC1 in methanol.

Table 8. Metabolites identified in soybean seed treated with [^{14}C]terbufos.

Components	Fraction Analyzed[a,b]	
	Acetonitrile (0.17 mg/kg)	Hexane (0.36 mg/kg)
Oil	2.5 (0.03)	8.8 (0.12)
CL 99,875	4.2 (0.05)	2.7 (0.4)
Origin-Bound	6.1 (0.08)	12.5 (0.16)
Other Unknown	0.3 (<0.01)	3.2 (0.04)

[a] The results of TLC analysis of the combined extracts of solvent mixtures 1 and 2 (40.3%, Table 9), after partition into acetonitrile (13.1%) and hexane fractions (27.2%) accounting for 40.3% TRR (0.53 mg/kg) in seed.
[b] The total extractable residue expressed as [^{14}C]terbufos was 40% (0.53 mg/kg) of total residue of 1.32 mg/kg in soybean seeds. It was partitioned between acetonitrile and hexane. The calculated residue levels in mg/kg are shown in parenthesis.

Metabolism in sugar beet

In a sugar beet metabolism studies (TE-640-003 and TE-640-010) by, Caballa, S. (1973 and 1974), plants were grown from seed in soil treated with [^{14}C]terbufos at a rate of 6.8 kg ai/ha. The levels of radioactivity in both foliage and roots were determined at 4.5, 8, l6, and 32 weeks after treatment and were found to decline rapidly with time.

The total radioactive residues (TRR) found in the various samples declined with time from 6.27 mg/kg to 1.07 mg/kg in foliage and from 7.44 mg/kg to 0.284 mg/kg in roots (Table 9). This decline was primarily due to dilution from plant growth. The increase in the absolute amount of radioactivity recovered in the 32-week roots was due to the fact that the roots were mature and very big at this stage. The radioactivity recovered in all the plants represented a total of only 2.3% of the applied dose.

Table 9. TRR in sugar beets grown in soil treated with [^{14}C]terbufos at 6.8 kg ai/ha.

Sugar beet matrix	Time Post-Treatment (Weeks)	TRR (mg/kg)
Foliage	4.5	6.27
	8	3.38
	16	2.22
	32	1.07
Roots	4.5	7.44
	8	1.92
	16	0.295
	32	0.284

Extraction and partitioning data showed that metabolism of CL 92100 occurred at a faster rate in the roots. Chromatographic data obtained at different stages of plant growth indicated that terbufos is degraded mainly by way of oxidation, hydrolysis and methylation followed by subsequent oxidation to yield principally non-toxic metabolite CL 99875.

The concentration of various metabolites found is summarized in Table 10. In terms of mg/kg the values for the phosphorylated metabolites at 4.5 weeks were 4.2 mg/kg in the foliage and 1.2 mg/kg in the roots. At the end of 32 weeks, the major metabolite found was CL 99875, a non-phosphate compound. It is believed to be formed from the hydrolysis, subsequent methylation, and further oxidation of the analogs of terbufos. This compound accounted for nearly 95% (0.596 mg/kg) of the organosoluble radioactivity in foliage.

In the roots, the low levels of organosoluble radioactivity (0.007 mg/kg) were predominantly due to metabolite CL 99875 (0.0044 mg/kg). The decline in the amount of metabolites belonging to the phosphorylated series was accompanied by an increase of the metabolites in the methylated mercaptan series, mainly metabolites CL 99843 and 99875. These compounds have the same basic structure but different oxidation states, and are of very low toxicity. The LD_{50} in the mouse, for example, of metabolite CL 99875 is 4660 mg/kg compared with 3.5 mg/kg, for technical CL 92100. At 32 weeks, the concentration of phosphorylated compounds in foliage and roots was 0.004 mg/kg and 0.001 mg/kg, respectively.

There is evidence of incorporation of terbufos-derived radioactivity into the sucrose fraction of sugar beets. In the 16-week roots, 4.8% (0.014 mg/kg) of the total radioactivity was found in the purified sucrose fraction. Most of the aqueous-soluble activity (0.233 mg/kg) is believed to be due to soluble and insoluble natural products together with 13.2% (0.038 mg/kg) of unidentified water-soluble metabolites.

Table 10. Metabolites identified in sugar beets treated with [^{14}C]terbufos at 6.8 kg ai/ha.

Metabolite	Foliage (mg/kg)				Roots (mg/kg)			
	Time Interval (weeks)				Time Interval (Weeks)			
	4.5	8	16	32	4.5	8	16	32
CL 202474	0.0187	0.0189	0.011	< 0.001	0.0169	0.0014	< 0.001	< 0.001
CL 99844	0.0174	0.0194	< 0.001	< 0.001	0.0093	0.0015	< 0.001	< 0.001
CL 99843	0.0497	0.1714	0.0650	0.0136	0.0260	0.0093	< 0.001	< 0.001
CL 99875	0.0240	0.3754	0.7024	0.5962	0.0080	0.0256	0.0047	0.0044
CL 94365	0.2742	0.0930	< 0.001	< 0.001	0.0404	< 0.001	< 0.001	< 0.001
CL 94302	0.1129	0.0215	0.0014	0.0023	0.01490	0.0089	< 0.001	< 0.001
CL 94301	2.6014	0.0279	< 0.001	0.0014	0.6666	0.0162	< 0.001	0.0013
CL 94221	< 0.001	< 0.001	< 0.001	< 0.001	0.0180	< 0.001	< 0.001	< 0.001
CL 94320	1.1957	0.0343	< 0.001	< 0.001	0.3236	0.0339	< 0.001	< 0.001
CL 92100	0.0083	0.009	< 0.001	< 0.001	0.0081	< 0.001	< 0.001	< 0.001

Metabolism in sweet corn

In sweet corn metabolism studies (TE-640-005 and TE-640-006) by North H. *et al.* (1972) and Barringer, D. F. (1973), corn was grown in a Wisconsin greenhouse, in soil contained in metal cylinders and treated with [thiomethylene-^{14}C]terbufos at 1.1 kg ai/ha. Two high-dose tests were also conducted at 6.7 kg ai/ha, one in metal cylinders and the other one in plastic pots, to facilitate isolation and identification of metabolites. Plants from the low-dose tests were harvested at post-treatment intervals of 2, 4, 7 and 10 weeks by cutting the stem at the soil level. Sweet corn grown in soil treated with [^{14}C]terbufos at 1.1 kg ai/ha contained 0.34, 2.64, 4.70 and 6.85% of the applied dose at 2, 4, 7 and 10 weeks of growth, respectively, as shown in Table 11 .

Table 11. Recovery of ^{14}C-activity from sweet corn plants treated with [^{14}C]terbufos at 1.1 kg ai/ha.

Sampling Interval (week)	% Dose Recovered		Total % of Dose Accounted For
	Corn Plants	Soil	
2	0.336	-	-
4	2.64	50.4	53
7	4.70	41.5	46
10	6.85	33.2	40

Sweet corn was grown in a Wisconsin greenhouse soil treated with [thiomethylene-^{14}C]terbufos at 1.1 kg ai/ha.

Radioactivity extracted from plants separated into at least 19 radioactive metabolites on TLC. The metabolites found in sweet corn plants are shown in Table 12. The expected oxidation products of terbufos, i.e., the sulfoxide (CL 94,301), the sulfone (CL 94,320), the oxygen analog sulfoxide (CL 94,365) and sulfone (CL 94,302), were confirmed by two-dimensional co-TLC in the corn plant. In the 10-week corn plant, these phosphorylated metabolites accounted for 34 percent of the chloroform-soluble extractable radioactivity.

Table 12. Metabolites found in sweet corn plants grown in soil treated with [^{14}C]terbufos at 1.1 kg ai/ha.

Compound	Residues [%] of chloroform-soluble radioactivity			
	2 Weeks 0.88 mg/kg	4 Weeks 2.70 mg/kg	7 Weeks 2.87 mg/kg	10 Weeks 5.51 mg/kg
CL 94,302	2.5	3.9	6.3	5.6
CL 94,301	28	29.9	14.6	8.1
CL 94,221	0	0	0.52	0.3
CL 94,320	5.4	7.9	5.1	2.8
CL 94,365	12.7	13.7	19.2	16.9
Terbufos (CL 92,100)	0.5	0.4	0.18	0.073
Non-phosphorylated metabolites	52	44	53	66

The corn plants were extracted with methanol-acetone and methanol, and these extracts were subsequently partitioned into chloroform and water fractions. Results in this table are expressed as mg/kg equivalent of CL 92100 based on fresh plant

tissue weight, and in terms of % chloroform-soluble radioactivity, which accounted to 57%, 65%, 61 and 55% of the total radioactivity in corn plants harvested at 2, 4, 7 and 10 weeks.

The major metabolites in the 10-week old sweet corn plants grown in soil treated with [^{14}C]terbufos at 1.1 kg ai/ha (TE-640-006, Barringer, D. F.,(1973) are shown below in Table 13.

Table 13. Metabolites identified in corn plants grown in soil treated with [^{14}C]terbufos at 1.1 kg ai/ha.

Compound	Concentration (mg/kg)	% Recovered Radioactivity
Corn Plants (10 weeks post-treatment)		
CL 94365	0.515	26
CL 94301	0.260	13
CL 94302	0.179	9
CL 94320	0.095	5
CL 94221	0.009	0.4
CL 99875	0.666	34
CL 99843	0.173	9
CL 99844	0.043	2
CL 202474	0.007	4
CL 92100	0.002	0.1

Metabolism in cabbage

In the cabbage metabolism study (TE-640-004) by Peterson, R. (1976), cabbage plants were grown in the greenhouse and outside from seed in soil treated with [^{14}C]terbufos at a rate of 2.2 kg ai/ha, using both a 15G granular formulation and a liquid concentrate.

The concentration of radioactive residues found in the cabbage plants, expressed as mg/kg equivalent of terbufos, decreased with time (4 to 16 weeks) from 3.93 mg/kg to 0.09 mg/kg for outside granular treatment, from 1.48 mg/kg to 0.04 mg/kg for outside liquid treatment, and from 1.71 to 0.07 mg/kg for the greenhouse liquid treatment. This decline is primarily due to dilution from plant growth. The absolute amounts of radioactivity (in µCi) recovered in plants did not vary much with time.

The recovered radioactivity represented a maximum of 1.5% of the total applied dose. Terbufos is readily metabolized by cabbage plants by way of oxidation, s-p hydrolysis, methylation followed by subsequent oxidation to yield the non-toxic metabolites CL 202474, CL 99843 and CL 99875.

At the end of 12 weeks, 92% (0.07 to 0.22 mg/kg) of the total radioactivity consisted of unidentified water-soluble metabolites and the total amount of phosphate compounds were less than 0.01 mg/kg. There was no apparent metabolic difference between granular (15G) or liquid-treated soil in growing cabbage. The only notable difference in the total metabolic pattern of the entire study was the early appearance of metabolites CL 99843 and CL 99875 in the greenhouse cabbage at 4 weeks while none were evident in the outside grown plants at this early time.

The metabolism of terbufos in cabbage is similar to that reported in sugar beet (TE-640-003) by Caballa, S. (1974). The proposed metabolic pathway is presented in Figure 4.

Metabolism in rape seed

In a rape metabolism study (TE-640-007 by Chiu, T. Y. (1980)), rape was grown in soil treated with [^{14}C]terbufos in the furrow at 0.28 kg ai/ha. The total residual radioactivity in rape plants expressed in terms of parent was 0.63 mg/kg and 0.68 mg/kg for 1 and 2 month samples respectively. Residues were 0.42 mg/kg in the 2 month pods sample. At harvest (3 months post-treatment), the residue levels in fodder, hull and seed were 3.21, 3.63 and 1.11 mg/kg, respectively. The TRR found in various matrices of rape are summarized in Table 14.

Table14. TRR in rape after in-furrow treatment with [^{14}C]terbufos at 0.28 kg ai/ha.

Sample	Time Interval (Month)	TRR (mg/kg)
Plants	1	0.63
Plants	2	0.68
Pods		0.42
Fodder	3[a]	3.21
Hull		3.63
Seed		1.11

[a] Harvest (normal maturity).

The extractable radioactivity from the 1-month rape plant was 90%, of which 48% was organosoluble and 42% was aqueous soluble. By two-dimensional TLC analysis, about 16.3% of the radioactive organosolubles migrated away from the plate origin and the remaining 31.7% of the radioactivity stayed at the origin. Among the migrating radiocomponents, CL 99875 predominated with 4.9%, CL 94365 accounted for 4.0% and, CL 99843 and CL 94301 contributed 1.7 and 1.3% of the resolved organoextractables, respectively. The remaining 4.4% of the migrating radioactivity was composed of at least 6 minor components.

The extractability of rapeseed residues with dichloromethane followed by methanol was about 52%. The PES was further extracted with a methanol-water solvent system with mild heating, providing an additional 22.4% of extractable radioactivity. The acid-methanol extraction produced only 1.2% of the radioactivity, thus leaving 24.3% of the radioactivity in the seed PES.

The combined extractable radioactivity of seeds from dichloromethane and methanol extractions (52%) was partitioned and separated into hexane, acetonitrile and methanol fractions containing 22.0, 11.6 and 18.4% of the radioactivity, respectively. In the hexane fraction the chromatographic pattern indicated the majority of radioactivity migrating along with the oil, suggesting the incorporation of radioactivity into natural lipids. The TLC pattern from the acetonitrile fraction demonstrated that CL 99,875 (1.3%) and the oil-incorporated radio spots (5.5%) were the major components in this fraction. Several other radio-metabolites, such as CL 943,20, CL 94,301, CL 94,302, CL 99,843 and CL 94,365 were found in trace amounts each in this fraction.

The identified components found in the organosoluble fractions of plant and seed extracts are summarized in Table 15 and Table 16.

Table 15. Metabolites identified in rape forage treated with [^{14}C]terbufos at 0.28 kg ai/ha.

Identified Component	% of Organosoluble Radioactivity	% Total Radioactivity[a]	mg/kg[b]
CL 94320	1.7	0.816	0.005
CL 94301	2.7	1.296	0.008
CL 94302	0.6	0.288	0.002
CL 99875	10.2	4.896	0.031
CL 99843	3.5	1.68	0.011
-	2.4	1.152	0.007
CL 94365	8.4	4.032	0.025
-	0.5	0.24	0.001
-	2.3	1.104	0.007
-	2.0	0.96	0.006
Origin	65.7	31.68	0.2
Total	**100**	**48**	**0.303**

[a] Identified components from TLC of organosolubles of 1-month plant extract (48% of Total Radioactivity).
[b] Calculated level based on 48% (0.303 mg/kg) of total residue of 0.63 mg/kg in 1-month plant expressed as parent equivalents.

Table 16. Metabolites identified in rapeseed treated with [^{14}C]terbufos at 0.28 kg ai/ha

Components	Distribution of organosoluble metabolites in various solvents[a]		
	Hexane (22%)	Acetonitrile (11.6%)	Methanol (18.4%)
Oil	22	5.48	2.04
Origin-Bound	Trace	1.53	16.36
CL 99875	ND[b]	1.3	ND
CL 94301	ND	Trace	ND
CL 94302	ND	Trace	ND
CL 94320	ND	Trace	ND
CL 99843	ND	Trace	ND

[a] Radioactivity (52% of TRR) in the combined dichloromethane and methanol extracts of rapeseed (3-months post-treatment) after partition and separation into hexane, acetonitrile and methanol fractions.
[b] ND = Not Detected

Rape plants can readily absorb terbufos and closely related metabolites from the soil. The absorbed compounds are then initially metabolized in plant tissues by oxidation to phosphorylated metabolites, such as CL 94365 and CL 94301. These oxidized products degrade further through hydrolysis, methylation and subsequent oxidation thus leading to the formation of certain non-phosphorylated metabolites, such as CL 99843 and CL 99875.

In the present study, the total radioactivity in one-month old plants was composed of components (about 16%) which migrated on the TLC plate, components (74%) which were too polar to migrate, and 10% radioactivity which could not be extracted from the plant marc. The principal metabolites were identified as CL 99875 and CL 94365, accounting for 4.9% (0.031 mg/kg) and 4.0% (0.025 mg/kg), respectively.

In rape seeds, the hexane fraction comprised 22% of the radioactivity, which was probably associated with fatty acids or lipid-type compounds. The acetonitrile fraction, accounting for about 12%, mainly consisted of the oil-related compounds and CL 99,875 along with trace amounts of several other minor components. The proposed metabolic pathway of terbufos in rape is shown in Figure 4.

The hydrolysis study (TE-630-001 by Miller, P. (1973)), indicated that [methylene-^{14}C]terbufos was hydrolyzed to formaldehyde, whereas soil studies (TE-620-006 by North, H. (1973)) demonstrated the degradation of [^{14}C]terbufos to $^{14}CO_2$. Thus, in rape plants, it is likely that incorporation of carbon14-formaldehyde or $^{14}CO_2$ derived from [^{14}C]terbufos into natural products of various rape tissues accounts for a very large fraction of the radioactivity present in the plants or seeds.

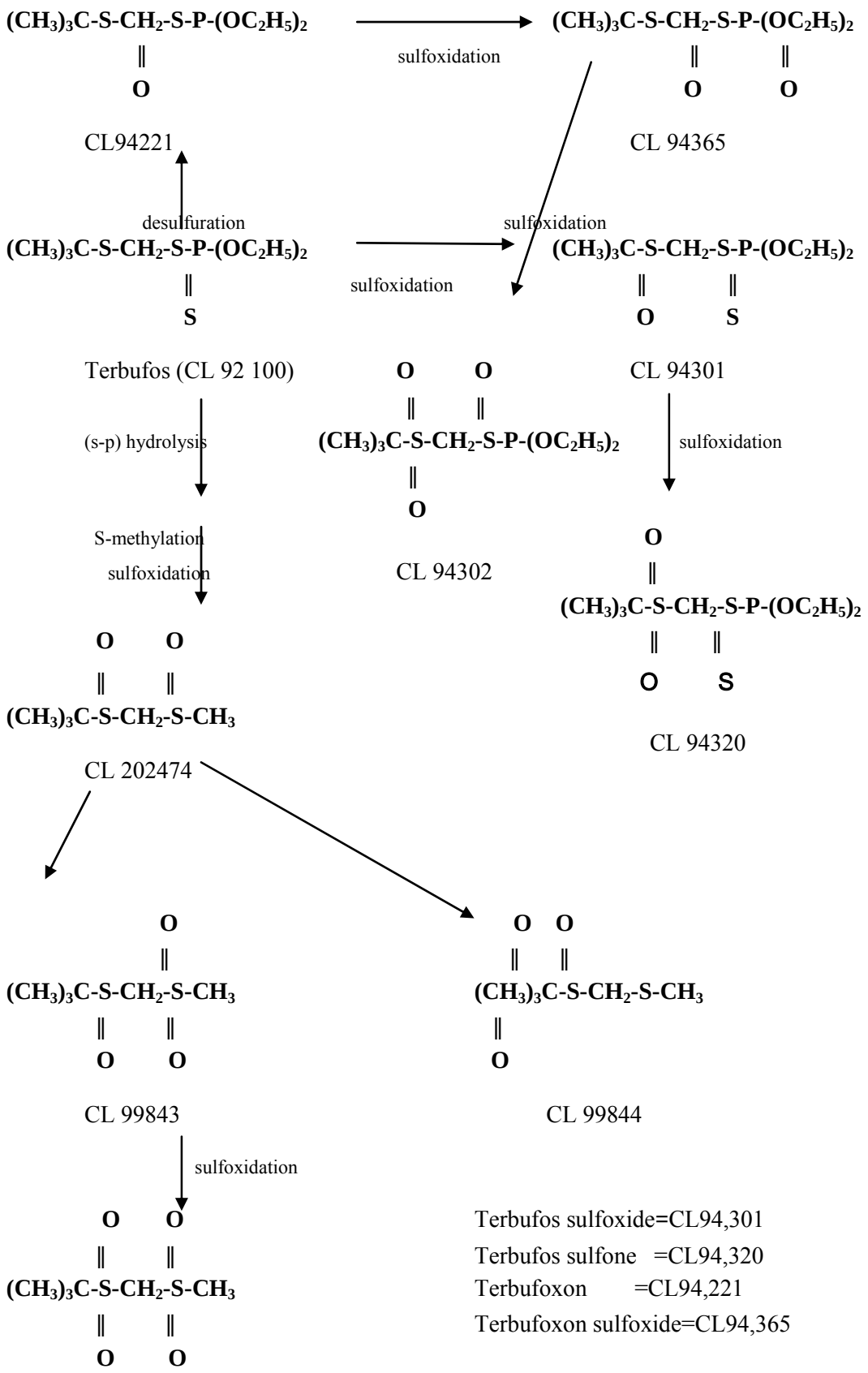


Figure 4 . Proposed metabolic pathway in plants.

Environmental Fate

Hydrolysis and biodegradation are the primary dissipation processes for terbufos in the environment when terbufos is incorporated into soil (US EPA, 1999). Under conditions favourable to microbial growth, the linear metabolic half-life in aerobic soil is approximately 27 days (5.6 days for nonlinear) and in anaerobic soil is 67 days (21 days for non-linear). Under abiotic conditions, the hydrolysis half-life is 12.3-13.7 days in the typical range of environmental pH values (pHs 5, 7, and 9).

The important metabolites terbufos sulfoxide and terbufos sulfone are more mobile and persistent than parent terbufos. The sulfoxide and sulfone half-lives are 116 and 96 days, respectively. These metabolites are also mobile in all tested soils and may reach ground water when terbufos is used in a location where irrigation or rain water moves through the soil profile to groundwater. In addition, terbufos and its metabolites may enter surface water as a result of run-off events.

Volatilization may be a major dissipation route for the portion of parent terbufos that remains on the surface of soil after incorporation. The relatively high vapour pressure (3.16×10^{-4} mm Hg) and observed Henry's Law Constant (6.58×10^{-3}) suggest that some of the parent compound will dissipate by diffusion into the atmosphere, but the amount that may volatilize will vary depending on the use site conditions and the mode of application.

Degradation in soil (aerobic)

The degradation route of methylene-^{14}C-Terbufos was investigated in silt loam soil in Wisconsin incubated under aerobic conditions for a period of 12 months (TE-620-004 by Peterson, R., 1983), ^{14}-C-Terbufos (specific activity 18.4 mcCi/mg and purity of 96.7%) in acetone was applied to 200 g of soil (wet weight basis) at a nominal rate of 5 mg/kg in the soil. Treated samples and controls were incubated in environmental control chambers maintained at an average temperature of 19 ± 2°C in the dark under continuous ventilation with moistened air. Systems were connected to gas washing bottles, containing ethylene glycol and monoethanolamine for collection of carbon dioxide and to trap radioactive volatiles from the reaction vessels.

Soil was sampled on days 0, 4, 7, 14, 30, 60, 120, 180, 270, and 365 post-treatment. Contents of the volatile traps and the carbon dioxide trap were also sampled at this time. To ensure efficient trapping of the carbon dioxide, a fresh portion of monoethanolamine was added to all remaining carbon dioxide traps at the 120-day sampling interval. The total of the 6, 9, and 12-month intervals was the sum of the two traps. All soil samples were either extracted immediately or stored at approximately 0°C until analysis.

Samples from all time points were extracted three times, first with aqueous methanol, next with methanol, and the third with 0.5% hydrochloric acid in methanol. After each extraction, the sample was vacuum filtered and rinsed with methanol and radioactivity was quantified in each filtrate by liquid scintillation counting (LSC).

The first two extracts were combined because they contained the majority of the radioactivity and after dilution with water, were partitioned into dichloromethane. As the sampling progressed, the amount of radioactivity increased in the acid extracts. Those extracts were partitioned separately with dichloromethane. All dichloromethane fractions were dried, concentrated, and analysed by thin layer chromatography (TLC).

Thin layer chromatography was performed on the various extracts, which were compared to the Rf values obtained from a series of TLC plates of the terbufos and metabolite standards. The standards were located by exposure to iodine vapours. The standard compounds appeared as brownish-yellow spots. The location of radioactive metabolites was by radioautography.

Based on the ^{14}C radioactivity present in the soil extracts, bound radioactivity and the volatiles, the mass balance for the applied radioactivity was determined to be in the range of 93 to 108

% of the applied dose of 5 mg/kg over the 365-day test period (Table 17). ^{14}C-carbon dioxide levels rose from 1.8% of the applied dose at the 4-day interval to 46% at 365 days, indicating extensive degradation of the applied ^{14}C-terbufos. Volatile organic components were found only at trace levels with a maximum of 0.5% of the applied dose found in the last sampling interval.

The distribution of dichloromethane-soluble ^{14}-C components of the combined aqueous/methanol and methanol soil extracts is presented in Table 18. Degradation of terbufos is quite rapid with a half-life of approximately 5 days. After 30 days, 4% of the applied dose remained as terbufos (CL 92,100) and after 365 days only 0.4% remained. The two major oxidative metabolites found were terbufos sulfoxide (CL 93, 201) and terbufos sulfone (CL 94,320). Concentrations of these metabolites decreased steadily until 365 days, when 0.3 g/kg of the sulfoxide and 0.1 mg/kg of the sulfone remained. The half-life of total CL 92,100-related compounds was approximately 100 days with an equivalent of about 8% of the applied dose remaining after one year.

TLC analyses of the dichloromethane partitioning phases of 60 and 120 day acid-methanol extracts showed only trace levels of terbufos sulfoxide and sulfone. These compounds were probably incompletely extracted with the first two extractions or slightly bound by the soil. No other unexpected metabolites were found in this fraction.

The presence of terbufoxon (oxygen analogue of terbufos) and terbufoxon sulfoxide were detected only at several early sampling intervals and never exceeded 0.04 mg/kg. Terbufoxon sulfone was not detected at all.

Table 17. Percent of applied dose of 5 mg/kg ^{14}C-CL 92,100 in aerobic soil at indicated time intervals.

Fraction	0-Day	14-Day	30-Day	120-Day	180-Day	270-Day	365-Day
Extract 1 (aqueous/methanol)	107.4	79.2	70.6	53.8	46.6	38.5	18.0
Extract 2 (methanol)	0.1	0.9	0.9	0.8	2.9	0.9	0.7
Extract 3 HCL/methanol	0.1	3.4	5.6	7.0	7.0	10.2	6.5
Soil Marc (air dried)	0.1	3.5	4.6	10.0	11.1	12.2	21.4
Volatiles (traps)	-	0.1	0.1	< 0.1	< 0.1	0.1	0.5
Carbon dioxide (trap)	-	9.0	13.5	22.0	25.3	33.6	45.9
TOTAL	**107.7**	**96.1**	**95.3**	**93.6**	**92.9**	**95.5**	**93.0**

Table 18. Nature and distribution of CL 92,100 and its metabolites in dichloromethane rextracts[1] of aerobic soil at various times.

Compound	0-Day		14-Day		30-Day		120-Day		180-Day		270-Day		365-Day	
	mg/kg[2]	%[3]	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%	mg/kg	%
CL 92,100	4.31	86.2	0.77	15.4	0.21	4.1	0.03	0.6	0.04	0.8			0.02	0.38
CL 94,301	0.31	6.2	2.55	50.9	2.62	52.3	1.47	29.4	1.24	24.7	0.88	17.7	0.29	5.9
CL 94,320			0.40	8.1	0.53	10.5	0.85	17.0	0.71	14.3	0.60	12.0	0.11	2.3
CL 94,221	0.04	0.8												
CL 94,365			0.02	0.4										
CL 94,302														
TLC origin	0.02	0.4	0.01	0.2	0.01	0.1	0.02	0.4	0.01	1.2	0.01	0.1	0.01	0.1
Unknowns[4]			0.03	0.6	0.03	0.6	0.08	1.6	0.08	1.5	0.06	1.2	0.07	1.4
TOTAL	**4.68**	**93.6**	**3.78**	**75.6**	**3.4**	**67.6**	**2.45**	**49.0**	**2.08**	**42.5**	**1.55**	**30.9**	**0.49**	**10.1**

[1] Soil extracts 1 and 2 were combined, diluted with water and extracted with dichloromethane.
[2] mg/kg of chemical in soil as calculated from the amount found in dichloromethane phase.
[3] Percent of applied dose based on mg/kg found divided by 5 mg/kg (applied dose).
[4] No individual compound was greater than 0.1% of applied dose.

Hydrolysis Rate and Products

The hydrolysis of ^{14}C-terbufos in sterile water at a pH of 5, 7, and 9 demonstrated that greatest stability occurs at pH 9, with a half-life for terbufos of 8.5 days (TE-630-001 by Miller, P., 1973). At a pH of 7 and 5, the half-life is 5.5 and 4.5 days respectively.

At the conclusion of a four-week study, 75.1, 72.4, and 68.3% of the radioactivity at pH 5, 7, and 9, respectively, was hydrophilic, with formaldehyde constituting the principal degradation product. Organophilic products consisted of the phosphorylated series of oxidative metabolites.

The existence of the principal hydrolysis products was demonstrated. Tert-butyl mercaptan and 0,0-diethylphosphorodithioic acid were converted to their benzyl derivatives with benzyl chloride and identified by mass spectrometry. Formaldehyde was converted to its 2,4-dinitrophenylhydrazone and identified by coincident thin-layer chromatography with an authentic standard.

The hydrolysis of ^{14}C-terbufos (CL 92,100), ^{14}C-terbufos sulfoxide (CL 94,301), and ^{14}C-terbufos sulfone (CL 94,320) in sterile buffer systems was studied under laboratory conditions (TE-630-005 by Marin, C. and Heim, D., 1999). Three buffers (pH 5, 7, and 9) and three temperature regimes (varying for each test substance and pH) were used to study the hydrolysis behaviour.

Hydrolysis of terbufos was strongly temperature dependent, and its rate of hydrolysis also increased slightly as the pH increased. Formaldehyde was the primary degradation product formed. Hydrolysis of terbufos sulfoxide and terbufos sulfone was strongly temperature and pH dependent. At pH 5 and pH 7, major degradates were des-ethyl terbufos sulfoxide, des-ethyl terbufos sulfone, and formaldehyde. Formaldehyde was the primary degradate at pH 9 for terbufos sulfoxide and terbufos sulfone systems.

The degradation pathways of terbufos sulfoxide and terbufos sulfone were pH dependent at elevated temperatures with de-esterification being the predominant reaction at pH 5 and 7, but only a minor reaction at pH 9.

Terbufos hydrolyzes rapidly under abiotic conditions at environmentally relevant temperatures and will not be expected to persist in aquatic systems. Hydrolysis of terbufos sulfoxide and terbufos sulfone occurs more slowly, but the des-ethyl derivatives that formed are not expected to be of toxicological concern.

The Arrhenius equation was used to estimate the DT_{50} values at 25° C. For terbufos, the hydrolysis half-lives at 25° C were estimated to be 1.20, 1.07, and 1.01 days for pH 5, 7, and 9 respectively. For terbufos sulfoxide, the hydrolysis half-lives at 25° C were estimated to be 239, 153, and 8.83 days at pH 5, 7, and 9 respectively. For terbufos sulfone, the hydrolysis half-lives at 25° C were estimated to be 127, 93.5, and 7.00 days at pH 5, 7, and 9, respectively.

Confined Rotational Crop Study

Confined rotational crop studies (TE-790-030 and TE-790-031) were conducted in Wisconsin and Nebraska by Lee, T and Belcher, D. (1984, 1986 a and b). Residues of CL 92,100-related compounds were determined in soil and rotational crops (cabbage, red beets, and wheat) from a treated corn field. In the study in Wisconsin, corn was planted in a silt loam soil and treated at planting with 2.24 kg ai/ha. After 30 days, the corn was destroyed and wheat, cabbage, and red beets were planted in the treated and untreated areas of the field.

At 127 days after treatment, cabbage was harvested, quartered, and stored within 2 hours at 0° C until shipment to the laboratory in about 4 months, where samples were frozen at -10° C to about -20° C until analysis about 14 months after sampling. Red beets and spring wheat were also harvested 127 days after treatment. Red beet tops were separated from roots and spring wheat heads and straw

were separated. Red beet and wheat samples were handled in the same manner as described for cabbage.

Soil samples were taken at 0-7.5 cm and 0-15 cm deep on the day of application, 33 and 127 days after treatment. The samples were stored at 0º C within 2 hours of sampling and handled as described for the plant samples.

The samples were analyzed using procedures described in Method M-1061 for soil, Method M-503 for cabbage, Method M-395 for red beets, and Method M-1592 for wheat straw and grain. Residues of terbufos-related compounds were analyzed using gas chromatography with flame photometric detection. Residues of CL-92,100 related compounds were less than the validated sensitivity of the method (0.05 mg/kg) in all cabbage, red beet and wheat grain samples. Wheat straw showed residues of 0.1 mg/kg. The soil half-life of CL-92,100-related compounds was calculated to be 30 days. Concurrent recovery tests were run with each group of samples to show that the analyses were performing properly throughout the study. For soils, they averaged 109% with a range of 88% to 140%. For cabbage, red beets roots, red beet tops, and spring wheat straw and heads, the recovery rates were 114%, 92%, 112%, and 102%, respectively. The results are summarized in Table 19 for soil and Table 20 for rotational crops.

In another study conducted in Nebraska, corn, planted in silt loam soil was treated at planting by soil incorporation with terbufos at the rate of 2.24 kg ai/ha (TE-790-031 by Lee, T and Belcher, D., 1986b). After 30 days, one area (Area I) of the corn was destroyed and planted with cabbage, sugar beets and wheat. At 130 days after treatment, cabbage and sugar beet samples were harvested and the samples frozen at -10°C within 2 hours of collection. The samples were shipped in dry ice and maintained frozen at -10 to -20°C until analysis about 14 months after sampling. Wheat green forage was harvested 69 days after treatment and wheat plants were harvested 95 days after treatment. The wheat samples were handled as described for cabbage and sugar beets.

One area of the originally planted corn (Area II) was harvested and planted with winter wheat. The wheat was allowed to mature and harvested 439 days after treatment. The samples were frozen and handled as described above for cabbage and sugar beets.

Soil samples were taken at 0-3 inches and 3-6 inches deep on the day of application, 30 and 125 days after treatment in the sugar beet and cabbage plots, and at day of treatment, 30, 69, and 97 days after treatment in wheat plots. Samples were handled as described for plant samples.

The samples were analyzed using procedures described in Method M-1061 for soil, Method M-503 for cabbage, Method M-395 for red beets, and Method M-1592 for wheat straw and grain. Residues of terbufos-related compounds were analyzed using gas chromatography with flame photometric detection. Residues of CL 92,100-related compounds were less than the validated sensitivity of the method (0.05 mg/kg) in all cabbage, sugar beet and wheat grain samples. Spring wheat forage showed residues of 0.15 mg/kg. No residues were detected in winter wheat straw and grain. The soil half-life of CL-92,100-related compounds was calculated to be 17 days in beet plots, 16 days in cabbage plots, and 10 days in wheat plots.

Concurrent recovery tests were run with each group of samples to show that the analyses were performed properly throughout the study. The average recoveries were 108% for soils, 80% for cabbage, 92% for beet roots and tops, 77% for spring wheat forage and heads, and 77% for winter wheat and grain. Results for both studies are summarized in Table 19 for soil and Table 20 for rotational crops.

Table 19. Summary of CL 92,100-related residues in soil.

Plot	Application rate (kg ai/ha)	Interval (days)	CL 92,100-Related Residues (mg/kg)			
			0 – 3”	3 – 6”	Average	Reference
	2.24	0	26.60	3.43	15.02	TE-790-030
	2.24	33	1.41	5.19	3.30	
	2.24	127	0.32	1.13	0.73	
Beet	2.24	0	7.70	4.02	5.86	TE-790-031
Beet	2.24	30	7.08	0.94	4.01	
Beet	2.24	125	0.06	< 0.05	0.06	
Cabbage	2.24	0	28.00	3.98	15.99	
Cabbage	2.24	30	15.70	0.38	8.04	
Cabbage	2.24	125	0.14	< 0.05	0.09	
Wheat	2.24	0	30.40	3.41	16.91	
Wheat	2.24	30	12.80	1.08	6.94	
Wheat	2.24	69	0.11	< 0.05	0.08	
Wheat	2.24	97	< 0.05	< 0.05	< 0.05	

Table 20. Summary of CL-92,100-related residues in rotational crops.

Commodity	Application rate (kg ai/ha)	Interval (days)	Residues (mg/kg)	Reference
Cabbage	2.24	127	< 0.05	TE-790-030
Red beet tops	2.24	127	< 0.05	
Red beet roots	2.24	127	< 0.05	
Spring wheat grain	2.24	127	< 0.05	
Spring wheat straw	2.24	127	0.10	
Cabbage	2.24	130	< 0.05	TE-790-031
Beet root	2.24	130	< 0.05	
Beet tops	2.24	130	< 0.05	
Spring wheat forage	2.24	69	0.15	
Spring wheat heads	2.24	95	< 0.05	
Winter wheat grain	2.24	439	< 0.05	
Winter wheat straw	2.24	439	< 0.05	

RESIDUE ANALYSIS

Analytical Methods

Plant Matrices

Several analytical methods have been developed for the determination of terbufos in plant commodities, which are suitable for data collection and some for enforcement (Table 21). Validation data are shown in (Table 22).

Similar data collection methods were used in the analysis of terbufos residues in or on crop commodities. All analytical methods for terbufos residues are designed to extract parent terbufos and its oxygenated metabolites: terbufos sulfoxide (CL 94301), terbufos sulfone (CL 94320), terbufoxon (CL 94221) and terbufoxon sulfoxide (CL 94365). Terbufos and its metabolites are oxidized to the common moiety metabolite of terbufoxon sulfone (CL 94302) using m-chlorobenzoic acid, which is then analyzed by gas chromatography. The methods vary slightly, usually in the extraction solvent used.

Residues of terbufos are extracted by blending, typically with methanol:chloroform (10:90, v/v), filtered, and then an aliquot of the filtrate is evaporated to dryness. The residue is reconstituted, or if necessary, is taken up in hexane and further cleaned by partitioning into acetonitrile before reconstitution. The residues are taken up in acetone, the solution treated with activated charcoal, filtered, and the solvent evaporated. For some substrates like maize, a charcoal/benzene treatment is used.

Residues are oxidized to terbufoxon sulfone using m-chloroperbenzoic acid. Excess reagent is destroyed with sodium sulfite. If further cleanup is necessary, the residue is dissolved in acetone and mixed with precipitating solution (aqueous 1.25 g/L ammonium chloride/2.1 g/L phosphoric acid). The filtrate from this solution is partitioned into the chloroform, which is evaporated and reconstituted in acetone. Final determination of terbufoxon sulfone is carried out on a gas chromatograph equipped with a phosphorus-selective detector, either flame ionization detector (FID) or a flame-photometric detector (FPD) in the phosphorus mode.

Table 21. Methods for the determination of terbufos in or on plant commodities

Method No.	Crop	Extraction	Detection Method	LOQ (mg/kg)	Reference
M-1340	Banana	10% Methanol in dichloromethane	GC/FPD	0.01	TE-244-005
M-3072	Banana	10% methanol in dichloromethane	GC/FPD	0.002	TE-244-025; TE 244-057
M-1360	Coffee	dichloromethane	GC/FPD	0.05	TE-244-015
M-1754	Maize	10% methanol in chloroform	GC/FPD	0.01 grain, 0.05 others	TE-244-049
M-336	Maize	10% methanol in chloroform	GC/FID ??	0.05	TE-244-054
M-1754	Sorghum	10% methanol in chloroform	GC/FPD	0.01 grain, 0.05 others	TE-244-049
M-995	Sorghum	10% methanol in chloroform	GC/FPD	0.05	TE-244-056
M 2457	Sugar beets[b]	10% methanol in chloroform	GC/FPD	0.01	TE-244-023
RLA10333V	Sugar beets[b]	10% methanol in chloroform	GC/FPD	0.05	TE-244-009
RLA-10156	Sugar beets[b]	10% methanol in chloroform	GC/FPD	0.05	TE-244-063
M-395	Sugar beets[b]	10% methanol in chloroform	GC/FID	0.05	TE-244-004, TE-244-064
M-1747	Sugar beets[a]	10% methanol in chloroform	GC/FPD	0.01	TE-244-007
M-336	Sweet corn	10% methanol in chloroform	GC/FPD	0.01 grain, 0.05 others	TE-244-054
M-1754	Sweet corn	10% methanol in chloroform	GC/FID	0.05	TE-244-049

[a] Methods for sugar beets (roots).
[b] Methods for sugar beets roots and tops.

The limit of determination for most of the reported trials was 0.05 mg/kg, but limits for some methods/substrates were 0.01 or 0.005 mg/kg. Recoveries of terbufos and its related metabolites were tested on all the sample types reported in the trials over the concentration range 0.01 – 1.0 mg/kg. Method validation data are summarized in Table 22.

Table 22. Validation of analytical methods for the determination of terbufos in plant products.

Crop	Method (Ref.)	Matrix [a]	Fort. Level (mg/kg)	% Recovery (Avg ± SD, Range, Number of Samples)[b]						
				All[c] Analytes	CL 92100	CL 94301	CL 94320	CL 94221	CL 94365	CL 94302
Banana	M 1340 (TE-244-005)	Whole banana	0.01, 0.5	93 ± 21 70-133 (n=8)					109 ± 19 79-140 (n=12)	
	M 1340 (PGD-183)	Whole banana	0.01	95 80-116 (%RSD= 14, n=5)						
			3.0	85 74-101 (%RSD= 13, n=5)						
		Banana pulp	0.01	125 117-135 (%RSD= 125,n=5)						

Crop	Method (Ref.)	Matrix [a]	Fort. Level (mg/kg)	% Recovery (Avg ± SD, Range, Number of Samples)[b]						
				All[c] Analytes	CL 92100	CL 94301	CL 94320	CL 94221	CL 94365	CL 94302
			3.0	80 73-92 (%RSD= 8, n=5)						
	M-3072 (TE-244-057)	Whole banana	0.002-0.02	84± 5.7 76 –89 n=6						
		Pulp	0.002-0.02	90 ± 5.5 83- 98 n=6						
Coffee	M 1360 (TE-244 -015)	Beans	0.05-0.5		114 ± 17 101-143 (n=6)				124 ±14 103-140 (n=8)	
Maize	M 1754 (TE-244 -049)	Dry plant	0.05-1.0	111 ± 22 86-137 (n=6)						
		Green plant	0.05-1.0	96 ± 4 90-102 (n=6)						
		Cannery waste	0.05-1.0	102 ± 17 85-133 (n=6)						
		Grain	0.01-0.2	97 ± 14 76-111 (n=6)						
	M-336 (TE-244-054)[e]	Silage	0.05-1.0		97 ± 20 71-130 (n=9)					110 ± 20 88-136 (n=6)
		Fodder (stover)	0.05-1.0		99 ± 32 68-134[f] (n=4)					90 ± 3 84-91 (n=5)
		Grain	0.05-1.0		101 ± 11 83-115 (n=9)					101 ± 14 83-118 (n=7)
Sorghum	M-995 (TE-244-056)	Grain	0.05-0.2		112± 22 90 – 136 n=4	88 ± 13 88 – 118 n = 4	109 ± 7 111 – 116 n = 4	102 ± 5 99 – 109 n = 4	105 ± 20 78 – 121 n=4	102 ± 11 92 – 114 n = 4
		Fodder	0.05-0.2		112 ± 10 97 – 118 n=4				110 ± 15 94 – 130 n=4	
		Silage	0.05-0.5		95 ± 19 73 –111 n=4				113 ± 14 93 – 125 n = 4	
Sorghum	M-1754 (TE-730-052)	Grain	0.01-0.4	105 ± 18 86 – 123 n=4						
		Forage	0.05-0.5	91 ± 5.0 86 – 96 n= 3						
		Fodder	0.05-0.50	80 ± 14 64 – 103 n=6						
Sugar Beet	M2457 (TE-244 -023)	Tops	0.01-0.2	76 ± 9 62-85 (n=8)						
		Roots	0.01-0.2	91 ± 21 56-128 (n=11)						

Crop	Method (Ref.)	Matrix [a]	Fort. Level (mg/kg)	% Recovery (Avg ± SD, Range, Number of Samples)[b]						
				All[c] Analytes	CL 92100	CL 94301	CL 94320	CL 94221	CL 94365	CL 94302
	M1747 (TE-244 -007)	Roots	0.01-1.0	84 ± 13 63-100 (n=12)						
Sugar Beets	M1747 (TE-244 -009)	Tops	0.05-1.0		89 ± 10 79-104 (n=5)					93 ± 10 83-106 (n=5)
	M-395 (TE-244 -004)	Roots	0.05-1.0		107 ± 15 84-133 (n=10)					84 ± 12 71-110 (n=11)
		Tops	0.05-1.0		100 ± 24 71-137 (n=11)					98 ± 19 62-130 (n=11)
Sweet corn	M1754 (TE-244 -049)	S. Corn K+C [d]	0.01-0.2	91 ± 17 69-116 (n=6)						
	M-336 (TE-244 -054)[e]	S. Corn (K+C)[d]	0.05-0.5		113 ± 11 101-120 (n=3)					100 ± 17 86-119 (n=3)

[a] Interferences in control samples were insignificant to none.
[b] All analytes fortified were converted by the method to the common moiety and detected as CL94301.
[c] Samples were fortified with terbufos, CL94301, CL94320, CL94221, CL94365, and CL94302, except for two validation studies on corn and sugar beets (TE-244-049 and -007) in which samples were fortified with a 1:1:1 mixture of terbufos, CL94301 and CL94365.
[d] K+C = Sweet corn kernel plus cob.
[e] Includes additional method validation recoveries provided in a field trial study report (TE-723-002).

Animal Matrices

All analytical methods for terbufos residues in animal tissues, milk, and egg are designed to extract parent, terbufos, and its oxygenated metabolites: terbufos sulfoxide, terbufos sulfone, terbufoxon, and terbufoxon sulfoxide. Terbufos and its metabolites are oxidized to the common moiety metabolite of terbufoxon sulfone using m-chlorobenzoic acid that is analyzed by GC. The methods vary slightly usually in the extraction solvent used. A brief description of the key points of the methods follows.

After extraction, the sample is filtered, and an aliquot of the filtrate is evaporated to dryness. Residues are oxidized to terbufoxon sulfone using m-chloroperbenzoic acid. The excess oxidizing agent is neutralized with sodium sulfite. The chloroform solution is evaporated and reconstituted in acetone. Final determination of terbufoxon sulfone is carried out on a gas chromatograph equipped with a phosphorus-selective detector, either flame ionization detector (FID) or a flame-photometric detector (FPD) in the phosphorus mode. Methods reported for the determination of terbufos in domestic animal commodities are shown in Table 23, with validation data in Table 24.

Table 23. Methods for the determination of terbufos and its metabolites in animal tissues.

Method Number (Reference Number)	Matrix	Extraction	Detection Method	LOQ (mg/kg)
M-372 (TE-705-002)	Cattle tissues	Acetonitrile	GC/FID	0.05
M-353 (TE-705-003)	Milk	Dichloromethane	GC/FID	0.01
M-1829 (TE-245-001)	Milk	CH_2Cl_2/acetone	GC/FPD	0.005
M-401 (TE-245-002)	Chicken tissues	Acetonitrile	GC/FID	0.05
M-396 (TE-705-001)	Egg	Acetonitrile	GC/FID	0.01

The LOQ for the milk method is 0.005 or 0.01 mg/kg, for the tissue methods, 0.05 mg/kg, and for the egg, 0.01 mg/kg. Recoveries of terbufos and its related metabolites were tested on the samples over the concentration range 0.005 – 1.0 mg/kg. Method validation data are summarized in Table 24.

Table 24. Validation of analytical methods for terbufos in animal products.

Matrix	Method (Ref.)[a]	Fort. Level (mg/kg)	Terbufos CL 92100	Terbufos Sulfoxide CL 94301	Terbufos Sulfone CL 94320	Terbufoxon CL 94221	Terbufoxon Sulfoxide CL 94365	Terbufoxon Sulfone CL 94302
Cattle								
Milk	M-1829 (TE-245-001)	0.005-1.0	88±12 67-110 (n=17)	95±6 87-101 (n=4)	---	---	---	---
	M-353 (TE-705-003)	0.01-0.50	79±13 58-97 (n=7)	---	---	---	---	88 ± 19 73-131 (n=7)
		0.10	71	74	98	100	78	73
Fat	M-372 (TE-705-002)	0.05-1.0	85±16 72-120 (n=7)	---	---	---	---	91 ± 19 71-126 (n=7)
		0.20	76	71	83	94	86	103
Kidney	M-372 (TE-705-002)	0.05-1.0	90±10 65-93 (n=7)	---	---	---	---	93 ± 16 69-110 (n=7)
		0.20	71	72	65	69	52	78
Muscle	M-372 (TE-705-002)	0.05-1.0	74±12 54-92 (n=8)	---	---	---	---	81 ± 11 65-96 (n=8)
		0.20	84	81	71	75	81	94
Liver	M-372 (TE-705-002)	0.05-1.0	70±10 60-81 (n=3)	---	---	---	---	95 ± 13 68-102 (n=5)
Poultry								
Fat	M-401 (TE-245-002)	0.05-1.0	80±19 58-100 (n=7)	---	---	---	---	101 ± 21 82-136 (n=7)
		0.2	94	86	95	105	104	86
Muscle	M-401 (TE-245-002)	0.05-1.0	84±10 67-94 (n=7)	---	---	---	---	93 ± 17 66-114 (n=7)
		0.2	67	74	101	98	93	85
Liver	M-401 (TE-245-002)	0.05-1.0	70±9 67-94 (n=7)	---	---	---	---	79 ± 18 48-109 (n=8)
		0.2	59	68	88	92	60	64
Skin	M-401 (TE-245-002)	0.05-1.0	85±10 72-98 (n=7)	---	---	---	---	93 ± 9 84-108 (n=7)
		0.2	85	92	103	93	97	84
Kidney	M-401 (TE-245-002)	0.05-1.0	64±10 52-86 (n=11)	---	---	---	---	78 ± 6 71-86 (n=7)
		0.2	58	60	74	73	70	71
Egg	M-396 (TE-705-001)	0.1	71	70	67	69	74	73
		0.01- 0.5	82±17 60-111 (n=7)					93 ± 20 65-119 (n=7)
		0.1	71	70	67	69	74	73

[a] The results reflect the validation data generated/reported with the feeding studies with the exception of recovery data for methods M-1829 and M-401, which appeared in separate method validation studies.

Environmental Samples

Methods were also reported for the determination of terbufos in environmental samples. The methods for soil and water are shown in Table 25, with method validation data in Table 26.

The methods that have used in the analysis of terbufos residues in soil and water are designed to extract parent terbufos and its oxygenated metabolites, terbufos sulfoxide and terbufos sulfone.

One soil method, M-1638, also determines terbufoxon, terbufoxon sulfoxide and terbufoxon sulfone. The limit of determination for total residues or individual analytes is 0.01 or 0.05 mg/kg in soil and 0.001 or 0.0001 mg/kg in water. A brief description of the key points of all of the methods follows.

Residues in soil are extracted with 10% aqueous methanol and partitioned into dichloromethane (CH_2Cl_2). For the water method, residues are extracted with CH_2Cl_2. The CH_2Cl_2 is evaporated and the residue reconstituted in acetone. If further clean up is necessary, an aliquot is passed through a silica solid phase extraction cartridge. Final determination is carried out using GC/FPD in the phosphorus mode or, in the case of water method M-2623, GC equipped with a mass selective detector (MSD). Two water methods (M-1615 and M-1144) convert all terbufos residues to the common moiety, terbufoxon sulfone, using m-chloroperbenzoic acid.

Table 25. Methods for the determination of terbufos in soil and water.

Method No. (Reference No.)	Matrix	Extraction[a]	Detection Method	Analytes determined (LOQ)
M-1912 (TE-242-006)	Soil	10% MeOH:H_2O	GC/FPD	Terbufos, CL94301 and CL94320 (each at 0.05 mg/kg)
M-1784 (TE-242-003)		10% MeOH:H_2O	GC/FPD	Terbufos, CL94221, CL94301 and CL94320 (each at 0.05 mg/kg)
M-1638 (TE-242-001)		10% MeOH:H_2O	GC/FPD	The LOQ is 0.010 mg/kg for terbufos and terbufoxon (CL 94221), and 0.050 mg/kg for terbufos sulfoxide (CL94301) and sulfone (CL94320) and terbufoxon sulfoxide (CL94365) and sulfone (CL94302).
M-1644 (TE-243-007)	Water	CH_2Cl_2	GC/FPD	Terbufos, CL94301 and Cl94320 (each at 0.001 mg/kg)
M-2623 (TE-243-004)		CH_2Cl_2	GC/MSD	
M-1149 (TE-243-002)		CH_2Cl_2	GC/FPD	Terbufos, CL94301 and Cl94320 (each at 0.001 mg/kg)
M-1615 (TE-243-003)		CH_2Cl_2	GC/FPD	Total terbufos-related residues (0.0001 mg/kg)
M-1144 (TE-243-001)		CH_2Cl_2	GC/FPD	

[a] MeOH = methanol; CH_2Cl_2 = dichloromethane.

Table 26. Validation of analytical methods for the determination of terbufos in soil and water.

Matrix	Method	Fort. Levels (mg/kg)	All	Terbufos CL92100	Terbufos Sulfoxide CL94301	Terbufos Sulfone CL94320	Terbufoxon CL94221	Terbufoxon Sulfoxide CL94365	Terbufoxon Sulfone CL94302
Soil	M-1912 (TE-242-006)	0.05-10		90 ± 6 78-100 (n=20)	101 ± 4 96-108 (n=20)	98 ± 3 95-104 (n=20)			
	M-1784 (TE-242-003)	0.05-20		97 ± 3 92-101 (n=9)	102 ±7 92-109 (n=7)	99 ± 5 91-105 (n=7)	97 ± 3 91-101 (n=7)		
	M-1638 (TE-242-001)	0.01-15[a] 0.05-5[b]		90 ± 7 81-101 (n=10)	93 ± 7 79-101 (n=10)	102 ± 11 87-115 (n=8)	93 ± 10 83-106 (n=8)	90 ± 10 80-108 (n=8)	91 ± 9 81-110 (n=8)
Water	M-1644 (TE-243-007)	0.0001-0.1		109 ± 9 100-125 (n=8)	106 ± 7 100-118 (n=6)	103 ± 8 97-113 (n=6)			
	M2623 (TE-243-004)	0.0001-0.1		87±5 78-91 (n=6)	98±6 91-106 (n=6)	96±4 90-100 (n=6)			
	M-1149 (TE-243-002)	0.0001-0.1		91 ± 4 85-96 (n=6)	96 ± 20 62-119 (n=6)	98 ± 15 72-114 (n=6)			
	M-1615	0.0001-	100 ±						

Matrix	Method	Fort. Levels (mg/kg)	All	Terbufos CL92100	Terbufos Sulfoxide CL94301	Terbufos Sulfone CL94320	Terbufoxon CL94221	Terbufoxon Sulfoxide CL94365	Terbufoxon Sulfone CL94302
	(TE-243-003)	00.010	15 77-121 (n=12)						

[a] Range of fortification levels for terbufos and CL94221.
[b] Range of fortification levels for terbufos, CL94301, CL94320, CL94302 and CL94365.

Enforcement methods

An adequate method is available for enforcement of terbufos MRLs in or on plant commodities. The GC-flame ionization detection method for determining terbufos and its phosphorylated metabolites is described in PAM (Pesticide Analytical Manual), Vol.II as Method I. The hazardous reagent, benzene, is specified in this method. Method M-1754, a modification of Method I in PAM, substitutes acetone for benzene and dichloromethane for chloroform. This method underwent successful method validation trial by the Residue Analytical Laboratory and was forwarded by the US EPA to FDA (Food & Drug Administration) for revision of PAM Vol II.

Multiresidue method

Terbufos and its metabolites were taken through the US FDA Multiresidue Method protocols described in PAM Volume 1 with some success (TE-244-059 by Gross, J., 1990). Terbufos and its metabolites were not tested through Protocols A and B since these protocols do not pertain to organophosphates. Terbufos sulfoxide and terbufoxon sulfoxide did not pass Protocol C.

Since terbufos sulfoxide and terbufoxon sulfoxide did not chromatograph adequately with any of the four columns, they were not tested by Protocol D and Protocol E. The other metabolites terbufos sulfone, terbufoxon sulfone, and terbufoxon did perform well through Protocols D and E and could be determined by the GC multi residue method.

Table 27 summarizes recovery data under Protocol D for terbufos sulfone, terbufoxon, and terbufoxon sulfone using sugar beet roots as non-fat food representative. Recoveries were run in duplicate with 0.05 mg/kg and 0.10 mg/kg of each compound.

Under Protocol E, Florisil had shown good recoveries and correct elution for standards of heptachlor epoxide and endrin. Only Terbufos sulfone was found to elute with one of the Florisil elution systems (PAM I,252.12b-dichloromethane solvents) and even then, the compound split between the second and third elution fractions.

Corn grain was used as a fatty food and sugar beet roots as a non-fat food. In three out of four recoveries, terbufos sulfone split between the second and third eluates. Table 28 summarizes the recovery data.

Table 27. Summary of recovery data with sugar beet roots using Protocol D

Fortification level (mg/kg)	Terbufos sulfone CL 94320	Terbufoxon CL 94221	Terbufoxon sulfone CL 94302
0.05	110	102	137
0.05	101	100	123
Average	105	101	130
0.10	117	109	122
0.10	121	115	132
Average	119	112	127

Table 28. Summary of recovery data for Terbufos Sulfone using Protocol E.

Sample	Fortification level (mg/kg)	Sugar beet roots (% recovery)
Eluant 2	0.05	38.6
Eluant 3	0.05	47.4
Eluant 3	0.05	77.0
	Average	54.3
Sample	**Fortification level (mg/kg)**	**Maize grain(% recovery)**
Eluant 2	0.05	46.8
Eluant 3	0.05	42.8
Eluant 2	0.05	48.9
Eluant 3	0.05	40.7
	Average	44.8

Stability of pesticide residues in stored analytical samples

Frozen storage stability studies were conducted in a variety of substrates including corn (grain, forage, fodder), sugar beets (tops and roots), banana (whole and pulp), milk, soil, and water samples. Control samples were fortified with known concentrations of terbufos and then placed in frozen storage at approximately -10 C or less. The fortified samples were analyzed periodically for total terbufos-related residues using the same analytical method as that used for the residue field trial or processing samples.

Plant commodities

The stability of terbufos residues has been determined in freezer storage stability studies in the representative plant commodities of corn (grain, plants, straw); sugar beet (tops and roots); peanut nutmeat, and banana (unpeeled and pulp).

Control samples were fortified with a mixed standard of terbufos (CL 92100), terbufoxon sulfoxide (CL 94365), and terbufoxon sulfone (CL 94302), at a concentration of either 0.1 or 0.5 mg/kg. Banana pulp and whole fruit were fortified with a mixture of all six analytes identified as residues of concern: terbufos, terbufos sulfoxide (CL 94301), terbufos sulfone (CL 94320), terbufoxon (CL 94221), terbufoxon sulfoxide, terbufoxon sulfone. In addition, a recently conducted study on sugar beets used samples fortified with a mixed standard containing CL 94301, CL 94320, and CL 94221.

The samples were stored frozen (< 0–10° C) and then removed from storage at various intervals and analyzed for total residues of terbufos. The methods of analysis were the same as those used for data collection. The storage intervals investigated were selected to follow the same intervals and conditions as the field crop trials.

The storage stability results for the representative commodities are summarized in Table 29. Terbufos residues fortified in representative crop samples (root, grain, watery and oily commodities) were shown to be stable in frozen storage for at least 18 months.

Table 29. Terbufos storage stability in various frozen plant commodities.

Commodity	Fortification level (mg/kg)	Storage (°C)	Interval (Months)	Concurrent Recovery	% Survived	Survived, %, corrected for recovery[a]	Reference (Method)
Banana (whole)[b]	0.1	≤-10	0	79	74, 73	94, 92	RES-99-070 TE-326-015 (M 3072)
			3	84	71, 81	85, 96	
			6	108	108, 109	100, 101	
			12	101	91, 90	90, 89	
			18	79; 107	40, 103; 84, 101	51, 130; 79, 94	
Banana Pulp[b]			0	75	79, 81	105, 108	
			3	93	76, 72	82, 77	

Commodity	Fortification level (mg/kg)	Storage (°C)	Interval (Months)	Concurrent Recovery	% Survived	Survived, %, corrected for recovery[a]	Reference (Method)
			6	100	67, 79	67, 79	
			12	74	48, 61	65, 82	
			18	93; 102	51, 28 40,78	55, 30; 39, 76	
Corn Plants[c] (Forage)	0.5	approx. -10	0	96	96	100	C-3299 TE-326-014 (M-336)
			6	137	83	83	
			8	76	108	142	
			12	30	97	97	
			23	111	72	65	
			25	96	78	81	
Corn Fodder/ Straw[c]	0.5		0	90	90	100	C-3299 TE-326-014 (M-336)
			6	98	106	108	
			8	70	89	127	
			12	136	70	70	
			23	114	82	72	
			25	118	122	103	
Corn Grain[c]	0.1		0	130	130	100	
			5	60	68	68	
			8	61	95	95	
			12	74	69	93	
			21	109	119	109	
			25	74	99	134	
Sugar Beet Roots[c]	0.1	approx. -10	0	85	85	100	C-3298 TE-326-012 (M-395)
			5	78	77	99	
			8	99	107	108	
			13	78	92	118	
			22	95	97	102	
			24	123	87	87	
Sugar Beet Tops[c]	0.5		0	70	71	101	
			5	82	102	124	
			8	94	89	95	
			13	111	71	64	
			22	69	74	74	
			24	84	92	110	
Sugar Beet Roots[d,e]	0.2	< 0	0.6	89	89	100	RES-97-017 TE-326-007 (M-2457)
			1	87	78	90	
			3	96	91	95	
			6	88	70	80	
			12	93	77	83	
			18	102	67	66	
			24	90	61	68	
Sugar Beet Tops[d,e]	0.5	< 0	0.6	109	88	81	RES-97-017 TE-326-007 (M-2457)
			1	80	74	93	
			3	92	79	86	
			6	87	70	80	
			12	82	51	62	
			18	90	66	73	
			24	83	51	61	

[a] Corrected percent recovery determined by dividing the percent recovered by the respective concurrent recovery and multiplying by 100. (No corrections were made when concurrent recoveries were not in the acceptable range of 70-120%.)

[b] Samples were fortified with a mixed standard containing terbufos (CL 92100) and its metabolites, terbufos sulfoxide (CL 94301), terbufos sulfone (CL 94320), terbufoxon (CL 94221), terbufoxon sulfoxide (CL 94365), terbufoxon sulfone.

[c] Samples were fortified with a mixed standard of terbufos, CL 94365, and CL 94302.

[d] Samples were fortified with a mixed standard containing CL 94301, CL 94320, and CL 94221.

[e] The samples were not successfully analyzed until the 0.6 month interval due to a low concurrent recovery on the initial analytical run. Also note that the "% recovery" is the average of duplicate analyses of the same sample, except at 12-months when two additional (contingency) tops stability samples were analyzed

Animal commodities

The stability of terbufos residues in cold storage has been determined for milk. Control samples were fortified with a representative mixed standard of terbufos and terbufos sulfoxide (CL 94301) at a concentration of 0.05 mg/kg, stored in 1.7 – 3.3 °C and samples removed and analyzed at various intervals. The results are summarized in Table 30.

Table 30. Terbufos frozen storage stability in milk

Commodity	Fortification level (mg/kg)	Storage (°C)	Interval (Days)	Survived residue %	Study Reference
Milk	0.05	1.7 - 3.3	0 7 14	94 84 79	TE-245-001

Soil and Water

The stability of terbufos residues in frozen storage has been determined for soil and water. Control samples were fortified with a representative mixed standard of terbufos, terbufos sulfoxide (CL 94301), and terbufos sulfone (CL94320), at a concentration of 0.250 mg/kg for soil and 0.010 mg/kg for water. The samples were stored at 0°C, and the samples were later removed and analyzed at various intervals. Soil samples were stored in glass while water was stored in plastic. The storage stability results (Table 31) indicate that terbufos residues are stable in frozen water and soil for at least 4 and 24 months, respectively.

Table 31. Terbufos Storage Stability in Soil and Water.

Fortification level (mg/kg)	Storage (°C)	Storage Interval	Residue remained in Stored Sample (%)[a]			Reference Number
			Terbufos	CL 94301	CL 94320	
Soil						
0.25 (each analyte)	0	0 months	90 (96) 92 (98)	104 (100) 107 (103)	99 (98) 100 (99)	TE-326-006
		3 months	85 (93) 86 (95)	112 (109) 118 (115)	100 (100) 102 (102)	
0.25 (each analyte)	0	6 months	91 (82) 90 (81)	126 (107) 128 (108)	112 (94) 113 (95)	
		12 months	72 (80) 72 (80)	134 (126) 134 (126)	100 (100) 100 (100)	
		14 months	71 (78) 68 (75)	128 (128) 125 (125)	98 (99) 96 (97)	
		18 months	65 (71) 66 (72)	134 (128) 133 (127)	102 (98) 101 (97)	
		24 months	62 (65) 64 (67)	136 (121) 136 (121)	99 (93) 101 (94)	
Water						
0.01 (each analyte)	-23 to -29	0 weeks	102 [100][b] 107 [99]	106 108	103 106	TE-326-010
		1 week	93	107	103	
		2 weeks	69 [98] 67 [102]	NA[c] NA	NA NA	
		3 weeks	69 63	111 110	109 100	
		4 weeks	77 [100]	100	99	
		5 weeks	76	104	104	
		8 weeks	55 [96] 52 [96]	108 103	103 102	
		16 weeks	52 [83] 59	109 106	109 109	

[a] Soil and water samples were analyzed by GC methods M-1912 and M-1644, respectively.

[b] After losses of parent were observed (probably due to adsorption to the plastic) another set of water samples was fortified with terbufos alone and analyzed to determine whether water could be stored in glass containers and also to determine if terbufos was being oxidized to CL94301 or CL94320. The results for terbufos fortified in water and stored in glass bottles

are shown in brackets; all other results are for distilled water samples fortified with each analyte and stored frozen in plastic bottles.

[c] NA = Not analyzed.

USE PATTERN

Terbufos is a systemic and contact organophosphorous insecticide/nematicide. It is formulated as a granule for application to crops and soil. It is usually applied once at planting or as a subsequent side-dressing.

Terbufos is registered in a number of countries and the registered uses are listed in Table 32.

Table 32. Registered uses of terbufos.

Crop	Country	Form type	Conc.	Application method[a]	Rate kg ai/ha	Number of application.	PHI (days)
Banana	Australia	G	150 g/kg	In established plantations, granules are spread in soil around follower plant; In new plantations, granules are spread in soil around the plant at sowing	3 g ai/plant	4	--
Banana	Brazil	G	50 g/kg 150 g/kg		3-4 g ai/plant	3	3
Banana	Philippines	G	100 g/kg		2 g ai/plant	4	--
Banana	Mexico	G	50 g/kg; 150 g/kg		3 g ai/plant	2-3	--
Banana	Guatemala Belize Honduras Nicaragua Costa Rica Panama	G	100 g/kg 150 g/kg		3-4 g ai/mat	2 – 3	--
Banana	Chile	G	100 g/kg		15-20	-	60
Coffee	Brazil	G	50 g/kg; 150 g/kg	In 10 cm under soil at planting or in crown projection	1.5-3.0 g ai/plant up to 7.5 kg ai/ha	1	90
Coffee	Guatemala Belize Honduras El Salvador Costa Rica Panama	G	100 g/kg; 150 g/kg	Broadcast in small radius around plant	0.75-1.05 g ai/tree	2	60
Coffee Seedbeds[b]	Guatemala Belize Honduras El Salvador Costa Rica Panama	G	100 g/kg 150 g/kg	At transplanting	1.2 – 1.5 g ai/m^2	1	--
Maize	Australia	G	150 g/kg	In-furrow at planting	0.26-0.3	1	--
Maize	Brazil	G	50 g/kg; 150 g/kg	In-furrow at planting	1.95-2	1	--
Maize	Chile Nicaragua	G	100 g/kg	In-furrow or banded at planting	1.5-2	1	60
Maize	Guatemala Belize Honduras El Salvador	G	100 g/kg	In-furrow at planting	1-1.5	1	

Crop	Country	Form type	Conc.	Application method[a]	Rate kg ai/ha	Number of application.	PHI (days)
	Costa Rica Panama						
Maize	Mexico	G	50 g/kg; 150 g/kg	In-furrow at planting	1	1	60
Maize	USA	G	150 g/kg; 200 g/kg	Banded or in-furrow, or knifed-in	1.5	1	30 (forage)
Sorghum	Australia	G	150 g/kg	Ground at sowing	0.255 – 0.3	1	--
Sorghum	Guatemala Belize Honduras El Salvador Costa Rica Panama	G	100 g/kg	In-furrow at planting	1-1.5	1	
Sorghum	South Africa	G	150 g/kg	In-furrow at plating	4.95 g ai/100 m plant row	1	80
Sorghum	USA	G	200 g/kg	Knife-in, banded, at bedding or at planting	2.0	1	50 (forage) 100 (grain, fodder)
Sugar beet	Chile	G	100 g/kg	Banded; in-furrow/ground	1.5-2	1	60
Sugar beet	USA	G	150 g/kg; 200 g/kg	Banded, in-furrow, knifed-in at planting or post-emergence	2.2	1	110 (banded application) 150 (knifed-in application
Sweet corn	USA	G	150 g/kg; 200 g/kg	Banded or in-furrow, or knife-in	1.5	1	60 (for post-emergence use)

[a] All treatments are at-planting (at seeding or transplanting), except for established banana and coffee crops, and reflect outdoor or field use, with application to the soil.

[b] For seeder coffee (*almacigo* coffee in Costa Rica, Honduras, and Panama) the label also allows 1-1.5 g ai/m2, incorporated 8 days before watering or immediately after transplanting.

RESIDUES RESULTING FROM SUPERVISED TRIALS ON CROPS

Supervised field trials were reported for numerous commodities. Where multiple samples were taken from a single plot or multiple analyses conducted on a single sample, the average value is reported. Where results from separate plots with distinguishing characteristics such as different formulations, varieties or treatment schedules were reported, results are listed for each plot. Results from trials at ± 30% of application rate or ± 30% of PHI were considered as complying with the GAP.

Most of the trials were conducted in the USA, where application rates were expressed in ounces active ingredient per 1000 ft. row (oz ai//1000 ft row). The labels provide limited tables to convert these to equivalent lbs ai/acre. When not specified in the study, or when the row width was not indicated, the rate in lbs/acre was estimated assuming 20-inch row spacing and applying the equation below. The resulting lbs/A is converted to kg/ha by multiplying by 1.12.

$$\text{Lbs/A} = [(\text{oz} / 1000 \text{ ft row}) \times (43560 \text{ ft}^2/\text{acre})] \div [(1000 \text{ ft row}) \times (16 \text{ oz/lb}) \times (\text{row width (feet)})]$$

The following tables summarize information on residues resulting from supervised trials, where underlined residues are from trials according to GAP and were used to estimate maximum residue levels. Results have not been corrected for concurrent method recoveries unless indicated.

Classification	Table	Commodity	CCN
Assorted tropical and sub-tropical fruits, inedible peel	Table 33	Banana	FI 0327
Root and tuber vegetables	Table 34	Sugar beets	VR 0596
Fruiting vegetables other than cucurbits	Table 35	Corn-on-the cob; Corn kernels	VO 0447 VO 1275
Cereal grains	Table 36	Maize	GC 0645
	Table 37	Sorghum	GC 0651
Seeds for beverages and sweets	Table 38	Coffee beans	SB 0716
Fodder and forage of cereal grains	Table 39	Maize forage and fodder	AF 0645 AS 0645
	Table 40	Sorghum forage and fodder	AF 0651 AS 0651
Miscellaneous forage and fodder crops	Table 41	Sugar beet tops	AV 0596

Assorted Tropical and Subtropical Fruit – Inedible Peel

Banana (FI 0327)

Field residue trials were conducted on bananas in Australia, Costa Rica, Ecuador, Honduras, Panama, Philippines, and Mexico, the main banana producing areas of the world, between 1984 and 1997. For trials conducted in 1984-1990, terbufos (10% G or 15% G) was applied to the soil around the base of daughter or follower banana plants at a rate of 3–4 g ai/plant/ application. A total of 2-3 treatments with a maximum of 12 g ai/ plant were applied per year. Some trials exceeded these total number of treatments and/or maximum amount applied. In one trial, up to 20 g ai/plant/application was used. One sample from treated plots was collected at each sampling interval, stored frozen for a maximum of 11 months, and analyzed for total terbufos residues by GC/FPD method M-1340. The method has been successfully validated on whole bananas to a lower limit of 0.01 mg/kg (see Table 22).

In banana field trials from Mexico and Ecuador in 1997, a single broadcast soil application of terbufos (15% G) was directed to the base of the daughter plants at 4 or 8 g ai/mat (2× rate). Duplicate samples were collected at selected intervals, stored frozen (<-10°C) for a maximum of 11 months, and analyzed by method M-3072. Method M-3072 is essentially the same method as M-1340; however, it was validated at 0.002 mg/kg. The method has also undergone a successful independent laboratory validation (Study no. TE-244-057 by Zheng, S. and Gross, J. 1998, Table 22). Recoveries of terbufos-related residues fortified simultaneously in whole banana and pulp at 0.002 and 0.02 mg/kg were 66-121% (92 ± 11%, n=72), with only three recoveries outside the range of 70 to 120%. Details of the trials are presented in Table 33, where results of trials according to GAP are underlined

Table 33. Total terbufos residues in or on bananas.

Crop Report no. Location/Year/var.	Application			PHI days	Residues (mg/kg)			Reference Number
	Form.	Max no. of Appl. or g ai/yr	Rate g ai/plant		Whole	Peel	Pulp	
Central American GAP (Guatemala, Belize, Dominican Rep, Honduras, Nicaragua, Costa Rica, Panama): 10G or 15G, at a rate of 3-4 g ai/plant around follower plant at max of 2-3 applications or 12 g ai/ plant /year								
C-2793 Limon, Costa Rica, 1986 Grand Naime	10G	1	9	1 2 3	< 0.01 < 0.01 < 0.01			TE-714-001
C-2789 Coyoles, Honduras,1986 Giant Cavendish	10G	1	2	1 2 4 8 14 28	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01			TE-714-002
		1	6	1 2 4	< 0.01 < 0.01 < 0.01			

Crop Report no. Location/Year/var.	Application			PHI	Residues (mg/kg)			Reference Number
	Form.	Max no. of Appl. or g ai/yr	Rate g ai/plant	days	Whole	Peel	Pulp	
				8 14 28	< 0.01 < 0.01 < 0.01			
C-2706 Coyoles, Honduras, 1986 Giant Cavendish	10G	1	10	14 33 47 89	0.02 0.02 0.02 0.01	0.04 0.03 0.02 0.01	0.02 0.01 0.02 < 0.01	TE-714-003
C-2705 Limon, Costa Rica, 1986 Giant Cavendish	10G	12 (41 g ai/yr)	2-4	20 32 43 46 88 90	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01			TE-714-004
C-2704 Rio Frio, Costa Rica, 1985 Giant Cavendish	10G	1	20	27 35 48 95	0.02 0.03 0.02 0.01	0.03 0.05 0.05 0.02	< 0.01 0.02 0.01 < 0.01	TE-714-005
C-2674 Limon, Costa Rica, 1984 Giant Cavendish	10G	8 (32 g ai/yr)	4	18 44 104	0.02 0.01 < 0.01	0.02 0.02	< 0.01 0.01	TE-714-006
		9 (36 g ai/yr)	4	57	< 0.01			
C-2622.1 Limon, Costa Rica, 1984 Giant Cavendish	10G	6 (24 g ai/yr)	4	18 44	0.02 0.01	0.02 0.02	< 0.01 0.01	TE-714-007
		7 (28 g ai/yr 7 (28 g ai/yr)	4 4	60 59	< 0.01 < 0.01			
		4 (16 g ai/yr)	4	43	< 0.01			
C-2621 Limon, Costa Rica, 1984 Giant Cavendish	10G	1	3	89 114	0.02 0.01 < 0.01	0.02 0.01	0.02 < 0.01	TE-714-008
C-2493 Limon, Costa Rica, 1984 Giant Cavendish	10G	4 (16 g ai/yr)	4	4 43	< 0.01 < 0.01			TE-714-009
C-2438 Limon, Costa Rica, 1983 Valery	10G	1	3	14 28 60	0.02 0.01 < 0.01			TE-714-010
		1	6	14 28 60	0.02 < 0.01 < 0.01			
C-2792 Davila, Panama, 1986 Grand Naime	10G	1	9	1 2 4 7 13	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01			TE-714-011
C-2494 Guapiles, Costa Rica, 1984 Grande Naime	10G	4 (14 g ai/yr)	4 (2x)+ 3 (2x)	95	< 0.01			TE-714-012
C-2622 Limon, Costa Rica, 1985 Giant Cavendish	10G	6 (24 g ai/yr) 6 (24 g ai/yr)	4	18 44 105	0.02 0.01 < 0.01	0.02 0.02	< 0.01 0.01	TE-714-013
		7	4	59	< 0.01			

Crop Report no. Location/Year/var.	Application			PHI days	Residues (mg/kg)			Reference Number
	Form.	Max no. of Appl. or g ai/yr	Rate g ai/plant		Whole	Peel	Pulp	
		(28 g ai/yr)						
C-3136 Guapiles, Costa Rica, 1987 Giant Cavendish	10G	1	2.5	33 68 89	< 0.01 < 0.01 < 0.01			TE-714-015
C-3614 Coyoles, Honduras, 1989 Giant Cavendish	10G	1	8	7 14 21 28 42 56 70 84	0.01 0.02 0.03 0.02 < 0.01 < 0.01 < 0.01 < 0.01			TE-714-017
Australian GAP: 150 g /kg G, at a rate of 2-3 g ai/plant applied around follower plant at max of 4 applications or 12 g ai/year								
TRR-93-005, 006, 007, 008 Palmerston, Queensland, Australia,1992 Giant Cavendish	15G	3 (9 g ai/yr)	3	1 3 7 14 21 28 56		< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	TE-714-018, 019, 020, 021
TRR-93-005, 006, 007, 008 Palmerston, Queensland, Australia,1992 Giant Cavendish (cont'd)		3 (18 g ai/yr)	6	1 3 7 14 21 28 56		< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	TE-714-018, 019, 020, 021
Philippines GAP: 100 g/kg G at the rate of 2 g ai/plant and a maximum of 4 total application or 8 g ai/year								
TTR-86-012 Philippines 1986 Giant Cavendish	10G	1	2	16 30 58 86	< 0.01 < 0.01 < 0.01 < 0.01			TE-714-014
	10G	2 (4 g ai/yr)	2	1 3 5 7	< 0.01 < 0.01 < 0.01 < 0.01			
TTR-87-025 Philippines, 1987 Giant Cavendish	10G	1	3	9 16 23 30 58 87 113 156 176	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	TE-714-022
		2 (6 g ai/yr)	3	23 58 87 114 163 191	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01 < 0.01 < 0.01 < 0.01	

Crop Report no. Location/Year/var.	Application			PHI	Residues (mg/kg)			Reference Number
	Form.	Max no. of Appl. or g ai/yr	Rate g ai/plant	days	Whole	Peel	Pulp	
		3 (9 g ai/yr)	3	25 74 102	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	< 0.01 < 0.01 < 0.01	
TTR-86-011 Twin Rivers Philippines, 1986 Giant Cavendish	10G	1	3	16 30 58 86	< 0.01 < 0.01 < 0.01 < 0.01			TE-714-023
		1	6	16 30 58 86	< 0.01 < 0.01 < 0.01 < 0.01			
Ecuador (Central America GAP): 10G or 15G, at a rate of 3-4 g ai/plant around follower plant at max of 2-3 applications or 12 g ai/ plant /year								
RES 97-062 La Peana Ecuador, 1997 Valery	15G	1	4	2 4 7 14 28 45	< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002		< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002	TE-714-024
		1	8	2 4 7 14 28 45	< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002		< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002	
RES 97-063 Rio Verde, Ecuador, 1997 Cavendish	15G	1	4	2 4 7 14 28 45	< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002		< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002	TE-714-025
		1	8	2 4 7 14 28 45	< 0.002 < 0.002 < 0.002 0.003 < 0.002 < 0.002		< 0.002 < 0.002 < 0.002 0.003 < 0.002 < 0.002	
Mexican GAP: 150 g/kg G at the rate of 3 g ai/plant and a maximum of 2-3 applications or 9 g ai/year								
RES 97-064 Teapa, Mexico, 1997 Enano Gigante	15G	1	4	2 4 7 14 30 45	< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002		< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002	TE-714-026
		1	8	2 4 7 14 30 45	< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002		< 0.002 < 0.002 < 0.002 < 0.002 < 0.002 < 0.002	

Root and Tuber Vegetables

Sugar beets (VR 0596)

Field trials were conducted in the USA and Canada during 1972-1975 in which terbufos (15% G) was applied in-furrow or banded at 1.1–2.5 kg ai/ha (approximating GAP) and also at exaggerated rates

(4.0–12.3 kg ai/ha). Several tests also depicted sequential at-planting and post-emergence banded applications, typically reflecting exaggerated rates. Treated samples were collected at each sampling interval, stored frozen for a maximum of 22 months, and analyzed for total terbufos residues by method M-395. This method was successfully validated on roots at 0.05 mg/kg (Table 22).

Seven additional sugar beet trials were conducted in the USA during the 1986 and 1989 growing seasons. In 1986, terbufos (15% G) was applied at planting (banded, knifed-in, or in-furrow) at 2.2 kg ai/ha. A single treated root sample was collected at each interval, stored frozen for a maximum of 10 months and analyzed for total terbufos residues by method M-1747. This method has been validated on roots at 0.01 mg/kg (Table 22). Concurrent recoveries of terbufos-related residues fortified in roots at 0.01 mg/kg were 82–108% (92 ± 14%, n=3).

In the trials conducted in 1989, terbufos (15%G) was knifed in as a band at planting at 4.9 kg ai/ha, in excess of the current GAP. A single treated sample was harvested by hand at maturity, 150–180 days after treatment. The samples were placed in frozen storage for a maximum of 6 months at about -17°C, and were analyzed for total residues of terbufos using method M-395. As noted above, method M-395 has been validated on roots at 0.05 mg/kg (Table 22). Concurrent recoveries of terbufos-related residues (parent and CL 94302) fortified in roots at 0.1 mg/kg were 64–126% (92 ± 24%, n=6).

In more recent field trials from the USA (1994), terbufos (15%G) was applied as a band over the row to sugar beets 15–58 cm tall at 2.2 to 2.4 or 4.4–4.9 kg ai/ha. The lower rate reflects the maximum GAP rate. Sugar beet root samples were collected at each sampling interval, stored frozen (about -8°C) for a maximum of 8 months, and analyzed by method M-2457. The validated sensitivity for the method was 0.01 mg/kg for roots. Concurrent recoveries of terbufos-related residues (parent, CL94221, CL94301, CL94302, CL94320, CL94365) fortified simultaneously in roots at 0.01 to 0.60 mg/kg were 78–130% (93 ± 12%, n=18). Additional data from a method validation study on method M-2457 are presented in Table 22. The residue results for sugar beet roots are presented in Table 34.

Table 34. Terbufos residues in sugar beet roots

Report No. Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G (150g/kg) at the rate of 0.6 – 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for 150 days for knifed-in applications.								
C-3064	15G	In furrow	1	2.2	1.2	162	< 0.01	TE-724-064
TE-724-064		Knifed-in	1	4.9	3	162	< 0.01	
Colorado, USA, 1986		Banded	1	2.2	1.2	162	< 0.01	
Mono-Hy A4		Banded Post	1	2.2	1.2	134	< 0.01	
C-3065	15G	In furrow	1	2.2	1.2	141	< 0.01	TE-724-065
TE-724-065		Knifed in	1	4.9	3	141	0.02	
ND, USA, 1986		Banded	1	2.2	1.2	141	< 0.01	
Bush Johnson 19		Banded-Post	1	2.2	1.2	91	< 0.01	
C-3066	15G	In furrow	1	2.2	1.2	148	< 0.01	TE-724-066
TE-724-066		Knifed in	1	4.9	3	148	0.01	
Idaho, USA, 1986		Banded	1	2.2	1.2	148	< 0.01	
Betaseed 8654		Banded-Post	1	2.2	1.2	115	< 0.01	
C-3067	15G	In furrow	1	2.2	1.2	139	0.01	TE-724-067
Minnesota		Knifed in	1	4.9	3	139	0.03	
USA, 1986		Banded	1	2.2	1.2	139	0.01	
Bush Johnson 19		Banded-Post	1	2.2	1.2	120	< 0.01	
C-3366	15G	Knifed-in	1	5.0		150	< 0.05	TE-724-068
ND, USA, 1989								
UltraMono								
C-3367	15G	Knifed-in	1	5.0		180	< 0.05	TE-724-069
Nebraska, USA,1989								
ACH 164								

Report No. Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G (150g/kg) at the rate of 0.6 – 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for 150 days for knifed-in applications.								
C-3368 Idaho, USA,1989 WS88	15G	Knifed-in	1	5.0		153	< 0.05	TE-724-070
C-3369 California, USA 1989, Z-1	15G	Knifed-in	1	5.0		170	< 0.05	TE-724-071
C-667 Colorado, USA 1974, Mono-HY-1	15G	In-furrow Banded	1 1	2 4		190 190	< 0.05 < 0.05	TE-724-004
C-666 Wyoming, USA 1975, Mono-HY	15G	In-furrow	1 1 1	1 2 12		142 142 142	< 0.05 < 0.05 < 0.05	TE-724-005
		Post	1 1 1	1 2 12		116 116 116	< 0.05 < 0.05 < 0.05	
		Banded	1 1 1	1 2 12		142 142 142	< 0.05 < 0.05 < 0.05	
		Post	1 1 1	1 2 12		116 116 116	< 0.05 < 0.05 < 0.05	
C-665 Idaho, USA 1973	15G	Banded	1	2.2	1.3	152	< 0.05	TE-724-006
C-664 Idaho, USA, 1974 AH-A1	15G	Banded	1 1	1.1 2.2		168 168	< 0.05 < 0.05	TE-724-007
C-964 Manitoba, Canada 1975	15G	In-furrow	1	1.12		117	< 0.05	TE-724-012
C-916 Manitoba, Canada 1974	15G	In-furrow	1	1.12		117	< 0.05	TE-724-013
C-694 North Dakota, USA 1973/ American Crystal Hybrid #1	15G	Banded	1 1 1	2.2 4.5 9.0	1.35 2.7 5.4	155 155 155	< 0.05 < 0.05 < 0.05	TE-724-014
		In-furrow	1 1	2.2 4.5	1.35 2.7	155 155	< 0.05 < 0.05	
		Post	1 1 1	2.2 4.5 9.0	1.35 2.7 5.4	124 124 124	< 0.05 < 0.05 < 0.05	
		Banded + Post	2 2	4.4+2.2 4.4+4.4		124 124	< 0.05 < 0.05	
C-695 North Dakota, USA, 1974/ American . Crystal Hybrid #2B	15G	Banded	1 1 1	2.5 5.0 12.3	1.35 2.7 6.75	129 129 129	< 0.05 < 0.05 < 0.05	TE-724-016
		In-furrow	1 1 1	2.5 5.0 12.3	1.35 2.7 6.75	129 129 129	< 0.05 < 0.05 < 0.05	
		Banded + Post	2 2 2	2.5+2.5 2.5+4.9 2.5+12.3		118 118 118	< 0.05 < 0.05 < 0.05	
C-693 Michigan, USA, 1974/	15G	In-furrow	1 1	1.8 3.6	1.35 2.7	174 174	< 0.05 0.11	TE-724-017

Report No. Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G (150g/kg) at the rate of 0.6 – 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for 150 days for knifed-in applications.								
Monitor common			1	8.5	5.4	174	< 0.05	
		Banded	1	1.8	1.35	174	< 0.05	
			1	3.6	2.7	174	< 0.05	
			1	8.5	5.4	174	< 0.05	
C-668 Colorado, USA, 1973/ Mono-Hy-1	15G	Banded	1	2.2	1.36	157	< 0.05	TE-724-018
			1	4.5	2.7	157	< 0.05	
		Post	1	2.2	1.36	126	< 0.05	
			1	4.5	2.7	126	< 0.05	
			1	9.0	5.4	126	< 0.05	
		Banded + Post	2	4.5+2.2		126	< 0.05	
			2	4.5+4.5		126	< 0.05	
C-914 Manitoba, Canada, 1973	15G	Banded	1	1.1		114	< 0.05	TE-724-029
C-917 Manitoba, Canada 1971	15G	In-Furrow	1	1.1		126	< 0.05	TE-724-030
			1	1.1		133	< 0.05	
C-656 North Dakota, USA, 1972	15G	Banded	1	1.1		135	< 0.05	TE-724-048
			1	2.2		135	< 0.05	
		Post	1	1.1		119	< 0.05	
			1	2.2		119	< 0.05	
C-657 Wyoming, USA, 1972 Mono-Hi	15G	Banded	1	0.56		156	< 0.05	TE-724-049
			1	1.1		156	< 0.05	
			1	6.7		156	< 0.05	
C-696 Minnesota, USA, 1973 American Crystal Hybrid #13	15G	Banded	1	2.2		102	< 0.05	TE-724-050
			1	4.4		102	< 0.05	
			1	8.9		102	< 0.05	
			1	2.2		138	< 0.05	
			1	4.4		138	< 0.05	
			1	8.9		138	< 0.05	
		Post	1	2.2		73	< 0.05	
			1	4.4		73	0.11	
			1	8.9		73	0.28	
			1	2.2		109	< 0.05	
			1	4.4		109	< 0.05	
			1	8.9		109	0.06	
		Banded+Post	2	4.5+2.2		109	< 0.05	
			2	4.5+4.5		109	< 0.05	
RES-95-046 Idaho, USA, 1994 HM-WS91	15G	Banded, Post	1	2.24	1.2	50	< 0.01	TE-724-035
						70	< 0.01	
						90	< 0.01	
		Banded, Post	1	4.9	2.7	50	0.04	
						70	0.02	
						90	0.02	
RES-95-039 Michigan, USA, 1993 H23	15G	Banded, Post	1	2.2	1.2	50	0.02	TE-724-036
						70	< 0.01	
						91	< 0.01	
		Banded, Post	1	4.4	2.4	50	0.06	
						70	0.02	
						91	< 0.01	
RES-95-040 Nebraska, USA, 1994 HM 1605	15G	Banded, Post	1	2.2	1.2	50	0.02	TE-724-037
						70	< 0.01	
						90	< 0.01	
				4.4	2.4	50	0.01	
						70	0.01	
						90	< 0.01	

Report No. Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G (150g/kg) at the rate of 0.6 – 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for 150 days for knifed-in applications.								
RES-95-045 North Dakota, USA, 1994 ACH 192	15G	Banded, Post	1	2.4	1.3	50 70 90	< 0.01 < 0.01 < 0.01	TE-724-038
				4.6	2.5	50 70 90	0.03 0.01 < 0.01	
GAP, USA: 150 g/kg at the rate of 0.6 – 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for 150 days for knifed-in applications.								
RES-95-047 Minnesota, USA, 1994 ACH 192	15G	Banded, Post	1	2.2	1.2	50 70 90	0.03 < 0.01 < 0.01	TE-724-039
				4.4	2.4	50 70 90	0.04 0.01 < 0.01	

Fruiting vegetables other than cucurbits

Sweet Corn, Corn-on-the-Cob (VO 0447) and Kernels (VO 1275)

In trials in the USA in 1972 - 1974, terbufos granules were applied in the furrow or in a band at the time of planting at rates of 1.1 to 9.0 kg ai/ha. In 1986 terbufos granules were applied to the soil at planting in furrow or in a band, at post-emergence or at cultivation at a combined rate of about 6 kg ai/ha. One sample was collected at each sampling interval, stored frozen for a maximum of 9 months, and analyzed by methods M-336 (1973-1974) and M-1754 (1986). The methods have been validated on sweet corn (kernels + cob) at 0.05 and 0.01 mg/kg, respectively (Table 22).

The results of the field trials on sweet corn are shown in Table 35. Total terbufos residues in sweet corn from trials according to the GAP (grain/ kernels, ears, or kernels + cob) were non-detectable (< 0.01 or < 0.05 mg/kg,). Residues from trials at higher application rates were also non-detectable, except in three samples of kernel + cob in which residues were detected at a level of 0.01 mg/kg.

Table 35. Terbufos residues in sweet corn (corn-on the-cob).

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP USA: 15G formulation at the rate of 1.2 oz ai/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. For post-emergent applications, the PHI is 30 days for forage, and 60 days for corn-on-the cob								
C-417 Illinois, USA, 1972	15G	Banded	1 1 1	1.1 2.2 4.5		88 88 88	< 0.05 < 0.05 < 0.05	TE-723-002
California, USA, 1972	15G	Banded	1 1	1.1 2.2		90 90	< 0.05 < 0.05	
Illinois, USA, 1973	15G	In-furrow	1 1	1.1 1.1		78 76	< 0.05 < 0.05	
Oregon, USA, 1973	15G	In-furrow	1 1	2.2 4.5		111 111	< 0.05 < 0.05	
	15G	Banded	1	2.2 4.5		111 111	< 0.05 < 0.05	
Wisconsin, USA, 1973	15G	In-furrow Banded	1 1	1.1 1.1		71 71	< 0.05 < 0.05	

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP USA: 15G formulation at the rate of 1.2 oz ai/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. For post-emergent applications, the PHI is 30 days for forage, and 60 days for corn-on-the cob								
C--642	15G	In-furrow	1	1.2	1.2	105	< 0.05	TE-723-003
Illinois, USA, 1974 Super sweet								
C--635	15G	Banded	1					
				1.5		95	< 0.05	TE-723-005
Iowa, USA, 1974			1	2.9		95	< 0.05	
Silver Queen			1	5.8		95	< 0.05	
	15G	In-furrow	1	1.5		95	< 0.05	
			1	2.9		95	< 0.05	
			1	5.8		95	< 0.05	
C-632	15G	In-furrow	1	2.2		75	< 0.05	TE-723-014
Florida, USA, 1974				4.5		75	< 0.05	
Tobelle				9.0		75	< 0.05	
C-425	15G	Banded	1	1.1		113	< 0.05	TE-730-002
Colorado, USA, 1973								
C-639	15G	In-furrow	1	1.1	1.2	69	< 0.05	TE-730-003
Minnesota, USA, 1974			1	2.2	2.4	69	< 0.05	
			1	4.5	4.8	69	< 0.05	
	15G	Banded	1	1.1	1.2	69	< 0.05	
			1	2.2	2.4	69	< 0.05	
			1	4.5	4.8	69	< 0.05	
C-638	15G	In-furrow	1	1.1	1.2	85	< 0.05	TE-730-005
Virginia, USA, 1974 Silver Queen			1	2.2	2.4	85	< 0.05	
	15G	Banded	1	1.1	1.2	85	< 0.05	
			1	2.2	2.4	85	< 0.05	
C-3096	15G	In-furrow	2	4 + 2	2.4 + 1.2	68	< 0.01	TE-723-004
Wisconsin, USA, 1986 Commander			2	2 + 4	1.2 + 2.4	68	< 0.01	
C--3109	15G	In-furrow +	2	4 + 2	2.4 + 1.2	41	< 0.01	TE-723-006
Florida, USA, 1986	15G	POST	2	2 + 4	1.2 + 2.4	41	0.01	
Silver Queen						41	0.01	
		In-furrow +	2	4 +2	2.4 + 1.2	41	0.01	
		Post	2	2 + 4	1.2 + 2.4	41	< 0.01	
						41	< 0.01	
C-3093	15G	In-furrow	2	4 + 2	2.4 + 1.2	72	< 0.01	TE-723-036
New York, USA, 1986, Jubilee	15G	In-furrow	2	2 + 4	1.2 + 2.4	72	< 0.01	

Cereal Grains

Maize (GC 0645)

A number of supervised trials on maize were conducted from 1972–1996 in the USA. In trials conducted from 1972–1974 and 1981–1986, terbufos granules were applied to the soil at planting, either in furrow or as a band, at the rate of 1.1 to 1.8 kg ai/ha. In some trials, additional plots were treated with terbufos at rates up to 5 times the recommended label rates. In one trial, a treatment at 11 kg ai/ha was applied. In trials conducted from 1990–1996 terbufos granules were applied post-emergent at the recommended rate of 1.5 kg ai/ha as well as at higher rates up to five times the recommended application rates. Treated samples of maize grain were collected at intervals, and the samples were stored frozen (-10°C), for a maximum of 8 months, prior to analysis.

Residues of terbufos-related compounds were determined either by method M-336 or M-1754, which have been validated to lower limits of 0.05 and 0.01 mg/kg, respectively (see Table 22). Additional method recoveries of terbufos residues from studies conducted during 1990-1996 further demonstrated the suitability of method M-1754. In the trials performed in 1995-1996, concurrent recoveries of terbufos-related residues in maize grain fortified at 0.01-0.4 mg/kg were 65–114% (94 ± 12%, n=22). Additionally, concurrent recoveries of parent, CL94301, CL94302, CL94320, CL94221, and CL94365 fortified in grain at 0.01 or 0.4 mg/kg were 82–92% (88 ± 4%, n=4).

Table 36 summarize results of trials on maize grain, with residues according to GAP, underlined. Treatments according to the GAP resulted in residues below the limit of determination (< 0.01 or < 0.05 mg/kg, depending on the method used).

Table 36. Terbufos residues in maize grain.

Location/Year/ Variety	APPLICATION					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type[a]	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP USA: 15G or 20G formulation at the rate of 1.2 oz ai/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage if applied post-emergent.								
C-2082 North Carolina, USA 1981 Pioneer 3184	15G 20G 20G 20G	Banded Banded In-furrow In-furrow	1 1 1 1	2.2 2.2 2.2 2.2		148 148 92 148	< 0.05 < 0.05 < 0.05 < 0.05	TE-723-026
C-2215 Nebraska, USA, 1982 Stauffer 6595	15G 15G	Infurrow/ Banded	2 2	2.2 + 2.2 4.4 + 2.2		105 105	< 0.05 < 0.05	TE-730-018
C-3038 Illinois, USA, 1986 Hybrid Funks G4507	15G 20G	Banded Banded	1 1	2.24 2.24	2.4 2.4	181 181	< 0.01 < 0.01	TE-730-010
C-3037 Nebraska, USA, 1986 Pioneer 337	15G 20G	Banded Banded	1 1	1.12 1.12	1.2 1.2	147 147	< 0.01 < 0.01	TE-730-011
C-3095 Minnesota, USA, 1986/ Cargill 809	15G 15G	Banded+POST Banded+POST	2 2	4.4+ 2.2 2.2 + 1.2	2.2 + 1.2 4.4 + 2.2	120 120	< 0.01 < 0.01	TE-730-012
RES-95-059 Wisconsin, USA, 1994 Pioneer Hybrid 3861	15G	Banded, POST	1	1.5	1.2	60 80	< 0.01 < 0.01	TE-730-028
	15G	Banded, POST	1	3	2.4	60 80	< 0.01 < 0.01	
RES-95-058 Michigan, USA, 1994 Pioneer 3921	15G	Banded, POST	1	1.5	1.2	59 80	< 0.01 < 0.01	TE-730-029
	15G	Banded, POST	1	3	2.5	60 80	< 0.01 < 0.01	
RES-96-021 Iowa, USA, 1995 434 VARIETY	15G	Banded, POST	1	1.5	1.2	56 80	< 0.01 < 0.01	TE-730-030
	15G	Banded, POST	1	3	2.4	60	< 0.01	

Location/Year/ Variety	APPLICATION					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type[a]	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP USA: 15G or 20G formulation at the rate of 1.2 oz ai/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage if applied post-emergent.								
						80	< 0.01	
RES-96-022 Nebraska, USA, 1995	15G	Banded, POST	1	1.5	1.2	64 79	< 0.01 < 0.01	TE-730-031
Northrup King N3803	15G	Banded, POST	1	3	2.4	64 79	< 0.01 < 0.01	
C-3566 Iowa, USA, 1990 Circle seed #7111	15G 15G	Banded, POST Banded, POST	1 1	1.5 7.3	1.2 5.9	132 113	< 0.01 < 0.01	TE-723-032
C-3567 Iowa, USA, 1990 DeKalb DK535	15G 15G	Banded, POST Banded, POST	1 1	1.5 7.3	1.2 5.9	119 119	< 0.01 < 0.01	TE-723-033
C-3568 Illinois, USA, 1990 Dockendorf 7670	15G 15G	Banded, POST Banded, POST	1 1	1.5 7.3	1.2 5.9	109 109	< 0.01 < 0.01	TE-723-034
C-3569 Illinois, USA, 1990 Pioneer 3615	15G 15G	Banded, POST Banded, POST	1 1	1.5 7.3	1.2 5.9	109 109	< 0.01 < 0.01	TE-723-035
RES-96-084 Illinois, USA, 1996	15G	Banded, POST	1	1.5	1.2	60 80	< 0.01 < 0.01	TE-730-051
Pioneer 3751	15G	Banded, POST	1	3	2.7	60 80	< 0.01 < 0.01	
C-1129 Maryland, USA, 1974 DeKalb 264	15G	In-furrow	1 1 1	1.3 2.6 5.2		134 134 134	< 0.05 < 0.05 < 0.05	TE-730-008
C-416: Illinois, USA, 1973	15G	In-furrow	1	1.12		124	< 0.05	TE-730-016
Nebraska, USA,1973	15G	In-furrow	1 1 1	1.12 2.24 5.6		168 168 168	< 0.05 < 0.05 < 0.05	
ND, USA, 1973	15G	In-furrow	1 1 1	1.12 1.7 2.2		159 159 159	< 0.05 < 0.05 < 0.05	
Nebraska, USA, 1973	15G	In-furrow	1 1 1	1.12 2.24 5.6		162 162 162	< 0.05 < 0.05 < 0.05	
Iowa, USA, 1973	15G	In-furrow	1 1 1 1	1.12 2.24 5.6 11.2		135 135 135 135	< 0.05 < 0.05 < 0.05 < 0.05	
C-415 Indiana, USA, 1972	15G	In-furrow	1	1.12 1.7		146 146	< 0.05 < 0.05	TE-730-017
South Dakota, USA, 1972	15G	In-furrow	1	1.1		131	< 0.05	
Missouri, USA, 1972	15G	In-furrow	1	1.7		184	< 0.05	
Nebraska, USA, 1972	15G	In-furrow	1	1.12		168	< 0.05	
NC, USA, 1972	15G	In-furrow	1 1	1.12 1.12		143 148	< 0.05 < 0.05	
ND, USA, 1972	15G	In-furrow	1 1	1.12 2.24		159 159	< 0.05 < 0.05	
C-631 Minnesota, USA, 1974	15G	In-furrow	1	1.12		115	< 0.05	TE-723-013
C-636	15G	In-furrow	1	1.1	1.2	143	< 0.05	TE-723-016

Location/Year/ Variety	APPLICATION					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type[a]	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP USA: 15G or 20G formulation at the rate of 1.2 oz ai/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage if applied post-emergent.								
Minnesota, USA, 1974			1 1	2.2 4.5	2.4 4.8	143 143	< 0.05 < 0.05	
C-637 ND, USA, 1974 NK 420	15G	In-furrow	1 1 1 1	1.2 1.8 2.5 4.9	1.2 1.8 2.4 4.8	134 134 134 134	< 0.05 < 0.05 < 0.05 < 0.05	TE-723-017
C-640 Michigan, USA, 1974	15G	In-furrow	1 1 1	1.1 2.2 4.5	1.2 2.4 4.8	151 151 151	< 0.05 < 0.05 < 0.05	TE-723-018
C-641 Maryland, USA, 1974 DeKalb 264	15G	In-furrow	1 1 1	1.5 2.9 5.8	1.2 2.4 4.8	130 130 130	< 0.05 < 0.05 < 0.05	TE-723-019
C-644 Colorado, USA, 1974 NC +	15G	In-furrow	1 1 1 1	1.1 1.5 2.9 5.8	0.9 1.2 2.4 4.8	179 179 179 179	< 0.05 < 0.05 < 0.05 < 0.05	TE-723-021
C-647 Kentucky, USA, 1973 Pioneer 3369A	15G	In-furrow	1 1	0.84 1.1	0.9 1.2	142 142	< 0.05 < 0.05	TE-723-022

Sorghum (GC 0651)

Supervised trials were conducted from 1978–1996 in major sorghum-growing areas in the USA. In trials conducted in 1996, terbufos granules were applied to the soil in a band during the vegetative stages of the plant, at the rate of 2.0 – 2.2 kg ai/ha. Grain samples (approximately 1 kg) were collected 88 to 90 days after the last application, frozen (-10°C) and stored up to a maximum of 8 months until analysis. A freezer storage stability study on the related crop, corn or maize grain, showed that residues of terbufos-related compounds are stable in corn grain up to at least 24 months when stored at approximately -10°C (Table 29, study no. TE-326-014 by Dixon, C 1990).

Terbufos residues were determined by Method M-1754, using a gas chromatograph equipped with a flame photometric detector. The validated sensitivity of the method was 0.01 mg/kg for sorghum grain (see Table 22). The average concurrent recovery from field samples was 105%.

In trials conducted in 1978-1979 and 1986-1991, terbufos granules were applied to the soil at planting, either in-furrow, knifed-in, or in a band, at rates ranging from 2.0 to 4.3 kg ai/ha. Samples of sorghum grain were harvested from 95 to 150 days after the application, immediately frozen (-10°C), and stored until analysis. Total terbufos-related residues were determined by Method 995, which had previously been validated (Table 22). The validated sensitivity for the method is 0.05 mg/kg for sorghum grain.

Results for all the trials are summarized in Table 37, with residue values from trials according to the GAP, underlined. Treatments according to the GAP resulted in residues below the limit of determination (< 0.01 or < 0.05 mg/kg, depending on the method used).

Table 37. Terbufos residues in sorghum grain

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP USA: 15G formulation at the rate of 1.1 oz ai/1000 ft row or a maximum of 2.0 kg ai/ha applied once and a PHI of 50 days for forage, and 100 days for grain and fodder.								
RES-96-082 Missouri, USA, 1996 KS 714Y	15G	Banded (POST)	1	2.2	1.2	72 90	< 0.01 (2) < 0.01 (2)	TE-730-057
RES-96-078 Texas, USA, 1996 F-200	15G	Banded (POST)	1	2.2	1.2	59 76 90	< 0.01 (2) < 0.01 (2) < 0.01 (2)	TE-730-053
RES-96-077 Texas, USA 1996 F 200	15G	Banded (POST)	1	2.2	1.2	58 73 88	< 0.01 (2) < 0.01 (2) < 0.01 (2)	TE-730-052
RES-96-081 Illinois, USA, 1996 Northrup King 1210	15G	Banded (POST)	1	2.2	1.2	60 75 90	< 0.01 (2) < 0.01 (2) < 0.01 (2)	TE-730-056
RES-96-079 Louisiana, USA, 1996 DeKalb 37	15G	Banded (POST)	1	2.0	1.2	60 75 90	< 0.01 (2) < 0.01 (2) < 0.01 (2)	TE-730-054
RES-96-080 Kansas, USA, 1996 6R55E	15G	Banded	1	2.1	1.2	62 76 90	< 0.01 (2) < 0.01 (2) < 0.01 (2)	TE-730-055
C-1626 Kansas, USA, 1978	15G	Banded Banded In-furrow In-furrow	1 1 1 1	2.0 4.0 2.0 4.0	1.2 2.4 1.2 2.4	95 95 95 95	< 0.05 < 0.05 < 0.05 < 0.05	TE-730-039
C-1742 Texas, USA, 1978 Mitchell Standking Y	15G	Banded	1	4.0	2.4	150	< 0.05	TE-730-040
C-1752 Texas, USA, 1978 Harpool 8409	15G	In-furrow Banded	1 1	4.0 4.0	2.4 2.4	104 104	< 0.05 < 0.05	TE-730-041
C-1773 Oklahoma, USA 1979 Rawhide	15G	In-furrow Banded	1 1	4.0 4.0	2.4 2.4	117 117	< 0.05 < 0.05	TE---730-042
C-1776 Colorado, USA, 1978 DeKalb A28+	15G	Banded In-furrow	1 1	4.0 4.0	2.4 2.4	175 175	< 0.05 < 0.05	TE-730-043
C-3374 Kansas, USA, 1989 FSIA +	15G	Knifed-in	1	4.3		132	< 0.05	TE-730-046
C-3375 Nebraska, USA, 1989 NC + 271	15G	Knifed-in	1	4.3		133	< 0.05	TE-730-047
C-3376 Missouri, USA, 1989 5511	15G	Knifed-in	1	4.3		139	< 0.05	TE-730-048
C-3851 Texas, USA,1991 F-270G	15G	Knifed-in	1	4.3		100 114 131	< 0.05 < 0.05 < 0.05	TE-730-049

Seed for beverages and sweets

Coffee beans (SB 0716)

Residue trials were conducted during 1982-1988 in the major coffee producing areas of the world: Costa Rica, Guatemala, and El Salvador.

In field trials in Costa Rica conducted in 1982-1983, a 10% granular formulation of terbufos was applied to the soil around the base of established coffee plants at the rate of 0.75–7.5 g ai/plant. Treated samples of berries were collected at intervals, field dried according to common practice, and the outer shell or pericarp removed, leaving the dried beans.

In the trials in El Salvador and Guatemala (1988), terbufos (10% G) was applied in band to plants after flowering but before bean formation, at the rate of 1 or 5 g ai/plant. Treated samples of berries were collected at each sampling interval, field dried (38–56 days for El Salvador; 163–197 days for Guatemala), and the outer shell removed.

The coffee bean samples from each trial were shipped ambient and stored frozen prior to analysis for total terbufos residues by method M-1360. The method (GC/FPD) has been successfully validated on coffee beans at 0.05 mg/kg (Table 22). Freezer storage stability studies in corn and sugar beets have shown that residues of terbufos are stable up to two years in frozen storage. Coffee bean samples in these studies were stored frozen for 12-16 months. In the studies performed in 1988, procedural recovery data were provided. Recoveries of terbufos in beans fortified at 0.05 mg/kg were 84-112% (99 ± 12%, n=4).

The results of the residue trials on coffee are presented in Table 38. Residue levels were below the LOQ (< 0.05 mg/kg) for all treated coffee bean samples collected 58–120 days after treatment with terbufos at 0.75-7.75 g ai/plant rate. At one site (TE-790-002a) where application rates of 5 and 10 times the label rate, i.e., 3.75 and 7.5 g ai/plant, were used maximum residues of 0.12 and 0.17 mg/kg, were found in coffee beans collected at 47 or 35 days after treatment, which represented a shorter PHI than the GAP of 60 days. For both these treatments residues declined to < 0.05 mg/kg at the next sampling interval, i.e., 124 or 53 days post-treatment, respectively.

Table 38. Terbufos residues in coffee beans

Location/Year/ Variety	Application				PHI days	Residues (mg/kg)	BASF Reference Number
	Form	Type Application	no. Appl.	Rate g ai/plant			
GAP Central America (Guatemala, Belize, Dominican Rep, Honduras, El Salvador, Costa Rica, Panama): 10G formulation applied up to 2 times per year, at the rate of 0.75 to 1.1 g ai/plant for a total of 1.5 to 2.2 g ai/year and a PHI of 60 days for established plantations							
C-2351 Costa Rica, 1982 Caturra	10G	Broadcast in soil around trunk	1	0.75	60 90	< 0.05 < 0.05	TE-790-001
			1	1.5	60 90	< 0.05 < 0.05	
C-2459 Costa Rica, 1983 Caturra	10G	Broadcast in soil around trunk	1	0.75	47 63 97	< 0.05 < 0.05 < 0.05	TE-790-002a
			1	2.25	47 124	< 0.05 < 0.05	
			1	3.75	47 124	0.12 < 0.05	
			2	7.5	35 53 114	0.17 < 0.05 < 0.05	
	10G	Broadcast in soil around trunk	1	0.75	24 58	< 0.05 < 0.05	

Location/Year/ Variety	Application				PHI days	Residues (mg/kg)	BASF Reference Number
	Form	Type Application	no. Appl.	Rate g ai/plant			
GAP Central America (Guatemala, Belize, Dominican Rep, Honduras, El Salvador, Costa Rica, Panama): 10G formulation applied up to 2 times per year, at the rate of 0.75 to 1.1 g ai/plant for a total of 1.5 to 2.2 g ai/year and a PHI of 60 days for established plantations							
					90	< 0.05	
			1	2.25	90	< 0.05	
			1	3.75	90	< 0.05	
			2	7.5	24	< 0.05	
					58	< 0.05	
					90	< 0.05	
C-3380 Guatemala, 1988 Catuai	10G	Broadcast in soil around trunk	1	1	60	< 0.05	TE-790-004
					94	< 0.05	
			1	5	60	< 0.05	
					94	< 0.05	
C-3379 El Salvador, 1988 Pacas	10G	Broadcast in soil around trunk	1	1	60	< 0.05	TE-790-005
					90	< 0.05	
					120	< 0.05	
			1	5	60	< 0.05	
					90	< 0.05	
					120	< 0.05	

[a] Samples of coffee beans from two nearby growers were composited as the quantity of each individual sample was not large enough for analysis.

Fodder and forage of cereal grains

Maize forage (AF 0645) and fodder (AS 0645)

The same GAP applies to both maize and sweet corn. Data from trials on maize and sweet corn for residues in fodder and forage were conducted in the USA during 1972-1990. Terbufos granules were applied to the soil either in-furrow or in a band during planting at the rate of 1.1 – 5.8 kg ai/ha. In a trial on maize in 1973 and another on sweet corn in 1974 terbufos was applied at rates ranging from 9– 11kg ai/ha. In a few trials, tests were performed where two applications were made to maize, one at planting and a second treatment 5–6 weeks after planting.

At each sampling interval, approximately 2.3 kg each of treated forage and fodder samples were collected using either a machete or pruning shears. The samples were frozen at -10°C and stored for a maximum of 8 months prior to analysis. In one trial (TE-723-014 by Higham, J. and Alvarez, C.G. 1975) forage samples were stored frozen for up to 24 months prior to analysis. A freezer storage stability study on corn or maize forage and fodder showed that residues of terbufos-related compounds are stable in these matrices up to at least 24 months when stored at approximately -10°C (Table 29, study no. TE-326-014 by Dixon, C. 1990).

The samples were analyzed by methods M-336 or M-1754, which have both been validated at 0.05 mg/kg for terbufos-derived residues in forage and fodder (Table 22). Additional method recoveries provided in studies conducted during 1990 further demonstrated the suitability of method M-1754. Concurrent recoveries of parent fortified in forage and fodder at 0.05 mg/kg, were 82–103% (97 ± 12%, n=8).

The residue data on maize and sweet corn forage and fodder are summarized in Table 39, with residue levels from trials within the GAP, underlined.

Table 39. Terbufos residues in maize forage and fodder.

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	**Appl. Type**	**no. Appl.**	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 6 oz/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage when applied post-emergent.								
Data from trials on maize								
C-2082	15G	Banded	1	2.2	Forage	92	< 0.05	TE-723-026
North Carolina, USA	20G	Banded	1	2.2	Forage	92	< 0.05	
1981	15G	In-furrow	1	2.2	Forage	92	< 0.05	
Pioneer 3184								
C-2215	15G	In-furrow/	2	2.2 + 2.2	Forage	30	0.25	TE-730-018
Nebraska, USA, 1982		Banded			Forage	60	< 0.05	
Stauffer 6595					Fodder	105	0.06	
		In-furrow/	2	4.4 + 2.2	Forage	30	< 0.05	
		Banded			Forage	60	< 0.05	
					Fodder	105	< 0.05	
C-3038	15G	Banded	1	2.24	Forage	31	0.07	TE-730-010
Illinois, USA, 1986					Forage	63	< 0.05	
Hybrid Funks G4507					Fodder	181	< 0.05	
	20G	Banded	1	2.24	Forage	31	< 0.05	
					Forage	63	< 0.05	
					Fodder	181	< 0.05	
C-3037	15G	Banded	1	1.12	Forage	31	0.07	TE-730-011
Nebraska, USA, 1986					Forage	62	< 0.05	
Pioneer 337					Fodder	147	< 0.05	
	15G	Banded	1	1.12	Forage	31	< 0.05	
					Forage	62	< 0.05	
	20G	Banded	1	1.12	Forage	31	< 0.05	
					Forage	62	< 0.05	
					Fodder	147	< 0.05	
C-3566	15G	Banded, POST	1	1.5	Forage	31	< 0.05	TE-723-032
Iowa, USA, 1990					Forage	46	< 0.05	
Circle seed #7111					Fodder	132	< 0.05	
C-3567	15G	Banded, POST	1	1.5	Forage	31	< 0.05	TE-723-033
Iowa, USA, 1990					Forage	45	< 0.05	
DeKalb DK535					Fodder	119	< 0.05	
C-3568	15G	Banded, POST	1	1.5	Forage	30	0.17	TE-723-034
Illinois, USA, 1990					Forage	45	0.08	
Dockendorf 7670					Fodder	109	< 0.05	
C-3569	15G	Banded, POST	1	1.5	Forage	30	0.07	TE-723-035
Illinois, USA, 1990					Forage	47	< 0.05	
Pioneer 3615					Fodder	109	< 0.05	
C-1129	15G	In-furrow	1	1.3	Forage	61	< 0.05	TE-730-008
Maryland, USA					Forage	106	< 0.05	
DeKalb 264					Fodder	134	< 0.05	
1974	15G	In-furrow	1	2.6	Forage	61	< 0.05	
					Forage	106	< 0.05	
					Fodder	134	< 0.05	
	15G	In-furrow	1	5.2	Forage	61	0.24	
					Forage	106	< 0.05	
					Fodder	134	< 0.05	
C-645	15G	Banded +	2	1.12+	Forage	10	0.31	TE-730-015
Colorado, USA, 1972		POST		1.12	Forage	30	< 0.05	
PAG 5X53B					Forage	40	< 0.05	
					Forage	60	< 0.05	
					Fodder	121	< 0.05	
	15G	Banded +		1.12 +	Forage	10	8.9	
		POST		2.24	Forage	30	0.21	

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	**Appl. Type**	**no. Appl.**	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 6 oz/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage when applied post-emergent.								
					Forage	40	< 0.05	
					Forage	60	< 0.05	
					Fodder	121	< 0.05	
C-645 Colorado, USA, 1972 PAG 5X53B (cont'd)	15G	Banded + POST		2.24 + 1.12	Forage	10	8.0	TE-730-015
					Forage	30	< 0.05	
					Forage	40	< 0.05	
					Forage	60	< 0.05	
					Fodder	121	< 0.05	
	15G	Banded + POST		2.24 + 2.24	Forage	10	6.1	
					Forage	30	< 0.05	
					Forage	40	< 0.05	
					Forage	60	0.11	
					Fodder	121	< 0.05	
	15G	Banded + POST		1.12 + 5.6	Fodder	121	< 0.05	
	15G	Banded + POST		2.24+ 5.6	Fodder	121	0.07	
C-416: Illinois, USA, 1973	15G	In-furrow	1	1.12	Fodder	124	< 0.05	TE-730-016
Nebraska, USA,1973	15G	In-furrow	1	1.12	Fodder	168	< 0.05	
			1	2.24	Fodder	168	< 0.05	
			1	5.6	Fodder	168	< 0.05	
ND, USA, 1973	15G	In-furrow	1	1.12	Fodder	159	< 0.05	
			1	1.7	Fodder	159	< 0.05	
			1	2.2	Fodder	159	< 0.05	
Nebraska, USA, 1973	15G	In-furrow	1	1.12	Fodder	162	< 0.05	
			1	2.24	Fodder	162	< 0.05	
			1	5.6	Fodder	152	0.10	
Iowa, USA, 1973	15G	In-furrow	1	1.12	Fodder	135	< 0.05	
			1	2.24	Fodder	135	< 0.05	
			1	5.6	Fodder	135	< 0.05	
			1	11.2	Fodder	135	0.09	
C-415								
Indiana, USA, 1972	15G	In-furrow	1	1.12	Fodder	146	< 0.05	TE-730-017
				1.7	Fodder	146	< 0.05	
Missouri, USA, 1972	15G	In-furrow	1	1.12	Fodder	131	< 0.05	
		In-furrow	1	1.7	Fodder	184	< 0.05	
Nebraska, USA, 1972	15G	In-furrow	1	1.12	Fodder	162	< 0.05	
			1	1.12	Fodder	168	< 0.05	
NC, USA, 1972	15G	In-furrow	1	1.12	Fodder	148	< 0.05	
			1	1.12	Fodder	143	< 0.05	
			1	2.24	Fodder	105	< 0.05	
			1	5.6	Fodder	105	0.24	
ND, USA, 1972	15G	In-furrow	1	1.12	Fodder	159	< 0.05	
			1	2.24	Fodder	159	< 0.05	
Iowa, USA, 1973	15 G	In-furrow	1	1.12	Fodder	135	< 0.05	
C-631 Minnesota, USA, 1974	15G	In-furrow	1	1.12	Forage	45	< 0.05	TE-723-013
					Forage	65	< 0.05	
					Fodder	115	< 0.05	
C-636	15G	In-furrow	1	1.2	Forage	71	0.23	TE-723-016

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	**Appl. Type**	**no. Appl.**	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 6 oz/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage when applied post-emergent.								
Minnesota, USA, 1974					Forage	88	< 0.05	
					Forage	111	< 0.05	
					Fodder	143	< 0.05	
	15G	In-furrow	1	2.2	Forage	71	0.16	
					Forage	88	< 0.05	
					Forage	111	< 0.05	
					Fodder	143	< 0.05	
	15G	In-furrow	1	4.5	Forage	71	0.24	
					Forage	88	0.06	
					Forage	111	< 0.05	
					Fodder	143	< 0.05	
C-637 ND, USA, 1974 NK 420	15G	In-furrow	1	1.2	Forage	40	< 0.05	TE-723-017
					Forage	57	< 0.05	
					Forage	90	< 0.05	
					Forage	106	< 0.05	
					Fodder	134	< 0.05	
	15G	In-furrow	1	1.8	Forage	40	0.45	
					Forage	57	0.07	
					Forage	90	< 0.05	
					Forage	106	< 0.05	
					Fodder	134	< 0.05	
	15G	In-furrow	1	2.5	Forage	40	0.23	
					Forage	57	0.09	
					Forage	90	< 0.05	
					Forage	106	< 0.05	
					Fodder	134	< 0.05	
	15G	In-furrow	1	4.9	Forage	40	0.484	
					Forage	57	0.13	
					Forage	90	< 0.05	
					Forage	106	< 0.05	
					Fodder	134	< 0.05	
C-640 Michigan, USA, 1974	15G	In-furrow	1	1.1	Fodder	151	< 0.05	TE-723-018
			1	2.2	Fodder	151	< 0.05	
			1	4.5	Fodder	151	0.33	
C-641 Maryland, USA, 1974 DeKalb 264	15G	In-furrow	1	1.5	Forage	60	< 0.05	TE-723-019
					Forage	103	< 0.05	
					Fodder	130	< 0.05	
	15G	In-furrow	1	2.9	Forage	60	< 0.05	
					Forage	103	< 0.05	
					Fodder	130	< 0.05	
	15G	In-furrow	1	5.8	Forage	60	0.24	
					Forage	103	< 0.05	
					Fodder	130	< 0.05	
C-643 New York, USA, 1974 DeKalb XL 12	15G	In-furrow	1	1.5	Forage	44	0.14	TE-723-020
					Forage	62	0.06	
					Forage	92	< 0.05	
					Forage	110	< 0.05	
					Fodder	134	< 0.05	
	15G	In-furrow	1	2.9	Forage	44	0.17	
					Forage	62	0.06	
					Forage	92	< 0.05	
					Forage	110	< 0.05	
					Fodder	134	0.05	
	15G	In-furrow	1	5.8	Forage	44	0.48	
					Forage	62	0.25	

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	**Appl. Type**	**no. Appl.**	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 6 oz/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage when applied post-emergent.								
					Forage	92	0.05	
					Forage	110	< 0.05	
					Fodder	134	0.12	
					Fodder	134	0.10	
C-644	15G	In-furrow	1	1.1	Forage	40	0.88	TE-723-021
Colorado, USA, 1974					Forage	60	0.32	
NC +					Forage	90	0.41	
					Forage	110	0.10	
					Fodder	179	< 0.05	
	15G	In-furrow	1	1.5	Forage	40	0.91	
					Forage	60	0.56	
					Forage	90	0.96	
					Forage	110	0.65	
					Fodder	179	0.08	
	15G	In-furrow	1	2.9	Forage	40	0.90	
					Forage	60	0.64	
					Forage	90	1.08	
					Forage	110	1.1	
					Fodder	179	< 0.05	
	15G	In-furrow	1	5.8	Forage	40	1.28	
					Forage	60	0.56	
					Forage	90	1.56	
					Forage	110	0.70	
					Fodder	179	0.56	
					Fodder	179	0.60	
C-647	15G	In-furrow	1	0.84	Fodder	142	< 0.05	TE-723-022
Kentucky, USA, 1973			1	1.1	Fodder	142	< 0.05	
Pioneer 3369A								
Data from trials on sweet corn								
C--642	15G	In-furrow	1	1.1	Fodder	105	< 0.05	TE-723-003
Illinois, USA, 1974								
Super sweet								
C--635	15G	Banded	1	1.5	Forage	51	< 0.05	TE-723-005
Iowa, USA, 1974					Forage	60	< 0.05	
Silver Queen					Fodder	95	< 0.05	
				2.9	Forage	51	< 0.05	
					Forage	60	< 0.05	
					Fodder	95	< 0.05	
				5.8	Forage	51	< 0.05	
					Forage	60	< 0.05	
					Fodder	95	< 0.05	
	15G	In-furrow	1	1.5	Forage	51	< 0.05	
					Forage	60	< 0.05	
					Fodder	95	< 0.05	
				2.9	Forage	51	< 0.05	
					Forage	60	0.057	
					Fodder	95	< 0.05	
				5.8	Forage	51	0.091	
					Forage	60	0.1	
					Fodder	95	< 0.05	
C-632	15G	In-furrow	1	2.2	Forage	30	0.06	TE-723-014
Florida, USA, 1974					Forage	44	0.06	
Tobelle					Forage	60	< 0.05	

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	**Appl. Type**	**no. Appl.**	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 6 oz/1000 ft row or a maximum of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage when applied post-emergent.								
					Forage	75	< 0.05	
	15G	In-furrow	1	4.5	Forage Forage Forage Forage	30 44 60 75	0.05 0.07 < 0.05 0.07	
	15G	In-furrow	1	9.0	Forage Forage Forage Forage	30 44 60 75	0.08 0.30 0.09 0.14	
C-639 Minnesota, USA, 1974	15G	In-furrow	1	1.1	Forage Fodder	40 69	< 0.05 < 0.05	TE-730-003
	15G	In-furrow	1	2.2	Forage Fodder	40 69	< 0.05 < 0.05	
	15G	In-furrow	1	4.5	Forage Forage Fodder	40 40 69	0.07 0.11 0.05	
C-639 Minnesota, USA, 1974	15G	Banded	1	1.1	Forage Fodder	40 69	< 0.05 < 0.05	TE-730-003
	15G	Banded	1	2.2	Forage Fodder	40 69	< 0.05 < 0.05	
	15G	Banded	1	4.5	Forage Forage Fodder	40 40 69	< 0.05 < 0.05 < 0.05	

Sorghum forage (AF 0651) and fodder (AS 0651)

Supervised trials on sorghum were conducted during 1978-1996. In the 1996 trials, terbufos granules were applied post-emergent, at the rate of 2.1 or 2.2 kg ai/ha. Forage samples were harvested 48 to 72 days after treatment while fodder samples were taken at normal grain harvest time, 88 to 90 days after treatment. In the rest of the trials (1978-1991), terbufos granules were applied at planting, at the GAP rate (2 kg ai/ha) and at twice that rate (4 – 4.3 kg ai/ka).

At each sampling interval, about 12 plants (forage) weighing approximately 1.4 kg were collected. Approximately 1.4 kg of dried stalks remaining after removal of the grain heads were collected for fodder/stover samples. All samples were immediately frozen (-10°) and stored up to a maximum of about 8 months until analysis. A freezer storage stability study on the related crop, maize, showed that residues of terbufos-related compounds are stable in corn forage and fodder/stover up to at least 24 months when stored at approximately -10°C (Table 29, study no. TE-326-014 by Dixon, C. 1990).

Terbufos residues from the 1996 trials were determined by Method M-1754, using a gas chromatograph equipped with a flame photometric detector. The validated sensitivity of the method was 0.05 mg/kg for sorghum forage and fodder (see Table 22). For the other trials, residues of

terbufos were determined by Method M-995, which had a validated sensitivity of 0.05 mg/kg for sorghum forage and fodder samples (Table 22).

Results of all trials are summarized in Table 40, with residue levels from trials according to the GAP, underlined.

Table 40. Terbufos residues in sorghum forage and fodder

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 1.0 oz ai/1000 ft row or a maximum of 2.0 kg ai/ha applied once and a PHI of 50 days for forage, and 100 days for grain and fodder.								
RES-96-082 Missouri, USA, 1996 KS 714Y	15G	Banded (POST)	1	2.2	Forage Forage Forage Fodder	50 61 72 90	< 0.05 (2) < 0.05 (2) < 0.05 (2) < 0.05 (2)	TE-730-057
RES-96-081 Illinois, USA, 1996 Northrup King 1210	15G	Banded (POST)	1	2.2	Forage Forage Fodder	50 60 90	< 0.05 (2) < 0.05 (2) < 0.05 (2)	TE-730-056
RES-96-080 Kansas, USA, 1996 6R55E	15G	Banded (POST)	1	2.1	Forage Forage Forage Fodder	52 52 62 90	0.05 < 0.05 < 0.05 (2) < 0.05 (2)	TE-730-055
RES-96-079 Louisiana, USA, 1996 DeKalb 37	15G	Banded (POST)		2.0	Forage Forage Forage Fodder	50 50 60 90	< 0.05 0.07 < 0.05 (2) < 0.05 (2)	TE-730-054
RES-96-078 Texas, USA, 1996 F-200	15G	Banded (POST)	1	2.2	Forage Forage Fodder	50 59 90	< 0.05 (2) < 0.05 (2) < 0.05 (2)	TE-730-053
RES-96-077 Texas, USA 1996 F-200	15G	Banded (POST)	1	2.2	Forage Forage Fodder Fodder	48 58 88 88	< 0.05 (2) < 0.05 (2) 0.19 0.12	TE-730-052
C-3374 Kansas, USA, 1989 FSIA +	15G	Knifed-in	1	4.3	Forage Fodder	60 132	< 0.05 < 0.05	TE-730-046
C-3375 Nebraska, USA, 1989 NC + 271	15G	Knifed-in	1	4.3	Forage Fodder	60 133	0.10 < 0.05	TE-730-047

Table 40. Terbufos residues in sorghum forage and fodder, cont'd

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Commodity			
GAP USA: 15G or 20G formulation at the rate of 1.0 oz ai/1000 ft row or a maximum of 2.0 kg ai/ha applied once and a PHI of 50 days for forage, and 100 days for grain and fodder.								
C-3376 Missouri, USA, 1989 5511	15G	Knifed-in	1	4.3	Forage Fodder	69 139	0.05 0.05	TE-730-048

C-3851 Texas, USA,1991 F-270G	15G	Knifed-in		4.3	Forage Fodder Fodder Fodder	50 100 114 131	0.88 0.49 0.13 0.18	TE-730-049
C-1626 Kansas, USA, 1978	15G 15G	Banded Banded	1 1	2.0 4.0	Fodder Fodder	95 95	< 0.05 < 0.05	TE-730-039
	15G 15G	In-furrow In-furrow	1 1	2.0 4.0	Fodder Fodder	95 95	< 0.05 0.14	
C-1742 Texas, USA, 1978 Standking Y	15G	In-furrow	1	4.0	Forage	150	< 0.05	TE-730-040
C-1752 Texas, USA, 1978, Harpool 8409	15G 15G	In-furrow Banded	1 1	4.0 4.0	Forage Forage	104 104	< 0.05 < 0.05	TE-730-041
C-1773 Oklahoma, USA, 1979; Rawhide	15G 15G	In-furrow Banded	1 1	4.0 4.0	Fodder Fodder	117 117	< 0.05 < 0.05	TE---730-042
C-1776 Colorado, USA, 1978 DeKalb A 28+	15G	Banded	1	4.0	Forage Forage	64 103	0.1 < 0.05	TE-730-043
	15G	In-furrow	1	4.0	Forage Forage	64 103	0.80 0.08	

Miscellaneous forage and fodder crops

Sugar beet tops (AV 0596)

Field trials were conducted in the USA and Canada during 1971-1975 in which terbufos (15%G) was applied in-furrow or banded at 1.0 to 2.5 kg ai/ha and also at exaggerated rates (4.0-12.3 kg ai/ha). Several trials were also conducted which consisted of sequential at-planting and post-emergence banded applications, typically reflecting exaggerated rates. Treated samples were collected at each sampling interval, stored frozen for a maximum of 22 months, and analyzed for total terbufos residues by method M-395. The freezer storage stability study conducted using this analytical method for sugar beet tops showed that samples are stable up to 24 months when stored frozen at -10°C (Table 29). The method was successfully validated for sugar beet tops at 0.05 mg/kg (Table 22).

Several trials were also conducted in the USA during the 1989 growing season in which terbufos (15%G) was knifed in at planting at 4.9 kg ai/ha. Treated samples were harvested by hand at maturity, 150–180 days after treatment. The samples were placed in frozen storage (< -17°C) for a maximum of 6 months, and were analyzed for total terbufos residues using method M-395. The only deviation from the method was the substitution of dichloromethane for chloroform. As noted above, the method has been validated for tops at 0.05 mg/kg. Residues were < 0.05 mg/kg in or on all tops control samples. Concurrent recoveries of terbufos-related residues (parent and CL94302) in tops at 0.1 mg/kg were 81-137% (101 ± 26%, n=4).

In more recent field trials in the USA in 1994, terbufos (15%G) was applied as a band over the row of sugar beets 6-23 inches tall at 2.2 – 2.4 or 4.4 – 4.9 kg ai/ha. The lower rate reflects the maximum GAP rate. Treated samples were collected at each sampling interval, stored frozen (< -8°C) for a maximum of 8 months, and analyzed by method M-2457, which had a validated sensitivity of 0.01 mg/kg for sugar beet tops. Concurrent recoveries of terbufos-related residues (parent, CL94221, CL94301, CL94302, CL94320, CL94365) fortified simultaneously in sugar beet tops at 0.01-0.60 mg/kg were 76-110% (88 ± 8%, n=26). Additional data from a method validation study on method M-2457 is presented in Table 22. A freezer storage stability study on sugar beet tops was conducted

using this method and results showed that residues in samples are stable up to at least 24 months (Table 29).

Results for all trials on sugar beet tops are summarized in Table 41, where residues from trials according to the GAP are underlined.

Table 41. Terbufos residues in sugar beet tops.

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G formulation at the rate of 0.6 to 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for knifed-in applications, where the PHI is 150 days.								
RES-95-046 Idaho, USA, 1994 HM-WS91	15G	Banded, POST	1	2.2	1.2	50 70 90	0.16 0.13 0.04	TE-724-035
		Banded, POST	1	4.9	2.7	50 70 90	0.37 0.20 0.18	
RES-95-039 Michigan, USA, 1994 H23	15G	Banded, POST	1	2.2	1.2	50 70 91	0.05 < 0.01 < 0.01	TE-724-036
		Banded, POST	1	4.4	2.4	50 70 91	0.16 0.02 < 0.01	
RES-95-040 Nebraska, USA, 1994 HM 1605	15G	Banded, POST	1	2.2	1.2	50 70 90	0.04 0.01 < 0.01	TE-724-037
				4.4	2.4	50 70 90	0.11 0.03 0.01	
RES-95-045 North Dakota, USA, 1994	15G	Banded, POST	1	2.4	1.3	50 70 90	0.13 0.05 0.01	TE-724-038
ACH 192				4.6	2.5	50 70 90	0.24 0.16 0.02	
RES-95-047 Minnesota, USA, 1994 ACH 192	15G	Banded, POST	1	2.2	1.2	50 70 90	0.02 0.02 < 0.01	TE-724-039
		Banded, POST	1	4.4	2.4	50 70 90	0.13 0.11 0.04	
C-3366 ND, USA, 1989 UltraMono	15G	Knifed-in	1	4.9		150	< 0.05	TE-724-068
C-3367 Nebraska, USA,1989 ACH 164	15G	Knifed-in	1	4.9		180	0.08	TE-724-069
C-3368 Idaho, USA,1989 WS88	15G	Knifed-in	1	4.9		153	0.06	TE-724-070
C-3369 California, USA 1989, Z-1	15G	Knifed-in	1	4.9		170	< 0.05	TE-724-071
C-667 Colorado, USA 1974, Mono Hy	15G	In-furrow Banded	1 1	2 4		190 190	< 0.05 < 0.05	TE-724-004
C-666 Wyoming, USA	15	In-furrow	1 1	1 2		142 142	< 0.05 < 0.05	TE-724-005

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G formulation at the rate of 0.6 to 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for knifed-in applications, where the PHI is 150 days.								
1975, Mono-HY			1	12		142	< 0.05	
		POST	1	1		116	< 0.05	
			1	2		116	< 0.05	
			1	12		116	< 0.05	
C-665 Idaho, USA 1973	15G	Banded	1	2.2	1.3	152	< 0.05	TE-724-006
C-664 Idaho, 1974 AH-A1	15G	Banded	1	1.1		60	0.05	TE-724-007
						90	< 0.05	
						168	< 0.05	
			1	2.2		60	0.21	
						90	0.15	
						168	< 0.05	
C-964 Manitoba, Canada 1975	15G	In-furrow	1	1.12		117	< 0.05	TE-724-012
C-916 Manitoba, Canada 1974	15G	In-furrow	1	1.12		117	< 0.05	TE-724-013
C-694 North Dakota, USA 1973	15G	Banded	1	2.2	1.35	121	< 0.05	TE-724-014
			1	4.5	2.7	121	< 0.05	
			1	9.0	5.4	121	< 0.05	
			1	2.2	1.35	155	< 0.05	
			1	4.5	2.7	155	< 0.05	
			1	9.0	5.4	155	< 0.05	
		In-furrow	1	2.2	1.35	121	< 0.05	
			1	4.5	2.7	121	< 0.05	
			1	2.2	1.35	155	< 0.05	
			1	4.5	2.7	155	< 0.05	
		POST	1	2.2	1.35	124	< 0.05	
			1	4.5	2.7	124	< 0.05	
			1	9.0	5.4	124	< 0.05	
		Banded + POST	1	4.4+2.2		124	< 0.05	
			1	4.4+4.4		124	< 0.05	
C-695 North Dakota, USA, 1974/ American . Crystal Hybrid #2B	15G	Banded	1	2.5	1.35	31	< 0.05	TE-724-016
			1	4.9	2.7	31	< 0.05	
			1	12.3	6.75	31	< 0.05	
			1	2.5	1.35	62	< 0.05	
			1	4.9	2.7	62	< 0.05	
			1	12.3	6.75	62	< 0.05	
			1	2.5	1.35	94	< 0.05	
			1	4.9	2.7	94	< 0.05	
			1	12.3	6.75	94	< 0.05	
			1	2.5	1.35	129	< 0.05	
			1	4.9	2.7	129	< 0.05	
			1	12.3	6.75	129	< 0.05	
		In-furrow	1	2.5	1.35	31	< 0.05	
			1	4.9	2.7	31	< 0.05	
			1	12.3	6.75	31	< 0.05	

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G formulation at the rate of 0.6 to 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for knifed-in applications, where the PHI is 150 days.								
			1	2.5	1.35	62	< 0.05	
			1	4.9	2.7	62	< 0.05	
			1	12.3	6.75	62	< 0.05	
			1	2.5	1.35	94	< 0.05	
			1	4.9	2.7	94	< 0.05	
			1	12.3	6.75	94	< 0.05	
			1	2.5	1.35	129	< 0.05	
			1	4.9	2.7	129	< 0.05	
			1	12.3	6.75	129	< 0.05	
		Banded + POST	2	2.5+2.5		51	< 0.05	
			2	2.5+4.9		51	< 0.05	
			2	2.5+12.3		51	< 0.05	
			2	2.5+2.5		83	< 0.05	
			2	2.5+4.9		83	< 0.05	
			2	2.5+12.3		83	< 0.05	
			2	2.5+2.5		118	< 0.05	
			2	2.5+4.9		118	< 0.05	
			2	2.5+12.3		118	< 0.05	
C-693 Michigan, USA, 1974 Monitor common	15G	In-furrow	1	1.8	1.35	40	2.78	TE-724-017
			1	3.6	2.7	40	3.75	
			1	1.8	1.35	60	1.36	
			1	3.6	2.7	60	1.04	
			1	1.8	1.35	91	0.12	
			1	3.6	2.7	91	0.09	
			1	1.8	1.35	174	< 0.05	
			1	3.6	2.7	174	< 0.05	
			1	7.2	5.4	174	0.06	
C-693 Michigan, USA, 1974 Monitor common		Banded	1	1.8	1.35	40	2.81	TE-724-017
			1	3.6	2.7	40	3.86	
			1	1.8	1.35	60	1.12	
			1	3.6	2.7	60	2.18	
			1	1.8	1.35	91	0.82	
			1	3.6	2.7	91	0.21	
			1	1.8	1.35	174	< 0.05	
			1	3.6	2.7	174	< 0.05	
			1	7.2	5.4	174	< 0.05	
C-668 Colorado, USA, 1973/ Mono-Hy-1	15G	Banded	1	2.2	1.36	60	0.06	TE-724-018
			1	4.5	2.7	60	0.16	
			1	9.0	5.4	60	0.58	
			1	2.2	1.36	90	< 0.05	
			1	4.5	2.7	90	< 0.05	
			1	9.0	5.4	90	< 0.05	
			1	2.2	1.36	119	< 0.05	
			1	4.5	2.7	119	< 0.05	
			1	9.0	5.4	119	< 0.05	
			1	2.2	1.36	157	< 0.05	
			1	4.5	2.7	157	< 0.05	
			1	8.96	5.4	157	< 0.05	
		POST	1	2.2	1.36	29	0.06	
			1	4.5	2.7	29	0.21	
			1	9.0	5.4	29	0.31	
			1	2.2	1.36	59	< 0.05	
			1	4.5	2.7	59	< 0.05	
			1	9.0	5.4	59	< 0.05	
			1	2.2	1.36	88	< 0.05	
			1	4.5	2.7	88	< 0.05	
			1	9.0	5.4	88	< 0.05	

Location/Year/ Variety	Application					PHI	Residues (mg/kg)	Reference Number
	Form.	Appl. Type	no. Appl.	Rate kg/ai/ha	Rate oz ai/1000 ft			
GAP, USA: 15G formulation at the rate of 0.6 to 1.2 oz ai/1000 ft row or an annual maximum of 2.2 kg ai/ha. PHI is 110 days, except for knifed-in applications, where the PHI is 150 days.								
			1	2.2	1.36	126	< 0.05	
			1	4.5	2.7	126	< 0.05	
			1	8.96	5.4	126	< 0.05	
		Banded + POST	2	4.5+2.2		29	0.12	
			2	4.5+4.5		29	0.30	
			2	4.5+2.2		59	< 0.05	
			2	4.5+4.5		59	< 0.05	
			2	4.5+2.2		88	< 0.05	
			2	4.5+4.5		88	< 0.05	
			2	4.5+2.2		126	< 0.05	
			2	4.5+4.5		126	< 0.05	
C-914 Manitoba, Canada, 1973	15G	Banded	1	1.12		114	< 0.05	TE-724-029
C-917 Manitoba, Canada 1971	15G	In-Furrow	1	1.1		126	< 0.05	TE-724-030
			1	1.1		133	< 0.05	
C-656 North Dakota, USA, 1972	15G	Banded	1	1.1		135	< 0.05	TE-724-048
			1	2.2		135	< 0.05	
		POST	1	1.1		119	< 0.05	
			1	2.2		119	< 0.05	
C-657 Wyoming, USA, 1972 Mono-Hi	15G	Banded	1	0.56		156	< 0.05	TE-724-049
			1	1.1		156	< 0.05	
			1	6.7		156	0.08	
C-696 Minnesota, USA, 1973 American Crystal Hybrid #13	15G	Banded	1	2.2		102	< 0.05	TE-724-050
			1	4.4		102	0.06	
			1	8.9		102	0.11	
			1	2.2		138	< 0.05	
			1	4.4		138	< 0.05	
			1	8.9		138	< 0.05	
		POST	1	2.2		73	0.09	
			1	4.4		73	0.78	
			1	8.9		73	1.23	
			1	2.2		109	< 0.05	
			1	4.4		109	< 0.05	
			1	8.9		109	0.20	
		Banded+POST	2	4.5 + 2.2		73	0.26	
			2	4.5 + 4.5		73	0.46	

FATE OF RESIDUES IN STORAGE AND PROCESSING

In storage

Terbufos is not registered for use in stored products.

In Processing

Since terbufos residues in maize grain, sweet corn kernels, corn-on-the-cob, coffee beans, sugar beets (roots) and sorghum grain were at non-detectable levels, processing studies were not relevant.

Residues in the Edible Portion of Food Commodities

For commodities belonging to the group with inedible peel, residue data on both the whole commodity and the edible portion are submitted to the Meeting. Although terbufos is systemic in nature, it is expected that some of the residues remain in the peel and are removed by peeling. In order

to determine the amount of terbufos residues in the edible portion (pulp), in some supervised trials conducted on bananas (Table 33), terbufos residues were determined in both whole bananas and pulp. In general, residue levels even in whole bananas were relatively low (< 0.01 – 0.03 mg/kg). Therefore, from trials according to the GAP, the level of residue actually remaining in the pulp was difficult to ascertain since the residues in the pulp were equal or only slightly less than those in whole bananas. However, in trials where exaggerated rates were used (study no. TE-714-003, 005, 006, 007, 008 and 013, respectively by Khunachak, A., 1986b, d; Khunachak, A., 1997, Bohn, W., 1985a, and Bohn, W. and Behm, J., 1985) and residues in the pulp and whole bananas were determined, results showed that an average of 79% of the residues of terbufos remained in the pulp. Twenty one percent was removed by peeling. The details are presented in Table 42.

Table 42. Estimated terbufos-related residues in banana pulp.

Terbufos-related residues, mg/kg		% Residues in pulp	Reference
Whole banana	**Pulp**		
0.02	0.02	100	TE-714-003
0.02	0.01	50	
0.02	0.02	100	
0.01	< 0.01	100	
0.02	< 0.01	50	TE-714-005
0.03	0.02	67	
0.02	0.01	50	
0.01	< 0.01	100	
0.02	< 0.01	50	TE-714-006
0.01	0.01	100	
0.02	< 0.01	50	TE-714-007
0.01	0.01	100	
0.02	0.02	100	TE-714-008
0.01	< 0.01	100	
0.02	< 0.01	50	TE-714-013
0.01	0.01	100	
Average		**79%**	

RESIDUES IN ANIMAL COMMODITIES

Metabolism studies on ruminants and poultry showed that terbufos was rapidly metabolized leaving no detectable residues in tissues, milk, and eggs. All residues in tissues, milk, and eggs were below the limit of determination for the corresponding analytical methods used. Based on these, feeding studies could have been waived. However, ruminant and poultry feeding studies were conducted and made available to the Meeting, the results of which confirm the findings from the metabolism studies.

Ruminant feeding studies

Beef cattle feeding study

In a beef cattle feeding study conducted in the USA, a mixture of terbufos and its phosphorus-containing metabolites was administered to two groups of three steers each for 21 days at a dose equivalent to 0.05 ppm body weight/day or 2 ppm dry weight in the diet (study no. TE-705-002 by Manuel, A., 1972b). The mixture was representative of the relative metabolite concentrations found in 10-week-old maize plants resulting from a terbufos soil treatment at planting. Tissues of fat, muscle, liver and kidney from treated animals sacrificed 24 hours after the last dose showed no detectable residues of terbufos and related metabolites (Table 43). The tissues were analyzed by method M-372, using a gas chromatograph equipped with an alkali flame ionization The method was validated for cattle tissues with a sensitivity of 0.05 mg/kg (Table 24).

Table 43. Summary of total terbufos-related residues in beef cattle edible tissues from cattle fed a nominal dose equivalent to 2 ppm for 21 days

Cattle No.	Dose (mg/kg in diet)	Total terbufos-related residues (mg/kg)			
		Muscle	Fat	Kidney	Liver
A-56	2	< 0.05	< 0.05	< 0.05	< 0.05
A-61	2	< 0.05	< 0.05	< 0.05	< 0.05
A-62	2	< 0.05	< 0.05	< 0.05	< 0.05

Dairy cattle feeding studies

In a dairy cattle feeding study the same mixture of terbufos and metabolites at the same dose level (2 ppm in the feed) was administered daily to two groups of three dairy cows for 21 days (Manuel, A., 1972c). Milk samples were taken on days 0 (pre-treatment), 7, 14, and 21 and analyzed by method M-353, using a gas chromatograph equipped with an alkali flame ionization detector. The method was validated for milk samples with a sensitivity of 0.01 mg/kg (Table 24). Results from whole milk analyses indicated that cows from both groups showed total apparent terbufos-related residues below the limit of determination (< 0.01 mg/kg) at days 7, 14 and 21 during dosing (Table 44).

Table 44. Summary of total terbufos-related residues in milk from dairy cattle fed a nominal dose equivalent to 2 ppm for 21 days

Cattle No.	Dose (mg/kg in diet)	Total terbufos-related residues (mg/kg)		
		7 DAY	14 DAY	21 DAY
A-1	2	< 0.01	< 0.01	< 0.01
A-3	2	< 0.01	< 0.01	< 0.01
A-4	2	< 0.01	< 0.01	< 0.01

A complementary study was conducted in 1987 where terbufos was administered to three dairy cows at a dose level of 50 ppm in the diet (study no. TE-705-004 by Peterson, R., 1989). The protocol called for 7 consecutive days of treatment followed by a withdrawal period of 7 days where no terbufos was fed. Milk samples were scheduled to be collected in the morning and in the after noon for 14 days. However, cow mortality prevented the study from being completed as proposed. Instead, milk samples were collected only for 3.5 days, at 0.5 day sampling intervals. Milk samples were analyzed by method M-1829, which had a validated sensitivity of 0.005 mg/kg. The method validation data is summarized in Table 24.

Residues of terbufos-related compounds in milk from this study are summarized in Table 45. Residues in milk samples were all below the limit of determination, except for two samples where residues were detected at levels of 0.011 mg/kg and 0.005 mg/kg.

Table 45. Terbufos-related residues in milk after dosing with terbufos at 50 ppm in the diet for a period of 3.5 days

Sampling interval from 1st treatment, days)	Dose (mg/kg in diet)	Total terbufos-related residues (mg/kg)		
		Cow # 365	Cow # 220	Cow # 367
0	50	< 0.005		
0.5	50	0.011	< 0.005	< 0.005
1	50	< 0.005	< 0.005	
1.5	50	< 0.005	0.005	< 0.005 (2)
2	50	< 0.005		
2.5	50	< 0.005		
3.5	50	< 0.005		

Poultry feeding study

A mixture of terbufos and its phosphorus-containing metabolites was administered by gavage to nine chickens for 21 days at a dose equivalent to 0.1 mg/kg body weight or 2 ppm in the diet on a dry weight basis (study no. TE-705-001 by Manuel, A., 1972a). The mixture was the same as that used in the cattle feeding studies. Egg samples were taken for analysis at 7, 14, and 21 days, and analyzed for terbufos-related residues by method M-396, using a gas chromatograph equipped with an alkali flame ionization detector. The method had been validated with a sensitivity of 0.01 mg/kg (Table 24). Results showed that all residues of terbufos-related compounds in eggs were below the limit of determination (< 0.01 mg/kg). Table 46 summarize the results for eggs.

Table 46. Summary of total terbufos-related residues in eggs from poultry fed a nominal dose equivalent to 2 ppm for 21 days

Sample No.	Dose (mg/kg in diet)	Total terbufos-related residues (mg/kg)		
		7 DAY	14 DAY	21 DAY
B-4	2	< 0.01	< 0.01	< 0.01
B-5	2	< 0.01	< 0.01	< 0.01
B-6	2	< 0.01	< 0.01	< 0.01

The chickens were sacrificed at the end of the feeding period and samples of fat, muscle, liver, kidney, and skin were taken and analyzed for total terbufos residues using method M-401, which had been validated at a sensitivity level of 0.05 mg/kg (Table 24). Results showed that residues of terbufos-related compounds are below the limit of determination (< 0.05 mg/kg) in poultry tissue samples taken after 21 days of continuous feeding with treated rations. Table 47 summarizes the results on poultry tissues.

Table 47. Summary of total terbufos-related residues in poultry edible tissues from chickens fed a nominal dose equivalent to 2 ppm for 21 days

Sample No.	Dose (mg/kg in diet)	Total terbufos-related residues (mg/kg)			
		Muscle	Fat	Kidney	Liver
B-7	2	< 0.05	< 0.05	< 0.05	< 0.05
B-8	2	< 0.05	< 0.05	< 0.05	< 0.05
B-9	2	< 0.05	< 0.05	< 0.05	< 0.05
B-10	2	< 0.05	< 0.05	< 0.05	< 0.05
B-11	2	< 0.05	< 0.05	< 0.05	< 0.05
B-12	2	< 0.05	< 0.05	< 0.05	< 0.05

RESIDUES IN FOOD IN COMMERCE AND AT CONSUMPTION

The Pesticide Data Program (PDP) of the US Department of Agriculture (USDA) collects data on pesticide residues in food (USDA, 2002). Table 48 summarizes the data for terbufos and its metabolites in the PDP database. The data represent the results of monitoring pesticide residues in food up to the year 2002.

Table 48. Monitoring data for terbufos from the US Pesticide Data Program (PDP)

Commodity	Total Samples Screened	Samples with Detection	% Samples with Detection	Range of values detected (mg/kg)	Range of LODs (mg/kg)
TERBUFOS					
Apples	556	0			0.006-0.014
Asparagus	622	0			0.004-0.006
Banana	727	0			0.006-0.014
Broccoli	125	0			0.006
Carrots	536	0			0.001-0.006
Celery	170	0			0.001-0.006
Cucumbers	129	0			0.006

Commodity	Total Samples Screened	Samples with Detection	% Samples with Detection	Range of values detected (mg/kg)	Range of LODs (mg/kg)
Mushrooms	642	0			0.001-0.06
Peaches	563	0			0.001-0.002
Pineapples	106	0			0.006
Potatoes	370	0			0.006-0.015
Spinach	363	0			0.015
Sweet bell peppers	186	0			0.002
Sweet corn, caned/frozen	727	0			0.006-0.015
Sweet peas. Canned/frozen	643	0			0.004-0.006
TOTAL	**6,465**	**0**			
TERBUFOS SULFONE					
Apples	556	0			0.004-0.007
Asparagus	623	0			0.004
Banana	727	0			0.004-0.007
Broccoli	125	0			0.004
Carrots	536	0			0.001-0.004
Celery	170	0			0.002-0.004
Cucumbers	129	0			0.004
Mushrooms	642	0			0.001-0.004
Peaches	563	0			0.001-0.002
Pineapples	106	0			0.004
Potatoes	370	0			0.004-0.048
Spinach	363	0			0.048
Sweet bell peppers	186	0			0.002
Sweet corn, caned/frozen	727	0			0.004-0.018
Sweet peas. Canned/frozen	643	0			0.004
TOTAL	**6,466**	**0**			

NATIONAL MAXIMUM RESIDUE LIMITS

The manufacturer reported MRLs for the following countries: Australia, Brazil, Chile, Japan, Korea and USA. Terbufos is not authorized for use on agricultural crops in the Netherlands.

APPRAISAL

Terbufos, a systemic nematicide and soil insecticide, was evaluated for the first time by JMPR in 1989. A further residue review was undertaken in 1990. At the 36th Session of the CCPR the compound was scheduled for a residue evaluation within the periodic review program for 2005. The toxicological review was conducted in 2003, which established an ADI of 0.0006 mg/kg bw/day and an ARfD of 0.002 mg/kg bw/day.

The Meeting received information on identity; metabolism and environmental fate; analytical methods; relevant storage stability studies; use pattern; residues resulting from supervised trials on a number of crops including bananas, coffee beans, sugar beets, maize, sorghum, and sweet corn; residues in food in commerce and at consumption and national maximum residue limits.

List of terbufos and related metabolites:

Terbufos	*S-tert*-butylthiomethyl *O,O*-diethyl phosphorodithioate
Terbufos sulfoxide	*S-tert*-butylsulfinylmethyl *O,O*-diethyl phosphorodithioate
Terbufos sulfone	*S-tert* -butylsulfonylmethyl *O,O*-diethyl phosphorodithioate
Terbufoxon	*S-tert*-butylthiomethyl, *O,O*-diethyl phosphorodithioate
Terbufoxon sulfoxide	*S-tert* -butylsufinylmethyl, *O,O*-diethyl phosphorodithioate
Terbufoxon sulfone	*S-tert*-butylsulfonylmethyl, *O,O*-diethyl phosphorodithioate

Animals Metabolism

The Meeting received information on the fate of [methylene-^{14}C]terbufos in rats, lactating goats and laying hens dosed orally.

Studies on metabolism in rats were evaluated by the WHO Expert Group of the 2003 JMPR, which concluded that absorption of single doses of ^{14}C-terbufos was rapid and fairly complete. Most of the radiolabel was excreted within 24 – 48 h. Excretion was primarily by the urinary route (about 70 – 80% of the administered dose). Terbufos was extensively metabolized and little radioactivity was found in the tissues. Sulfoxidation and desulfuration of terbufos is followed by hydrolysis of the thiolophosphorus bond, enzymatic S-methylation and then additional S-oxidation. On the basis of a 14-day study of repeated doses, terbufos showed little potential for accumulation.

[Methyllene-^{14}C]terbufos at doses equivalent to 0.281 and 2.53 mg/kg body weight, were administered via capsule to two lactating goats separately, i.e., one dose regime per goat. Each goat was dosed once daily for seven consecutive days. The major route of excretion was via the urine, which accounted for 96.0 and 86.9% of the administered radioactivity respectively. The main metabolic pathway in lactating goats and rats is qualitatively similar, thus suggesting a common metabolic pathway. Neither terbufos nor any of the phosphorylated oxidative metabolites - sulfoxide, sulfone, oxygen analog and its sulfoxide and sulfone - were observed in milk. None of the phosphorylated oxidative metabolites were detected in tissues. However, terbufos (parent) was observed at low concentrations in liver (< 0.01 mg/kg eq) and in kidney (< 0.01 mg/kg eq).

The total radioactive residue (TRR) in daily milk samples were < 0.01 mg/kg eq (low dose, 0.28 mg/kg eq in diet, day 7) and 0.02-0.03 mg/kg eq (high dose, 2.53 mg/kg eq in diet, day 7). Residues in the liver, kidney, muscle and fat of the low dose animal were all < 0.01 mg/kg eq. In the high dose animal, residues were 0.08, 0.04, < 0.01 and < 0.01 mg/kg eq, respectively.

Two groups of laying hens were dosed via capsules with [methyllene-^{14}C]terbufos for five consecutive days with the feed equivalent of 0.35 ppm for one group (Group B) and an exaggerated level of 1.05 ppm equivalent for the second group (Group C). Recovery of [^{14}C] residues in excreta over the 5-day treatment period averaged 91.4% of the total administered dose for the 1st group, and 88.9% for the 2nd group. For both dose levels, residues in eggs (days 1 through 5, both white and yolk), skin with adhering fat, muscle, liver or kidney tissues were all less than the LOQ of the radioassay (< 0.05 mg/kg eq).

The results of the hen study showed that terbufos when orally ingested at highly-exaggerated levels does not give rise to residues in the eggs or edible tissues of the laying hen.

Plant metabolism

The Meeting received information on the metabolic fate of ^{14}C-terbufos in soybeans, sugar beet, sweet corn, cabbage and rape seed.

Soybean plants were grown under field conditions from seed treated in the furrow at a rate of 1.1 kg ai/ha with [methylene-^{14}C]terbufos. The TRR levels found in the plant, expressed as terbufos equivalent, were 13.3 and 1.5 mg/kg in plants at one and two months after treatment, respectively. At harvest, residue levels were 1.8 mg/kg in fodder, 1.6 mg/kg in hulls and 1.3 mg/kg in the seed.

At the one-month sampling, 43% of the total extractable residue was identified as the phosphorylated metabolites: sulfoxide, sulfone, oxygen analog sulfone, and oxygen analog sulfoxide. The non-phosphorylated metabolites accounted for 11% of the residue. The remaining residue was comprised of five unknown metabolites (4%) and origin-bound compounds (17%). At harvest only non-phosphorylated metabolites were identifiable at low (< 10%) levels in all three commodities, i.e., hulls, fodder and seed. The remaining residue was shown to be very polar extractable materials or to have the ^{14}C incorporated into the cellulose and lignin of the hulls, fodder and protein and oil of the seed.

In conclusion, soybean seedlings can readily take up terbufos applied to the soil. The absorbed compound is then translocated and metabolized by oxidation, hydrolysis, methylation and subsequent oxidation to eventually yield principally non-phosphorylated, non-toxic metabolites.

In sugar beet metabolism studies, plants were grown from seed in soil treated with [methyllene-^{14}C]terbufos at a rate of 6.8 kg ai/ha. The levels of radioactivity in both foliage and roots were determined at 4.5, 8, l6, and 32 weeks after treatment. The TRR levels found in the various samples declined with time from 6.27 to 1.07 mg/kg eq in foliage and from 7.44 to 0.284 mg/kg eq in roots. The levels of ^{14}C recovered in all plants represented a total of only 2.3% of the applied dose. The data showed that metabolism of terbufos occurred at a faster rate in the roots. Chromatographic data obtained at different stages of plant growth indicated that terbufos is degraded mainly by way of oxidation, hydrolysis and methylation followed by subsequent oxidation to yield principally non-phosphorylated, non-toxic metabolites.

There is also evidence of incorporation of terbufos-derived radioactivity into the sucrose fraction of sugar beets.

In sweet corn metabolism studies, corn was grown in metal cylinders contained in greenhouses and treated with [methylene-^{14}C]terbufos at 1.1 kg ai/ha. Sweet corn contained 0.34, 2.64, 4.70 and 6.85% of the applied dose at 2, 4, 7 and 10 weeks of growth. The identified phosphate esters found as metabolites in sweet corn accounted for about 89% of the radioactivity. Levels of ^{14}C extracted from plants were separated into at least 19 radioactive metabolites using thin layer chromatography (TLC). The expected oxidation products of terbufos, i.e., the sulfoxide, the sulfone, the oxygen analog of sulfoxide and sulfone, were confirmed to be present as residues in the corn plants. In the corn plants sampled at 10 weeks the phosphorylated metabolites, terbufos sulfoxide (8.1 mg/kg eq), terbufos sulfone (2.8 mg/kg eq), terbufoxon (0.3 mg/kg eq), terbufoxon sulfoxide (16.9 mg/kg eq) and terbufoxon sulfone (5.6 mg/kg eq) accounted for 34% of the chloroform-soluble extractable radioactivity. A significant amount of the total hydrophilic radioactivity could be in the form of natural products.

In the cabbage metabolism study, plants were grown in a greenhouse and externally from seed in soil treated with [methyllene-^{14}C]terbufos at a rate of 2.2 kg ai/ha, using both a 15-G granular formulation and a liquid concentrate. The levels of radioactivity found in the cabbage plants, expressed as mg/kg equivalent of terbufos, declined with time (4 to 16 weeks) from 3.93 to 0.09 mg/kg eq for external granular treatment, from 1.48 to 0.04 mg/kg eq for the external liquid treatment and from 1.71 to 0.07 mg/kg eq for the greenhouse liquid treatment. The absolute amounts of radioactivity (in µCi) recovered in plants did not vary much with time. The recovered radioactivity represents a maximum of 1.5% of the total applied dose. At the end of 12 weeks, 92% (0.07 to 0.22 mg/kg eq) of the total radioactivity consisted of unidentified water-soluble metabolites and the total amount of phosphate compounds were less than 0.01 mg/kg eq. There was no apparent metabolic difference between granular (15-G) or liquid-treated soil in developing cabbage. The metabolism of terbufos in cabbage is similar to that reported for sugar beet.

In a rape metabolism study, rape seed was grown in soil treated with [methylene^{14}C]terbufos in the furrow at 0.28 kg ai/ha. The total residual radioactivity in rape plants expressed as parent was 0.63 and 0.68 mg/kg eq for 1 and 2 month post-treatment samples respectively. Residues were 0.42 mg/kg eq in the 2 month hulls sample. At harvest (3-months post treatment), the residue levels in fodder, hull and seed were 3.21, 3.63 and 1.11 mg/kg eq, respectively. The extractable radioactivity from the 1-month old rape plant was 90%, of which 48% was organosoluble and 42% was aqueous soluble. By two-dimensional TLC analysis, about 16.3% of the radioactive organosolubles migrated away from the plate origin and the remaining 31.7% of the radioactivity stayed at the origin. Among the migrating radiocomponents, non-phosphorylated compounds predominated with 4.9%, terbufoxon sulfoxide accounted for 4.0% and non-phosphorylated compounds and terbufos sulfoxide contributed to 1.7 and 1.3% of the resolved organoextractables respectively. The remaining 4.4% of the migrating radioactivity was made up of at least 6 minor components.

Rape plants can readily take up terbufos and closely related metabolites from the soil. The absorbed compounds are then initially metabolized in plant tissues by way of oxidation to phosphorylated metabolites such as terbufos sulfoxide and terbufoxon sulfoxide. These oxidized products degrade further through hydrolysis, methylation and subsequent oxidation thus leading to the formation of certain non-phosphorylated metabolites. In rape seeds, the hexane fraction comprised of 22% of the radioactivity which was probably associated with fatty acids or lipid-type compounds. The acetonitrile fraction, accounting for about 12%, mainly consisted of oil-related compounds and a non-phosphorylated compound along with trace amounts of several other minor components. The hydrolysis study indicated that incorporation of ^{14}C-formaldehyde or $^{14}CO_2$ derived from [^{14}C]terbufos, into natural products of various rape tissues accounts for a very large fraction of the radioactivity present in the plants or seeds.

In conclusion, the metabolic pathway for the formation of observed metabolites arises from sulfoxidation and desulfuration of terbufos, hydrolysis of the thiol-phosphorous bond (S=P), enzymatic S-methylation and finally S-oxidation. The studies evaluated show that the same oxidative phosphorylated metabolites of terbufos occur in plants and in animals. In addition, terbufos has been shown to be taken up by the roots, with the residues and metabolites translocated to all parts of the plants examined.

Environmental fate

The Meeting received information on aerobic degradation in soil, hydrolysis rates and products and a confined rotational crop study.

Degradation in soil (aerobic)

The metabolic fate of terbufos in soil was investigated in silt loam soil under aerobic conditions using [methylene-^{14}C]terbufos. The half-life of terbufos was approximately 5 days and of the total terbufos related residues was approximately 100 days. Major degradation products were carbon dioxide and the oxidative metabolites terbufos sulfoxide and terbufos sulfone. The concentration of terbufos sulfoxide in soil increased rapidly to a maximum of 2.6 mg/kg eq (52% of the applied dose) after 30 days and then declined to 0.3 mg/kg eq (6% of dose) after one year. Terbufos sulfone residues increased slowly to a maximum level of 1.0 mg/kg eq. (20% of applied dose) at 60 days and then decreased to 0.1 mg/kg eq (2.3% of dose) after one year.

Hydrolysis Rate and Products

Terbufos hydrolyses rapidly under abiotic conditions at environmentally relevant temperatures and would not be expected to persist in aquatic systems. Hydrolysis of terbufos sulfoxide and terbufos sulfone occurs more slowly, but the des-ethyl derivatives that formed are not expected to be of toxicological concern.

Confined Rotational Crop study

Residues of terbufos and related compounds were determined in soil and rotational crops (cabbage, red beets, and wheat) from a treated corn field. In the study in Wisconsin, corn was planted in a silt loam soil and treated at planting with 2.24 kg ai/ha. Residues of terbufos and related compounds were less than the LOQ of the method (0.05 mg/kg) in all cabbage, red beet and wheat grain samples. Wheat straw contained residues of 0.1 mg/kg. The soil half-life of terbufos and related compounds was calculated to be 30 days.

In another study conducted in Nebraska, corn planted in silt loam soil was treated at planting by soil incorporation with terbufos at the rate of 2.24 kg ai/ha. Residues of terbufos and related compounds were less than the LOQ of the method (0.05 mg/kg) in all cabbage, sugar beet and wheat grain samples. Spring wheat forage contained residues of 0.15 mg/kg. No residues were detected in winter wheat straw and grain. The soil half-life of terbufos and related compounds was calculated to be 17 days in beet plots, 16 days in cabbage plots, and 10 days in wheat plots.

Methods of analysis

The Meeting received information on validated methods of analysis of terbufos in plant matrices, animal matrices and environmental samples that were used in supervised trials, rotational crops studies and storage stability studies. Enforcement methods and multiresidue methods of analysis were also submitted to the Meeting.

Several analytical methods have been developed for the determination of terbufos in plant commodities and animal tissues, suitable for data collection and enforcement. All analytical methods for terbufos residues are designed to extract parent terbufos and its oxygenated metabolites: terbufos sulfoxide, terbufos sulfone, terbufoxon and terbufoxon sulfoxide. Terbufos and its metabolites are oxidized to the common moiety terbufoxon sulfone using m-chlorobenzoic acid, which is then analysed by gas chromatograph equipped with a phosphorus-selective detector. The methods vary slightly, usually in the extraction solvent used.

In plant samples, the LOQ for most of the reported trials was 0.05 mg/kg, but limits for some methods/substrates were 0.01 or 0.005 mg/kg. Recoveries of terbufos and its related metabolites were tested over the concentration range of 0.01 – 1.0 mg/kg on samples from all plant commodities reported in the trials.

In animal tissue samples, the LOQ for the milk is 0.005 or 0.01 mg/kg, for the tissue, 0.05 mg/kg, and for eggs, 0.01 mg/kg. Recoveries of terbufos and its related metabolites were tested on the samples over the concentration range of 0.005 – 1.0 mg/kg.

An adequate method is available for enforcement of terbufos MRLs in or on plant commodities. The GC method for determining terbufos and its phosphorylated metabolites is described in the Pesticide Analytical Manual (PAM), Vol.II as Method I modified by Method M-1754 substituting acetone for benzene and dichloromethane for chloroform.

Terbufos and its metabolites were taken through the US FDA Multiresidue Method with limited success.

Stability of pesticide residues in stored analytical samples

The stability of terbufos residues has been determined in freezer storage stability studies (from < 0 to -10ºC or -17ºC) in the representative plant commodities of corn (grain, plants and straw); sugar beet (tops and roots); and banana (unpeeled and pulp). Terbufos residues fortified in representative crop samples (root, grain, watery and oily commodities) were shown to be stable in frozen storage for approximately 18 months.

The stability of terbufos residues in milk (1.7–3.3ºC) has been determined and 79% of the residues were recovered after 14 days.

No stability studies were submitted to the Meeting on other animal matrices.

Definition of the residue

Metabolic studies on animals and plants have demonstrated that terbufos is metabolized in much the same way in all the biological systems studied. The decrease in the parent compound is accompanied by a short-term build-up of the sulfoxide and sulfone metabolites. The corresponding oxygen analogues are also formed, but at a much slower rate. Cleavage of the P=S bond yields, after methylation of the resulting thiol, a series of methylated metabolites differing in the oxidation state of the sulfur atoms.

Terbufos and all oxidation products are considered potent anticholinesterase agents.

Terbufos is readily metabolized in both plant and animal tissues by way of oxidation, hydrolysis and methylation which is then followed by further oxidation to principally non-toxic metabolites.

All analytical methods used to determine terbufos residues are designed to extract parent terbufos, and its oxygenated metabolites terbufos sulfoxide, terbufos sulfone, terbufoxon, and terbufoxon sulfoxide.

The Meeting confirmed the previous (JMPR 1989) residue definition for terbufos, both for enforcement and for risk assessment and for both animal and plant commodities as follows:

The sum of terbufos, its oxygen analogue and their sulfoxides and sulfones expressed as terbufos.

Although terbufos has a log k_{ow} of 4.71 based on the parent terbufos, the total residue of terbufos and related metabolites are not considered fat soluble.

Results of supervised trials on crops

Supervised residue trials were available for bananas, sugar beets, sweet corn, cereal grains (maize and sorghum); coffee beans, fodder and forage of cereal grains (maize and sorghum); and miscellaneous forage and fodder crops (sugar beet tops). A large number of trials were submitted from the 1970s based on analytical methods with an LOQ of 0.05 mg/kg. More recent trials were provided which had an improved LOQ of 0.01 and were used in estimating residues and establishing MRLs. In cases of finite residues, then relevant data from trials with an LOQ of 0.05 were considered acceptable to include in the data set. Supervised trials on the remaining commodities that currently have CXLs were not provided. The Meeting decided to withdraw the current recommendations for broccoli, cabbages (head), mustard seed, onion (bulb), peanut, peanut fodder, peanut forage (green), popcorn, rape seed, rapeseed oil (crude), soy beans (dry); straw and fodder of cereal grains, sugar beet fodder and wheat.

In situations where residues from supervised trials from GAP show nil residues, the MRL was chosen to reflect a level of sensitivity that is compatible with enforcement activities. Where analytical methods applied had different LOQs, the lowest value was chosen only if the nil residue could be expected. In this case, the High Residue value would be recommended at the highest LOQ used in the study unless a majority of the observations were derived from the more sensitive LOQ.

In situations where supervised trials from GAP showed nil residues, even at exaggerated rates, the MRL was chosen to reflect an LOQ that is compatible with enforcement activities. However, both the STMR and high residue values were recommended at zero.

Banana

Thirty six field trials were submitted to the Meeting from banana producing areas of the world including Australia, Costa Rica, Ecuador, Honduras, Panama, Philippines and Mexico. In the trials 100 g ai/kg (10G) or 150 g ai/kg (15G) granule (G) terbufos was applied to the soil at the base of daughter banana plants at 1-9 g ai/plant/application. Application rates varied with a maximum rate of application per plant per year at of 41 g ai. GAP application rates ranged from 2-4 g ai/plant with a maximum of 12 g ai/year in Australia and Central America, 2 g ai/plant with a maximum of 8 g ai/year in Philippines and 3g ai/plant to the maximum of 9 g ai/year in Mexico. No PHI was specified in the various national GAPs.

Residue levels ranged from <LOQ (< 0.01 or < 0.002) to 0.03 mg/kg for those trials where substantially exaggerated rates (2-3 times GAP) were applied. However, the majority of the trials did not conform to GAP. The residues from trials that were conducted according to GAP were <u>< 0.01</u>(6) and 0.02(2) mg/kg.

The meeting estimated a maximum residue level for bananas of 0.05 mg/kg, and STMR of 0.01 mg/kg and a HR of 0.02 mg/kg.

Sugar beets (roots)

Field trials involving at-planting and post-emergence treatments with terbufos were made available to the Meeting from the USA. The trials were conducted during the 1986, 1989 and 1994 growing seasons. In 1986, terbufos (15G) was applied at planting (banded, knifed-in, or in-furrow) at 2.2 kg ai/ha. In the trials conducted in 1989, terbufos (15G) was knifed in as a band at planting at 4.9 kg ai/ha, in excess of the current US GAP. Residues reflecting GAP were < 0.01(6) and 0.01(2) mg/kg where the PHI was considered equivalent to GAP, i.e., from 91-141 days.

In more recent field trials (1994), terbufos (15G) was applied as a band over the row to sugar beets at 2.2 to 2.4 or 4.4-4.9 kg ai/ha. The lower rate reflects the maximum GAP rate. Again, residues reflecting GAP were < 0.01(5) mg/kg. The PHI was considered equivalent to GAP at 90 days.

For knifed-in applications data was available at only 2 times the GAP rate where low finite residues could be found in some cases (< 0.01, 0.01, 0.02 and 0.03). Another knifed-in application trial had residues at < 0.01. The PHI for these trials ranged from 139-180 days (GAP is 150 days).

For all trials conducted according to GAP, total terbufos-related residues were: < 0.01(11) and 0.01(2) mg/kg.

The meeting withdrew its previous recommendation of 0.1 mg/kg and estimated a maximum residue level for sugar beets of 0.02 mg/kg, an STMR of 0.01 mg/kg and a highest residue of 0. 01 mg/kg.

Sweet corn Kernels and Corn-on-the Cob

Field trials involving at-planting and post-emergence treatments with terbufos were made available to the Meeting from the USA. In trials from 1972–1974, terbufos granules were applied in the furrow or in a band at the time of planting at rates of 1.1 to 9.0 kg ai/ha. In 1986 terbufos granules were applied to the soil at planting (in furrow or in a band), at post-emergence or at cultivation at a combined rate of about 6.0 kg ai/ha. GAP in the USA for 15G or 20G (200 g ai/kg) terbufos formulations is at a maximum rate of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. For post-emergent applications, the PHI is 30 days for forage, and 60 days for corn-on-the cob.

For post-emergent use, samples were analysed only where the PHI was less than that for GAP. Residue values from the majority of trials (7) were lower than the LOQ (0.01 mg/kg). For two trials, where the equivalent of three times the GAP rate was applied in two applications, residues found were 0.01 mg/kg (2).

The meeting withdrew its previous recommendation of 0.01 (*) mg/kg and estimated a maximum residue level for sweet corn of 0.01(*) mg/kg, an STMR of 0.01 mg/kg and a HR of 0.01 mg/kg.

Cereal Grains

Maize grain

Field trials involving at-planting and post-emergence treatments with terbufos were made available to the Meeting from the USA. GAP in the USA for terbufos 15G or 20G formulations is at the maximum rate of 1.5 kg ai/ha applied once at planting, post-emergent, or at cultivation. A PHI of 30 days is required for forage if applied post-emergent. In trials conducted from 1981 to 1986, terbufos granules were applied to the soil at planting, either in furrow or as a band, at the rate of 1.1 to 1.8 kg ai/ha. In some trials, additional plots were treated with terbufos at rates up to five times the recommended label rates. In trials conducted from 1990 to 1996 terbufos granules were applied post-emergent at the

recommended rate of 1.5 kg ai/ha as well as at higher rates up to five times the recommended application rates.

In all the trials conducted on maize grain according to GAP, total terbufos-related residues were below the LOQ of the analytical method: < 0.01 mg/kg (13). In trials where higher rates of application or more than one application was made, the residue levels were also below the LOQ. Since there were finite residues found in the trials for sweet corn at exaggerated rates, the use pattern for maize grain is not considered a nil residue situation and relevant values for STMR and HR have been proposed.

The meeting confirmed its previous recommendation for a maximum residue level of 0.01(*) mg/kg and estimated an STMR of 0.01 mg/kg and a highest residue of 0.01 mg/kg for maize.

Sorghum grain

Field trials involving at-planting and post-emergence treatments with terbufos were made available to the Meeting from the USA. GAP in the USA for terbufos 15G or 20G formulation consists of a maximum rate of 2.0 kg ai/ha applied once with a PHI of 50 days for forage, and 100 days for grain and fodder.

Results of all trials conducted according to the GAP for sorghum grain, including post-emergent applications, showed total terbufos-related residues below the LOQ: < 0.01 mg/kg (5). Residues were at non-detectable levels even in trials where higher rates of application or shorter PHI 58-76 days (6 trials) were used.

The meeting estimated a maximum residue level for sorghum grain of 0.01(*) mg/kg, an STMR of 0.

Coffee beans

Residue trials were conducted during 1982–1988 in Costa Rica, Guatemala, and El Salvador.

In field trials in Costa Rica conducted in 1982–1983, a 10G granular formulation of terbufos was applied to the soil at the base of established coffee plants at the rate of 0.75–7.5 g ai/plant. Berries were collected from treated plants at various intervals, field dried according to common practice, and the outer shell removed from the dried beans.

In the trials in El Salvador and Guatemala (1988), terbufos (10G) was band applied to plants after flowering but before bean formation, at the rate of 1 or 5 g ai/plant. From treated plants field dried berries, with outer shell removed, were collected at 38–56 days in El Salvador and at 163-197 days in Guatemala.

GAP in coffee bean plantations permits the application of terbufos at a maximum rate of 1.1g ai/plant for up to 2 applications with a PHI of 60 days. No trials were conducted at the maximum GAP. However, residue levels were below the LOQ (< 0.05 mg/kg) in all coffee bean samples (10) collected 58–120 days after treatment with terbufos at 0.75–7.75 g ai/plant rate. At one site, where coffee beans had been treated with 3.75 and 7.5 g ai/plant and shorter than GAP PHI of 60 days (47 or 35 days after treatment), maximum residues of 0.12 and 0.17 mg/kg respectively, were found. Residues declined to < 0.05 mg/kg at the next sampling interval, 124 or 53 days post-treatment.

The meeting confirmed its previous recommendation for a maximum residue level of 0.05 (*) mg/kg and estimated an STMR of 0.05 mg/kg for coffee beans.

Animal feed commodities

Fodder and forage of cereal grains

As maize forage, sorghum forage and sugar beet tops are not moving in international trade the Meeting made no recommendations regarding maximum residue levels for these commodities.

Maize forage and fodder

The GAP for terbufos 15G or 20G formulation in the USA allows for a maximum application rate of 1.5 kg ai/ha applied once either at-planting, early post-emergence, or at cultivation. A PHI of 30 days is required for forage when applied post-emergent. The same GAP applies to both maize and sweet corn. Trials on maize and sweet corn for residues in fodder and forage were conducted in the USA during 1972–1990. Terbufos granules were applied to the soil either in-furrow or in a band during planting at the rate of 1.1 – 5.8 kg ai/ha. In a few trials, tests were performed where two applications were made to maize one at planting and a second treatment 5–6 weeks after planting.

The residues deriving from trials conducted in sweet corn and maize were found to represent similar populations which could be combined (Mann-Whitney U-test). Residues, on a fresh weight basis, from trials conducted according to GAP were, with median underlined, <u>< 0.05</u> (11), 0.07(2), 0.14, 0.16, 0.17, 0.23, 0.32 and 0.96 mg/kg. The highest residue value (HR) was 0.96 mg/kg from trials in Colorado, USA from forage samples taken 90 days after treatment at planting at a rate of 1.5 kg ai/ha. Applying the default percent dry matter content (average between %DM of sweet corn forage and field corn forage, as listed in the *FAO Manual* (FAO, 2002) for maize forage (44%)), the highest residue on dry weight basis is estimated as 2.2 mg/kg.

The Meeting withdrew its previous recommendation of 1 mg/kg and estimated an STMR of 0.10 mg/kg and a highest residue of 2.2 mg/kg for maize forage.

Residue levels from trials according to GAP for maize fodder were: < LOQ i.e., < 0.05(38) and 0.08 mg/kg (from one trial in Colorado, USA, sampled at harvest after treatment at the rate of 1.5 kg ai/ha at planting). Applying the default percent dry matter value of 83% for corn fodder, as listed in the *FAO Manual* (FAO, 2002), the highest residue on dry weight basis was calculated as 0.10 mg/kg.

The meeting withdrew its previous recommendation of 0.1 mg/kg and estimated, on a dry weight basis, a maximum residue level of 0.2 mg/kg, an STMR of 0.06 mg/kg and a highest residue of 0.10 mg/kg for maize fodder.

Sorghum forage and fodder

Supervised trials on sorghum were conducted during 1978–1996. In the 1996 trials, terbufos granules were applied post-emergent, at the rate of 2.1 or 2.2 kg ai/ha. Forage samples were harvested 48 to 72 days after treatment while fodder samples were taken at normal grain harvest time, 88 to 90 days after treatment. In the rest of the trials (1978–1991), terbufos granules were applied at planting, at the GAP rate (2 kg ai/ha) and at twice that rate (4 – 4.3 kg ai/ka).

All trials according to the GAP resulted in residues below the LOQ for sorghum forage (<u>≤ 0.05</u> mg/kg), except one trial (Louisiana, USA) where a level of 0.07 mg/kg was recorded. This highest residue value was from forage samples taken 50 days after treatment with terbufos at a rate of 2.0 kg ai/ha at the vegetative stage. The moisture content of samples was only determined from some trials with the results showing wide variations. The Meeting therefore decided to use the default percent dry matter for sorghum forage (35%), as listed in the *FAO Manual* (FAO, 2002) to estimate the highest residue value.

The Meeting estimated an STMR for sorghum forage, on a dry weight basis, of 0.14 mg/kg and a highest residue of 0.20 mg/kg.

Residue levels in sorghum fodder ranged from < 0.05 to 0.19 mg/kg. Residues from trials conducted according to GAP were < 0.05 (12), 0.12 and 0.19 mg/kg. The highest residue value was 0.19 mg/kg from trials where fodder samples were taken 88 days after a post-emergent treatment at a rate of 2.2 kg ai/ha. Applying the default percent dry matter for sorghum fodder/stover of 88%, as listed in the *FAO Manual* (FAO, 2002), the highest residue on dry weight basis was estimated as 0.22 mg/kg.

The Meeting estimated, on a dry weight basis, a maximum residue level of 0.3 mg/kg, an STMR of 0.057mg/kg and a highest residue of 0.22 mg/kg for sorghum fodder.

Sugar beet tops

Field trials were conducted in the USA and Canada during 1971–1975 in which terbufos (15G) was either applied in-furrow or banded at 1.0 to 2.5 kg ai/ha or at exaggerated rates of 4.0–12.3 kg ai/ha. Several trials were also conducted which consisted of sequential at-planting and post-emergence banded applications, typically utilizing exaggerated rates.

Several trials were also conducted in the USA during the 1989 growing season in which terbufos (15G) was knifed in at-planting at 4.9 kg ai/ha. Samples were harvested by hand at maturity, 150–180 days after treatment. Residues found in all control samples of tops were < 0.05 mg/kg.

In US field trials in 1994, terbufos (15G) was applied as a band over the row to sugar beets at the maximum GAP rate of 2.2 to 2.4 kg ai/ha and at 2× GAP rates of 4.4 to 4.9 kg ai/ha. Residue levels ranged from < LOQ (0.01 or < 0.05) to 0.82 mg/kg for sugar beet tops samples. Residues found from trials conducted according to GAP were < 0.01(3), 0.01, 0.04, < 0.05 (18), 0.12, 0.15 and 0.82 mg/kg. The highest residue value (HR) found was 0.82 mg/kg, from samples taken 91 days following an at-planting treatment of 1.8 kg ai/ha Applying the default percent dry matter for sugar beet tops (23%), as listed in the *FAO Manual* (FAO, 2002), the highest residue on dry weight basis was estimated as 3.57 mg/kg.

The Meeting withdrew its previous recommendation for a maximum residue level of 1 mg/kg for fodder beet leaves or tops and estimated, on a dry weight basis, an STMR of 0.22 mg/kg for sugar beet tops and a highest residue of 3.6 mg/kg.

Dietary burden in farm animals

The Meeting estimated the dietary burden of terbufos residues in farm animals on the basis of the diets listed in Appendix IX of the *FAO Manual* (FAO, 2002). One feed commodity from each Codex Commodity Group was used. Calculation from the HR values provides the concentrations in feed suitable for estimating MRLs for animal commodities, while calculation based on STMR values for feed is suitable for estimating the STMR values for animal commodities.

Table 49. Estimated maximum dietary burden of farm animals.

Commodity	Codex group	Residue (mg/kg)	Basis	DM (%)	Residue, dry wt. (mg/kg)	*Diet content (%)*			Residue Contribution (mg/kg)		
						Beef cattle	*Dairy cows*	*Poultry*	Beef cattle	Dairy cows	Poultry
Maize forage	AF	0.96	highest residue	44%	2.2	*40%*	*50%*	*NU*	0.88	1.1	
Maize fodder	AS	0.08	highest residue	83%	0.10			*NU*			
Maize grain	GC	0.01	highest residue	88%	0.011	*40%*	*40%*	*80%*	0.004	0.004	0.009
Sorghum	GC	0.0	highest residue	86%	0			*20%*			0
Sorghum forage	AF	0.07	highest residue	35%	0.20			*NU*			
Sorghum fodder	AS		highest	88%	0.22			*NU*			

Commodity	Codex group	Residue (mg/kg)	Basis	DM (%)	Residue, dry wt. (mg/kg)	*Diet content (%)*			Residue Contribution (mg/kg)		
						Beef cattle	*Dairy cows*	*Poultry*	Beef cattle	Dairy cows	Poultry
Sugar beet tops	AV	0.19 0.82	residue highest residue	23%	3.60	*20%*	*10%*	*NU*	0.72	0.36	
TOTAL						*100%*	*100%*	*100%*	1.60	1.47	0.009

Table 50. Estimated median dietary burden of farm animals.

Commodity	Codex group	Residue (mg/kg)	Basis	DM (%)	Residue, dry wt. (mg/kg)	Diet content (%)			Residue Contribution (mg/kg)		
						Beef cattle	Dairy cows	Poultry	Beef cattle	Dairy cows	Poultry
Maize forage	AF	0.05	STMR	44%	0.10	40%	50%	NU	0.04	0.05	
Maize fodder	AS	0.05	STMR	83%	0.06			NU			
Maize grain	GC	0.01	STMR	88%	0.011	40%	40%	80%	0.004	0.004	0.009
Sorghum	GC	0.0	STMR	86%	0.0			20%			0
Sorghum forage	AF	0.05	STMR	35%	0.14			NU			
Sorghum fodder	AS	0.05	STMR	88%	0.057			NU			
Sugar beet tops	AV	0.05	STMR	23%	0.22	20%	10%	NU	0.044	0.022	
TOTAL						100%	100%	100%	0.088	0.076	0.009

Estimation of Dietary Burdens

The highest residues or STMR values for feed commodities were used in calculating the worst-case dietary burden for dairy cows, beef cattle and poultry while the STMR values were used in the estimation of the median dietary burdens. The respective dietary burdens were then compared with the results of the feeding studies at various dose levels (mg/kg in diet) to estimate the maximum residue levels and STMR in animal commodities.

The dietary burdens of terbufos for estimates of STMR and highest residue level values in animal commodities (residue levels in animal feeds expressed as dry weight) are 0.088 mg/kg and 1.60 mg/kg for beef cattle, 0.076 mg/kg and 1.47 mg/kg for dairy cows and 0.009 mg/kg and 0.009 mg/kg for poultry.

Farm animal feeding studies

Feeding studies indicated that at a dose (2 ppm for 21 days) approximately equivalent to the calculated animal diets, no residues (< 0.05 mg/kg) of terbufos or its metabolites were detectable in cattle tissues and milk. In another study, done at an exaggerated rate (50 ppm), only one milk sample had a finite residue (0.011 mg/kg) while one sample had residue at the LOQ (0.005 mg/kg) and the rest were below the LOQ.

The Meeting received a feeding study in poultry. Hens were fed at 2 ppm terbufos for 21 days and residues were determined in poultry tissues and eggs. The LOQ was 0.05 and 0.01 mg/kg for tissues and eggs, respectively. All tissues and eggs samples contained residues below the LOQ value.

MAXIMUM RESIDUE LEVELS

The estimated maximum dietary burdens for beef cattle (1.60 mg/kg) and for dairy cows (1.47 mg/kg) matched the feeding level from the respective cattle feeding studies (2 mg/kg). As a result the Meeting decided to use the residue levels from the feeding studies as estimates of the maximum residue levels for cattle tissues and milk. Residues in cattle tissues and milk in the feeding studies were all below the LOQ (< 0.05 mg/kg for cattle fat, muscle, liver, and kidney, and < 0.01 mg/kg for milk). The

calculated median dietary burdens were lower than the actual feeding level in both transfer studies, 0.088 mg/kg for beef cattle and 0.076 mg/kg in dairy cattle therefore the calculated median residues would also be expected to be lower.

The actual feeding level of laying hens was (2 ppm for 21 days), the calculated maximum and median dietary burdens (0.009 ppm) were lower than the residue levels in both tissue and eggs. Consequently, no detectable residues are expected in both tissues and eggs. Therefore, residues are expected to be well below the LOQ for the method used (< 0.05 mg/kg for poultry tissues and < 0.01 mg/kg for eggs).

The calculations confirmed the findings of the animal metabolism studies as well as the results of the feeding studies, that showed no residues of terbufos or its metabolites were detectable in cattle tissues, poultry tissues, milk, and eggs. The MRL and STMR for residues of terbufos in animal commodities are proposed at the limit of quantification of the analytical method.

The Meeting withdrew its previous recommendation of 0.05 (*) mg/kg for cattle meat, cattle edible offal, chicken meat and chicken edible offal and 0.01 (*) mg/kg for cattle milk. The Meeting confirmed its previous recommendation of 0.01 (*) mg/kg for eggs and estimated a maximum residue level of 0.05 (*) mg/kg for meat from mammals other than marine mammals and mammalian edible offal, and 0.01(*) mg/kg for milks. The Meeting recommended an STMR of 0.05 mg/kg for mammalian meat and edible offal and poultry tissues and 0.01 mg/kg for milk and eggs. The estimated high residues are 0.05 mg/kg for mammalian meat, edible mammalian offal, chicken meat and edible chicken offal and 0.01 mg/kg for milks and eggs.

RECOMMENDATIONS

Definition of residue is for compliance with MRLs and for estimation of dietary intake for plant and animal commodities: the sum of terbufos, its oxygen analogue, and their sulfoxides and sulfones, expressed as terbufos.

Table 51. Summary of recommendations.

Commodity		MRL mg/kg		STMR ,	HR ,
CCN	**Name**	**New**	**Previous**	**mg/kg**	**mg/kg**
FI 0327	Banana	0.05	0.05	0.01	0.02
VB 0400	Broccoli	W	0.05(*)		
VB 0041	Cabbages, head	W	0.05(*)		
	Cattle meat	W	0.05 (*)		
	Cattle milk	W	0.01 (*)		
	Cattle, Edible offal of	W	0.05 (*)		
	Chicken meat	W	0.05 (*)		
	Chicken, Edible offal of	W	0.05 (*)		
SB 0716	Coffee beans	0.05(*)	0.05(*)	0.05	
PE 0112	Eggs	0.01(*)	0.01 (*)	0.01	0.01
AV 1051	Fodder beet leaves or tops	W	1		
GC 0645	Maize	0.01(*)	0.01(*)	0.01	
AF 0645	Maize forage,	W	1		
AS 0645	Maize fodder,(dry)	0.2	0.1		
MO 0105	Edible offal(mammalian)	0.05(*)	0.05(*)	0.05	0.05
MM 0095	Meat (from mammals other marine mammals)	0.05(*)	0.05 (*)	0.05	0.05
ML 0106	Milks	0.01(*)	0.01 (*)	0.01	
SO 0485	Mustard seed	W	0.05(*)		
VA 385	Onion, bulb	W	0.05(*)		
SO 0697	Peanut	W	0.05(*)		

Commodity		MRL mg/kg		STMR ,	HR ,
CCN	Name	New	Previous	mg/kg	mg/kg
AL 0697	Peanut fodder	W	1		
AL 1270	Peanut forage (green)	W	1		
	Popcorn	W	0.01		
PM 0110	Poultry meat	0.05(*)		0.05	0.05
PO 0111	Poultry edible offal of	0.05(*)		0.05	0.05
PE 0112	Eggs	0.01(*)		0.01	0.01
SO 0495	Rape seed	W	0.05(*)		
	Rape seed	W	0.05		
	Rape seed oil, Crude	W	0.05		
VD 0541	Soybeans (dry)	W	0.05(*)		
GC 0651	Sorghum	0.01(*)		0	
AS 0651	Sorghum straw and fodder,(dry)[1]	0.3			
AS 0081	Straw and fodder of cereal grains	W	1		
VR 0596	Sugar beet	0.02	0.1	0.01	0.01
VO 0447	Sweet corn (corn-on-the-cob)	0.01	0.01(*)	0.01	0.01
GC 0654	Wheat	W	0.01(*)		

1Expressed on dry weight basis

DIETARY RISK ASSESSMENT

Long-term intake

The International Estimated Dietary Intakes (IEDIs) were calculated for the five GEMS/Food regional diets using the STMR for banana, coffee beans, edible offal (mammalian), eggs, maize (fresh, flour), meat from mammals other than marine mammals, milks, poultry meat, poultry edible offal, sorghum, sugar beet and sweet corn (corn on the cob) estimated by the current Meeting (Annex 3 of the 2005 JMPR Report). The ADI is 0–0.0006 mg/kg and the calculated IEDIs were 9–40% of the maximum ADI. The Meeting concluded that the intake of residues of terbufos resulting from the uses considered by the current JMPR were unlikely to present a public health concern.

Short-term intake

The International Estimated Short-Term Intakes (IESTIs) of terbufos by the general population and by children were calculated for commodities by the current Meeting (Annex 4 of the 2005 JMPR Report). This was based on HRs estimated by the Meeting from available information on consumption. The ARfD is 0.002mg/kg and the calculated IESTIs for children up to 6 years range from 0–60% and those for general population from 0–30% of the ARfD. The Meeting concluded that the short-term intake of residues of terbufos resulting from the uses considered by the current Meeting were unlikely to present a public health concern.

REFERENCES

Anonymous. (1973). Gas Chromatographic Procedure for the Determination of CL 92,100-Related Compounds in Sugar Beet Tops (Greens) and Roots. [TE-244-009]

Anonymous. (1986). Gas Chromatographic Determination of AC 92100 Related Compounds in Sugar beet Tops and Roots. [TE-244-063]

Babbitt, B. (1986). Counter Terbufos (CL 92,100): Validation of GC Method M-1615 for the Determination of Total CL 92,100 Related Residues in Drinking Water. Report C-2678. [TE-243-003]

Barringer, D. F. (1973). COUNTER ® Insecticide: The Identification of the Major Metabolites Found in Mature Sweet Corn Plants and in Soil, American Cyanamid Company, PD-M Volume 10, (Princeton). [TE-640-006]

Bohn, R. (1981). Counter Terbufos (CL 92,100): Validation of GC Method M-1144 for the Determination of Total CL 92,100 Related Residues in Water. Report C-1833. [TE-243-001]

Bohn, R. (1981). Counter Terbufos (CL 92,100): Validation of GC Method M-1149 for the Determination of CL 92,100, CL 94,301 and CL 94,320 Residues in Water. Report C-1892. [TE-243-002]

Bohn, W. (1979). COUNTER Terbufos CL 92,100: Solubility of CL 94, 301 (terbufos sulfoxide) and CL 94,320 (terbufos sulfone) in Distilled Water. Report C-1600. [TE-311-003]

Bohn, W. (1984). Counter (CL 92,100/10 G): Residues of Total CL 92,100-Related Compounds in Green Coffee Beans (Costa Rica, 1983). ARD Princeton, NJ. USA. Report C-2459. Unpublished. [TE-790-002]

Bohn, W. (1985). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1984). ARD Princeton, NJ. USA. Report C-2622. Unpublished. [TE-714-007]

Bohn, W. (1985). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1984). ARD Princeton, NJ. USA. Report C-2621. Unpublished. [TE-714-008]

Bohn, W. (1984). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1984). ARD Princeton, NJ. USA. Report C-2493. Unpublished. [TE-714-009]

Bohn, W. (1984). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (GND; Costa Rica; 1984). ARD Princeton, NJ. USA. Report C-2494. Unpublished. [TE-714-012]

Bohn, W. and Behm, J. (1985). Counter Terbufos (CL 92,100/10G): Residues of Total CL 92,100-Related Compounds in Bananas (Costa Rica, 1984). ARD Princeton, NJ. USA. Report C-2622. Unpublished. [TE-714-013]

Bohn, W. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica, 1986). ARD Princeton, NJ. USA. Report No. C-2793. Unpublished. [TE-714-001]

Bohn, W. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1984). ARD Princeton, NJ. USA. Report C-2674. Unpublished. [TE-714-006]

Bohn, W. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1986). ARD Princeton, NJ. USA. Report C-2792. Unpublished. [TE-714-011]

Bohn, W. (1987). Counter Terbufos (CL 92,100): Validation of GC Method M-1747 For The Determination of Total CL 92,100-Related Residues in Sugar Beet Roots (0.01 ppm). Report C-2973. [TE-244-007]

Bohn, W. and Zummo, G. (1988). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar Beet Roots (Colorado). . ARD Princeton, NJ. USA. Report C-3064. Unpublished. [TE-724-064]

Bohn, W., and Zummo, G. (1988). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar Beet Roots (North Dakota). . ARD Princeton, NJ. USA. Report C-3065. Unpublished. [TE-724-065]

Bohn, W., and Zummo, G. (1988). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar Beet Roots Idaho). . ARD Princeton, NJ. USA. Report C-3066. Unpublished. [TE-724-066]

Bohn, W., and Zummo, G. (1988). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar Beet Roots (Minnesota). ARD Princeton, NJ. USA. Report C-3067. Unpublished. [TE-724-067]

Brindle, P. (1990). Terbufos (CL 92,100): Metabolic Fate of Carbon-14 CL 92,100 in Tissues, Blood and Eggs of the Laying Hen, PD-M Volume 27-13, (Princeton). [TE-440-003]

Brindle, C. (1990). Terbufos 10G: Residues of Total CL 92,100-Related Compounds in Dry Processed Coffee (Guatemala, 1988). ARD Princeton, NJ. USA. Report C 3380. Unpublished. [TE-790-004]

Brindle, C. (1990). Terbufos 10G: Residues of Total CL 92,100-Related Compounds in Dry Processed Coffee (El Salvador, 1988.). ARD Princeton, NJ. USA. Report C 3379. Unpublished. [TE-790-005]

Caballa, S. (1973). COUNTER® Insecticide (15-G): Metabolism of Carbon-14 Labeled CL 92,100 in Sugar Beets. American Cyanamid Company. Report C-405. [TE-640-010]

Caballa, S. (1974). COUNTER® Insecticide (15-G): Metabolism of Carbon-14 Labeled CL 92,100 in Sugar Beets. PD-M 11: 418-440 (Princeton). [TE-640-003]

Cheng, T., (1992). Metabolism of 14C-Terbufos (CL 92,100) in Rats (Preliminary and Definitive Phases), Princeton, NJ. [TE-440-004]

Chiu, T. Y. (1980). COUNTER® Insecticide (CL 92,100): Metabolism of Carbon-14 CL 92,100 in Rape, PD-M Volume 17-8 (Princeton). [TE-640-007]

Chiu, T. (1981). COUNTER® Terbufos (CL 92,100): Metabolism of Carbon-14 Labeled CL 92,100 in Soybean. PD-M 18-19; 1-65 (Princeton). [TE-640-001]

Dixon, C. (1989). Freezer Stability of Total CL 92,100-Related Residues in Sugar Beet Tops and Roots. Report C-3298. [TE-326-012]

Dixon, C. (1990). Freezer Stability of Total CL 92,100 Related Residues in Corn Grain Plants and Straw. Report C-3299. [TE-326-014]

Dixon, C. (1990). Terbufos (CL 92,100): Analysis of Total CL 92,100-Related Residues in Bananas Treated with Counter 10G Insecticide. ARD Princeton, NJ. USA. Report C-3509. Unpublished. [TE-714-016]

Elenewski, C. and Walgenbach, P. (1982). Counter Terbufos (CL 92,100/15-G, 20G): Residues of Total CL 92,100-Related Residues in Corn Plants and Grain (North Carolina). American Cyanamid Company. Report C-2082. Unpublished. [TE-723-026]

Elenewski,C. (1983). Counter Terbufos (CL 92,100): Validation of GC Method M-1340 for the Determination of CL 92,100-Related Residues in Whole Bananas. Report C-2260. [TE-244-005]

Elenewski,C. (1983). Counter Terbufos (CL 92,100): Validation of GC Method M-1360 for the Determination of CL 92,100-Related Residues in Coffee Beans. Report C-2305. [TE-244-015]

Elenewski, C. and Walgenbach, P. (1983). Counter terbufos (CL 92,100/15-G): Residues of Total CL 92,100-Related Compounds in Field Corn Plants, Fodder and Grain (Nebraska). Report C-2215. American Cyanamid Company. Unpublished. [TE-730-018]

Fletcher, P. (1998). CL 92,100 (Terbufos): Total CL 92,100-Related Residues in Corn Grain after Treatment at Cultivation with COUNTER 15G Systemic Insecticide-Nematicide in Illinois. Report RES 96-084. American Cyanamid Company. Unpublished. [TE-730-051]

Fletcher, P. (1997). CL 92100 Terbufos: Total CL 92100-Related Residues in Sorghum Forage, Grain, and Stover after Treatment at Cultivation with Counter 15G Systemic Insecticide-Nematicide in Texas. American Cyanamid Company, NJ, USA. Report RES-96-077. [TE-730-052]

Fletcher, P. (1997). CL 92100 Terbufos: Total CL 92100-Related Residues in Sorghum Forage, Grain, and Stover after Treatment at Cultivation with Counter 15G Systemic Insecticide-Nematicide in Texas. American Cyanamid Company, NJ, USA. Report RES-96-078. [TE-730-053]

Fletcher, P. (1997). CL 92100 Terbufos: Total CL 92100-Related Residues in Sorghum Forage, Grain, and Stover after Treatment at Cultivation with Counter 15G Systemic Insecticide-Nematicide in Louisiana. American Cyanamid Company, NJ, USA. Report RES-96-079. [TE-730-054]

Fletcher, P. (1997). CL 92100 Terbufos: Total CL 92100-Related Residues in Sorghum Forage, Grain, and Stover after Treatment at Cultivation with Counter 15G Systemic Insecticide-Nematicide in Kansas. American Cyanamid Company, NJ, USA. Report RES-96-080. [TE-730-055]

Fletcher, P. (1997). CL 92100 Terbufos: Total CL 92100-Related Residues in Sorghum Forage, Grain, and Stover after Treatment at Cultivation with Counter 15G Systemic Insecticide-Nematicide in Illinois. American Cyanamid Company, NJ, USA. Report RES-96-081. [TE-730-056]

Fletcher, P. (1997). CL 92100 Terbufos: Total CL 92100-Related Residues in Sorghum Forage, Grain, and Stover after Treatment at Cultivation with Counter 15G Systemic Insecticide-Nematicide in Missouri. American Cyanamid Company, NJ, USA. Report RES-96-082. [TE-730-057]

Gross, J. (1990). Terbufos (CL 92,100): Characteristics of Terbufos CL 92,100 and Its Phosphorylated Metabolites through FDA Multiresidue Methods. Report C-3363. [TE-244-059]

Higham, J.W. (1973). Counter 15G: Total Counter (CL 92,100)-Related Residues in Sweet Corn (California, Illinois, Oregon and Wisconsin). Report C-417. American Cyanamid Company. Unpublished. [TE-723-002]

Higham, J. (1973). Counter (CL 92,100)-Related Residues in Field Corn Treated In-Furrow (Illinois, Iowa, Nebraska, New York, and North Dakota). American Cyanamid Company, NJ, USA. Report No. C-416. [TE-730-016]

Higham, J. (1973). Counter 15G: Total Counter (CL92100) Related Residues in Field Corn Treated "in a Band" (Indiana, Iowa, Missouri, Nebraska, New York, North Carolina, North Dakota and South Dakota). Report C-415. American Cyanamid Company. Unpublished. [TE-730-017]

Higham, J. (1974). Counter 15G: Total Counter (CL 92100) Related Residues in Irrigated Field Corn, Sweet corn and Popcorn (Colorado). Report C-425. American Cyanamid Company. Unpublished. [TE-730-002]

Higham, J. (1974). Counter (CL 92,100): The Gas Chromatographic Determination of Total CL 92,100 Related Residues in Fortified Sugar Beet Tops (Greens) and Roots. ARD Princeton NJ USA. Report C-532. [TE-244-004]

Higham, J. (1975). Counter (CL 92,100): The Gas Chromatographic Determination of CL 92,100 Related Residues in Fortified Corn Silage Corn Fodder Field Corn Grain Popcorn Grain and Sweet Corn Kernels Plus Cob With Husk Removed. ARD Princeton NJ USA. Report C-607. [TE-244-054]

Higham, J. (1975). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet (Tops And Roots) (North Dakota). ARD Princeton, NJ. USA. Report C-694. [TE-724-014]

Higham, J. (1975). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots Following Band, In-Furrow And Post Emergent Applications (ND). ARD Princeton, NJ. USA. Report C-695. [TE-724-016]

Higham, J. and Alvarez, C.G. (1975). Counter (CL 92,100): Determination of CL 92,100(S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate) Related Residues in Sweet Corn Plant and Ears following "In-furrow" Treatment at Planting (Florida). Report C-632. American Cyanamid Company. Unpublished. [TE-723-014]

Higham, J., and Alvarez, C. (1975). Counter CL92100 Determination Of Total CL92100 Related Residues In Sugar Beet Tops And Roots (North Dakota). ARD Princeton, NJ. USA. Report C-656. [TE-724-048]

Higham, J. and Alvarez, C. (1975). Counter CL92100 Determination Of Total CL92100 Related Residues In Sugar Beet Tops And Roots (Wyoming). ARD Princeton, NJ. USA. Report C-657. [TE-724-049]

Higham, J. and Nau, H. (1975). Counter CL92100 Determination Of Total CL92100 Related Residues In Sugar Beet Tops And Roots (Minnesota). ARD Princeton, NJ. USA. Report C-696. [TE-724-050]

Higham, J. and Nau, H. (1975). Counter (CL92100): Determination of CL92100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate) Related Residues In Field Corn Following "In-Furrow" Application (Minnesota). Report C-631. American Cyanamid Company. Unpublished. [TE-723-013]

Higham, J. and Nau, H. (1975). Counter (CL92100): Determination of CL92100(S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate) "Terbufos" Residues in Corn. (North Dakota). Report C-637. American Cyanamid Company. Unpublished. [TE-723-017]

Higham, J. and Nau, H. (1975). Counter (CL92100): Determination of CL92100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate) Related Residues in "No-Tillage" Field Corn Following "In-Furrow" Treatment at Planting (Kentucky). Report C-647. American Cyanamid Company. Unpublished. [TE-723-022]

Higham, J. and Nau, H. (1975). Counter (CL 92,100): Determination of CL 92,100 (S-[[(1,1-dimethylethyl)thio] methyl] 0,0-diethyl phosphorodithioate) Related Residues in Field Corn Following Treatments at Planting and at Cultivation Time (Colorado). American Cyanamid company, NJ, USA. Report No. C-645. [TE-730-015]

Higham, J. (1984). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1983). ARD Princeton, NJ. USA. Report C-2438. Unpublished. [TE-714-010]

Higham, J. (1987). Counter Terbufos (CL 92,100): Validation of GC Method M-1754 for the Determination of Total CL 92,100 Related Residues in Corn Commodities (Field Corn Grain Sweet Corn Kernels Plus Cob Cannery Waste and Green and Dry Corn Plants) ABC Lab. Report C-2961. [TE-244-049]

Higham, J. (1988). Terbufos (CL 92,100): Validation of GC Method M-1912 for the Determination of CL 92,100-Related Residues in Soil. Report C-3544. [TE-242-006]

Higham, J. and Fisher, R. (1988). CL 92,100 (Terbufos/15-G): Residues of Total CL 92,100-Related Compounds in Sweet Corn Kernels plus Cob (Wisconsin). Report C-3096. American Cyanamid Company. Unpublished. [TE-723-004]

Higham, J. and Fisher, R. (1988). CL92100 (terbufos/15-G): Residues of Total CL92100 Related Residues In Sweet Corn Kernels Plus Cob (BAND + POST; FL, 1986 (C-2961). Report C-3109. American Cyanamid Company. Unpublished. [TE-723-006]

Higham, J. and Fisher, R. (1988). CL 92,100 (Terbufos/15-G): Residues of Total CL 92,100-Related Compounds in Field Corn Grain (Minnesota). Report C-3095. American Cyanamid Company. Unpublished. [TE-730-012]

Higham, J. and R. Fisher. 1988. CL92100 (terbufos/15-G): Residues of Total CL92100 – Related Compounds In Sweet Corn Kernels Plus Cob (BAND + POST; NY, 1986) C-2961 [TE-723-036]

Higham, J. and Zummo, G. (1988). CL 92,100 Terbufos (15-G, 20-PG): Residues of Total CL 92,100-Related Compounds in Green Corn Plants, Dry Corn Plants and grain (Illinois). Report C-3038. American Cyanamid Company. Unpublished. [TE-730-010]

Higham, J. and Zummo, G. (1988). CL 92,100 Terbufos (15-G, 15-PG, 20-PG): Residues of Total CL 92,100-Related Compounds in Green Corn Plants, Dry Corn Plants and Grain (Nebraska). (C-2961). Report C-3037. American Cyanamid Company. Unpublished. [TE-730-011]

Higham, J. (1991). Terbufos (CL 92,100): Validation of GLC Method M-1912 for the Determination of Terbufos (CL 92,100) and Related Residues (CL 93,401 and CL 94,320) in Soil. . American Cyanamid Company, NJ, USA. Report No. C-3544. [TE-242-006]

Higham, J. (1996). Terbufos Validation of Method M 2457 for the Determination of Total CL 92,100 Related Residues in Sugar Beet Tops and Roots. RES 95-118. [TE-244-023]

Higham, J. (1997). Freezer Storage Stability of Residues of Terbufos-Related Compounds (CL 94,301, CL 94,320, and CL 94,221) in Sugar Beet Tops and Roots. American Cyanamid Company. USA. Unpublished. Report RES 97-017. [TE-326-007]

Horton, W., and Kleiner, A. (1998). Total CL 92,100-Related Residues in Bananas after Treatment with Counter 15G Systemic Insecticide-Nematicide in Ecuador. Central Analytical Labs State College, PA. USA. Report RES 97-062. Unpublished. [TE-714-024]

Horton, W., and Kleiner, A. (1998). Total CL 92,100-Related Residues in Bananas after Treatment with Counter 15G Systemic Insecticide-Nematicide in Ecuador. Central Analytical Labs State College, PA. USA. Report RES 97-063. Unpublished. [TE-714-025]

Horton, W. and Kleiner, A. (1998). Total CL 92,100-Related Residues in Bananas after Treatment with Counter 15G Systemic Insecticide-Nematicide in Mexico. Central Analytical Labs State College, PA. USA. Report RES 97-064. Unpublished. [TE-714-026]

Hui, T. 1973. COUNTER Soil Insecticide: Soil-Leaching Studies of CL 92,100, ARD Princeton NJ USA Project #2-402 [TE-620-005]

Jones, A.(2005). Validation of Analytical Methodology to Determine Terbufos and Metabolites in Whole Banana and Banana Pulp. Central Science Laboratory, UK. Exponent International. Report No. PGD-183. [PGD-183]

Khunachak, A. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Honduras; 1986). ARD Princeton, NJ. USA. Report C-2789. Unpublished. [TE-714-002]

Khunachak, A. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas, Peel and Pulp (Honduras; 1985). ARD Princeton, NJ. USA. Report C-2706. Unpublished. [TE-714-003]

Khunachak, A. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (Costa Rica; 1986). ARD Princeton, NJ. USA. Report C-2705. Unpublished. [TE-714-004]

Khunachak, A. (1986). Counter Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas, Peel and Pulp (Costa Rica; 1985). ARD Princeton, NJ. USA. Report C-2704. Unpublished. [TE-714-005]

Khunachak, A. (1998). CL 92,100/CL 35024: Validation of GC/MS Method M-2623 for the Determination of Residues of CL 35,024 and CL 92,100 and their Sulfoxides (CL 18,177 and CL 94,301) and Sulfones (CL 18161 and CL 94,320) in Water. American Cyanamid Company, NJ, USA. Report No. RES 97-074. [TE-243-004]

Khunachak, A. and Behm, J.(1988). Terbufos (CL 92,100/10-G): Residues of Total CL 92,100-Related Compounds in Whole Bananas (GND; Costa Rica; 1987). ARD Princeton, NJ. USA. Report C-3136. Unpublished. [TE-714-015]

Khunachak, A. (1997). Freezer Storage Stability of Residues of Terbufos CL 92,100 and Its Related Compounds CL 94,301 and CL 94,320 in Soil. Report RES 96-073.01. [TE-326-006]

Kleiner, A. (1990). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar beet Roots and Foliage (North Dakota). ARD Princeton, NJ. USA. Report C-3366. Unpublished. [TE-724-068]

Kleiner, A. (1990). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar beet Roots and Foliage (Nebraska). ARD Princeton, NJ. USA. Report C-3367. Unpublished. [TE-724-069]

Kleiner, A. (1990). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar beet Roots and Foliage (Idaho). ARD Princeton, NJ. USA. Report C-3368. Unpublished. [TE-724-070]

Kleiner, A. (1990). Terbufos 15-G: Residues of Total CL 92,100-Related Compounds in Sugar beet Roots and Foliage (California). ARD Princeton, NJ. USA. Report C3369. Unpublished. [TE-724-071]

Kleiner, A. (1990). CL 92,100 (terbufos/15G): Residues of Total CL 92,100-Related Compounds in Dual Purpose Sorghum. American Cyanamid, NJ, USA. Report No. C-3374. [TE-730-046]

Kleiner, A. (1990). CL 92,100 (terbufos/15G): Residues of Total CL 92,100-Related Compounds in Grain Sorghum. American Cyanamid, NJ, USA. Report No. C-3375. [TE-730-047]

Kleiner, A. (1990). CL 92,100 (terbufos/15G): Residues of Total CL 92,100-Related Compounds in Grain Sorghum. American Cyanamid, NJ, USA. Report No. C-3376. [TE-730-048]

Kleiner, A. (1992). CL 92,100 (terbufos/15G): Residues of Total CL 92,100-Related Compounds in Dual Purpose Sorghum. American Cyanamid, NJ, USA. Report No. C-3851. [TE-730-049]

Lee, T and Belcher, D (1986). COUNTER Terbufos (CL 92,100): Residues of CL 92,100-Related Compounds in Soil and Rotational Crops (cabbage, Red Beets, and Wheat) from a Treated Corn Field (Waunakee, WI, 1984). American Cyanamid Company, Princeton, NJ, USA. Report No. C-2658. [TE-790-030]

Lee, T and Belcher, D (1986). COUNTER Terbufos (CL 92,100): Residues of CL 92,100-Related Compounds in Soil and Rotational Crops (cabbage, Sugar Beets, and Wheat) from a Treated Corn Field (York, NE, 1984). American Cyanamid Company, Princeton, NJ, USA. Report No. C-2721. [TE-790-031]

Leonard, R. (1991). CL 92,100 (Terbufos/15G): Residues of Total CL 92,100-Related Residues in Field Corn after Application at the Maximum Labelled Use Rate and at 5X the Maximum Labelled Use Rate (Iowa). Report C-3566. American Cyanamid Company. Unpublished. [TE-723-032]

Leonard, R. (1991). CL 92,100 (Terbufos/15G): Residues of Total CL 92,100-Related Residues in Field Corn after Application at the Maximum Labelled Use Rate and at 5X the Maximum Labelled Use Rate (At Cultivation; IA, 1990). Report C-3567. American Cyanamid Company. Unpublished. [TE-723-033]

Leonard, R. (1991). CL 92,100 (Terbufos/15G): Residues of Total CL 92,100-Related Residues in Field Corn after Application at the Maximum Labeled Use Rate and at 5X the Maximum Labeled Use Rate (Illinois). Report C-3569. American Cyanamid Company. Unpublished. [TE-723-035]

Leonard, R. (1991). CL 92,100 (Terbufos/15G): Residues of Total CL 92,100-Related Residues in Field Corn after Application at the Maximum Labelled Use Rate and at 5X the Maximum Labelled Use Rate (At Cultivation; IL, 1990). American Cyanamid Company. Report C-3568. Unpublished. [TE-723-034]

Luckhowec, J. (1989). Pesticide Assessment Guidelines Subdivision D: Product Chemistry Requirements for the Technical Grade Active Ingredient (TGAI) and Manufacturing Use Product (MP) COUNTER terbufos: Section 63-2 to 63-21, Physical and Chemical Characteristics. American Cyanamid Company. [TE-301-007]

Manuel, A. (1972). CL 92,100 and its Metabolites in Chicken Fat, Muscle, Liver, Kidney, Skin, and Eggs. American Cyanamid Company, NJ, USA. Report No. C-372. [TE-705-001]

Manuel, A. (1972). CL 92,100 and its Metabolites in Cattle Fat, Muscle, Liver and Kidney. American Cyanamid Company, NJ, USA. Report No. C-337. [TE-705-002]

Manuel, A. (1972). CL 92,100 and its Metabolites in Milk; American Cyanamid Company, NJ, USA. Report No. C-336. [TE-705-003]

Manuel, A. (1973). Determination of Total CL 92,100 and Oxidative Metabolites in Chicken Fat, Muscle, Skin, Liver and Kidney by Gas Liquid Chromatography: Recommended Method of Analysis. ARD Princeton NJ USA. Report M-401. [TE-245-002]

Manuel, A. and Nau, H. (1975). Counter (CL92100): Determination of CL92100(S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "terbufos" residue in corn (Minnesota). Report C-639. American Cyanamid Company. Unpublished. [TE-730-003]

Manuel, A. and Nau, H. (1975). Counter (CL92100): Determination of CL92100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "terbufos" residue in corn (Virginia). Report C-638. American Cyanamid Company. Unpublished. [TE-730-005]

Manuel, A., Peterson, R. and Nau, H. (1975). Counter (CL 92,100): Determination of CL 92,100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "Terbufos" Residue in Sweet Corn and Popcorn(Iowa). Report C-642. American Cyanamid Company. Unpublished. [TE-723-003]

Manuel, A.J and Nau, H. (1975). Counter (CL 92,100): Determination of CL 92,100(S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "Terbufos" Residue in Corn (Minnesota). Report C-636. American Cyanamid Company. Unpublished. [TE-723-016]

Manuel, A. and Nau, H. (1975). Counter (CL92100): Determination of CL92100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "terbufos" Residue in Corn (New York). Report C-641. American Cyanamid Company. Unpublished. [TE-723-019]

Manuel, A.J. and Nau, H.H. 1975. Counter (CL92100): Determination of CL92100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "terbufos" residue in corn (Maryland). Report C-643. American Cyanamid Company. Unpublished, [TE-723-020]

Manuel, A. and Nau, H. (1975). Counter (CL92100): Determination of CL92100 (S-[[(1,1-dimethylethyl) thio]methyl] O,O-diethyl phosphorodithioate "Terbufos" Residue in Corn (Colorado). Report C-644. American Cyanamid Company. Unpublished. [TE-723-021]

Manuel, A. (1976). Counter 15G: Determination Of Total CL 92,100- Related Residues In Sugar Beet (Root Pulp And Tops) Manitoba, Canada, 1975. ARD Princeton, NJ. USA. Report C-964. [TE-724-012]

Miller, P. (1973). CL 92,100 COUNTER Insecticide: Metabolic Studies of 14-C-Labeled CL 92,100 in Hydrolytic and Photolytic Environments, ARD Princeton NJ USA PD-M Volume 10 P 959-1007. [TE-630-001]

Marin, C. and Heim, D. (1999). 14C-Terbufos (CL 82,100) and its Sulfoxide (CL 94,301) and Sulfone (CL 94,320) Metabolites: Hydrolysis in Sterile pH 5, 7, and 9 Buffers. American Cyanamid Company. Report No. ENV 97-017. [TE-630-005]

Minoura, M. (1986).). Counter Terbufos (CL 92,100): Residues of Total CL 92,100-Related Compounds in Whole Banana Fruits in the Philippines. Cyanamid Japan, Ltd. Report TTR-86-012. Unpublished. [TE-714-014]

Minoura, M. (1986). Counter Terbufos (CL 92,100): Residues of Total CL 92,100-Related Compounds in Whole Banana Fruits in The Philippines. Cyanamid Japan Ltd., Tahara, Japan. Report Ttr-86-011. Unpublished. [TE-714-023]

Minoura, M. (1987). Counter Terbufos (CL 92,100/10G): Residues of Total CL 92,100-Related Compounds in Banana Fruits in the Philippines. Cyanamid Japan Ltd., Tahara, Japan. Report TTR-87-025. Unpublished. [TE-714-022]

North H., Barringer, D., and Gatterdam, P. (1972). Fate of Carbon-14 Labeled CL 92,100 in Sweet Corn Plants. PD-M 9: 249-301 (Princeton). [TE-640-005]

North, H. (1973). COUNTER Soil Insecticide: Metabolism of CL 92,100 in Soils, ARD Princeton NJ USA Project #2-402 Oct 1973. BASF Ref. No. 1973/7000281. [TE-620-006]

Ohba, K. (1993). Terbufos (CL 92,100): Analysis of Total CL 92,100-Related Residues in Banana Pulp Treated With Counter 15G Insecticide/ Palmerston, Queensland, Australia (3g Ai Per Stool). Tahara Agricultural Center, Tahara Japan. Report TTR-93-005. Unpublished. [TE-714-018]

Ohba, K. (1993). Terbufos (CL 92,100): Analysis of Total CL 92,100-Related Residues in Banana Skin Treated With Counter 15G Insecticide/ Palmerston, Queensland, Australia (3g Ai Per Stool). Tahara Agricultural Center, Tahara Japan, Report TTR-93-006. Unpublished. [TE-714-019]

Ohba, K. (1993). Terbufos (CL 92,100): Analysis of Total CL 92,100-Related Residues in Banana Pulp Treated with Counter 15G Insecticide/ Palmerston, Queensland, Australia (6g ai/stool). Tahara Agricultural Center, Tahara, Japan. Report TTR-93-007. Unpublished. [TE-714-020]

Ohba, K. (1993). Terbufos (CL 92,100): Analysis of Total CL 92,100-Related Residues in Banana Skin Treated With Counter 15G Insecticide/ Palmerston, Queensland, Australia. Tahara Agricultural Center, Tahara, Japan. Report TTR-93-008. Unpublished. [TE-714-021]

Peterson, R. (1973). Gas Chromatographic Procedure for the Determination of CL 92,100-Related Compounds in Sugar Beet Tops Greens and Roots. Recommended Method of Analysis M-395. [TE-244-064]

Peterson, R. (1974). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots (Colorado). ARD Princeton, NJ. USA. Report C-667. [TE-724-004]

Peterson, R. (1975). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots (Wyoming). ARD Princeton, NJ. USA. Report C-666. [TE-724-005]

Peterson, R. (1975). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots (Idaho). ARD Princeton, NJ. USA. Report C-665. [TE-724-006]

Peterson, R. (1975). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots (Idaho). ARD Princeton, NJ. USA. Report C-664. [TE-724-007]

Peterson, R. (1975). Counter: (CL 92,100) Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots (Michigan). ARD Princeton, NJ. USA. Report C-693. [TE-724-017]

Peterson, R. (1975). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet Tops And Roots (Colorado). ARD Princeton, NJ. USA. Report C-668. [TE-724-018]

Peterson, R. and Nau, H. (1975). Counter (CL92100): Determination of total CL92100 (S-[[(1,1-dimethylethyl) thio)methyl] O, O-diethylphosphorodithioate) "terbufos" Related Residues in Corn (Michigan). Report C-640. American Cyanamid Company. Unpublished. [TE-723-018]

Peterson, R. (1976). COUNTER Insecticide 15 G and Liquid (CL 92,100): Metabolism of 14C-Labeled CL 92,100 in Cabbage Plants, American Cyanamid Company, PD-M Volume 13-1 (Princeton). [TE-640-004]

Peterson, R. (1976). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beets (Tops And Roots) (Winnipeg, Manitoba, Canada). ARD Princeton, NJ. USA. Report C-914. [TE-724-029]

Peterson, R. (1976). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beets (Tops And Roots) (Plum Coulee And Altona, Manitoba, Canada). ARD Princeton, NJ. USA. Report C-917. [TE-724-030]

Peterson, R. (1976). Counter: Determination Of Total CL 92,100 Related Residues In Sugar Beet (Root And Tops) (Gnadenthal, Manitoba, Canada). ARD Princeton, NJ. USA. Report C-916. [TE-724-013]

Peterson, R. and Byrne, D. (1977). Counter 15-G (CIr92100): Determination of total CL92100 Related Residues in no-Till Field Corn Tissues (Maryland, 1974). Report C-1129. American Cyanamid Company. Unpublished. [TE-730-008]

Peterson, R. and Baugher, D., (1979). Counter Terbufos (CL 92100/15G): Residues of Total CL 92,100-Related Compounds in Sorghum Silage, Fodder, and Grain . American Cyanamid Company. Report No. C-1626. [TE-730-039]

Peterson, R. (1979). Counter Terbufos (CL 92,100): Validation of GC Method M-0995 for the Determination of Total CL 92,100 Related Residues in Sorghum Tissues (Silage, Fodder, and Grain). American Cyanamid Company, NJ, USA. Report C-1592. [TE-244-056]

Peterson, R. (1981). COUNTER Terbufos (CL 92,100): Aerobic Radiobalance and Metabolism Study with Carbon-14 Labeled CL 92,100 in a Silt Loam Soil. ARD Princeton NJ USA. Report C-1857. [TE-620-002]

Peterson, R. 1983. COUNTER, terbufos (CL 92,100): Aerobic and Anaerobic Metabolism of CL 92,100 in a Silt Loam Soil, ARD Princeton NJ USA PD-M Volume 20-4. [TE-620-004]

Peterson, R. (1988). Validation of GC Method M-1829 For The Determination of Total CL 92,100 Related Residues in Cow's Milk. American Cyanamid Co., USA. Report C-3140. [TE-245-001]

Peterson, R. (1989). Terbufos/15G (CL 92,100): Residues of Total CL 92,100-Related Compounds in Cow's Milk (Feed; NJ, 1987). American Cyanamid Company, NJ, USA. Report No. C-3247. [TE-705-004]

Picard, G. and Kim, D. 1997. Terbufos GC/FPD Determinative Method and LC/MS/MS Confirmatory Method for Total Terbufos CL 92,100-Related Residues in Whole Banana and Banana Pulp. [TE-244-025]

Poepell, M. and Nau, H. (1975). Counter (CL 92,100): Determination of Total CL 92,100 (S-[[(1,1-dimethylethyl) thio)methyl] O, O-diethylphosphorodithioate) "Terbufos"-Related Residues in Sweet Corn Ears and Fodder (Iowa). Report C-635. American Cyanamid Company. Unpublished. [TE-723-005]

Potts, C. (1984). Counter (CL 92,100/10 G): Residues of Total CL 92,100-Related Compounds in Green Coffee Beans (Costa Rica, 1982) (C-2305). ARD Princeton, NJ. USA. Report C-2351. Unpublished. [TE-790-001]

Roman, M. and Lublinkhof, J. (1980). Counter Terbufos (CL 92100/15G): Residues of Total CL 92,100-Related Compounds in Sorghum Plant and Grain . American Cyanamid Company. Report No. C-1742. [TE-730-040]

Roman, M. and Lublinkhof, J. (1980). Counter Terbufos (CL 92100/15G): Residues of Total CL 92,100-Related Compounds in Sorghum Plant and Grain. American Cyanamid Company. Report No. C-1776. [TE-730-043]

Roman, M. and Lublinkhof, J. (1980). Counter Terbufos (CL 92100/15G): Residues of Total CL 92,100-Related Compounds in Sorghum Plant and Grain . American Cyanamid Company. Report No. C-1752. [TE-730-041]

Roman, M. and Lublinkhof, J. (1980). Counter Terbufos (CL 92100/15G, 15G/C): Residues of Total CL 92,100-Related Compounds in Sorghum. American Cyanamid Company. Report No. C-1773. [TE-730-042]

Roman, M. (1986). Counter Terbufos (CL 92,100): Validation of GC Method M-1644 for the Separate Determination of CL 92,100, CL 94,301, CL 94,320 Residues in Water. Report. C-2769. [TE-243-007]

Roman, M. (1987). Counter Terbufos (CL 92,100): Validation of GC Method M-1784 for the Separate Determination of CL 92,100 and Metabolites (CL 94,221, CL 94,301, and CL 94,320) in Soil. American Cyanamid Company, NJ. Report No. C-3020. [TE-242-003]

Roman, M. (1987). Freezer Stability of CL 92,100, CL 94,301 CL 94,320 Residues in Water. Report C-3032. [TE-326-010]

Skorczynski, S. (1991). Terbufos (CL 92,100/10G): Residues of Total CL 92,100-Related Compounds in Whole Bananas. ARD Princeton, NJ. USA. Report C-3614. Unpublished. [TE-714-017]

Shimel, K. (1986). Counter Terbufos (CL 92,100): Validation of GC Method M-1784 for the Separate Determination of Residues of CL 92,100 and Its Metabolites (CL 94,221, CL 94,301, CL 94,365, CL 94,302 and CL 94,320) in Soil. American Cyanamid Company, NJ. Report No. C-2766. [TE-242-001]

United State Department of Agriculture. Pesticide Data Program Annual Summary Calendar Years 2002 , page 40. Agricultural Marketing Service.

United States Environmental Protection Agency. (1999). Revised Environmental Fate and Effects Assessment (Section C: Environmental Assessment).

York, C. (1995). Total CL 92,100-Related Residues in Sugar Beets after Treatment with Counter 15 G Applied Post emergence (Michigan). CARC Princeton, NJ. USA. Report RES 95-039. Unpublished. [TE-724-036]

York, C. (1995). Total CL 92,100-Related Residues in Sugar Beets after Treatment with Counter 15 G Applied Post emergence (North Dakota). CARC Princeton, NJ. USA. Report RES 95-045. Unpublished. [TE-724-038]

York, C. (1995). Total CL 92,100-Related Residues in Sugar Beets after Treatment with Counter 15 G Applied Post Emergence (Minnesota). CARC Princeton, NJ. USA. Report RES 95-047. Unpublished. [TE-724-039]

York, C. (1996). Total CL 92,100-Related Residues in Sugar Beets after Treatment With Counter 15 G Applied Post emergence (Nebraska). CARC Princeton, NJ. USA. Report RES 95-040. Unpublished. [TE-724-037]

York, C. (1996). CL 92,100 (Terbufos/15G): Total CL 92,100-Related Residues in Corn Grain after Treatment with COUNTER 15G Insecticide Applied Post emergence (Wisconsin). Report RES 95-059. American Cyanamid Company. Unpublished. [TE-730-028]

York, C. (1996). CL 92,100 (Terbufos/15G): Total CL 92,100-Related Residues in Corn Grain after Treatment with COUNTER 15G Insecticide Applied Post emergence (MI, 1994). Report RES 95-058. American Cyanamid Company. Unpublished. [TE-730-029]

York, C. (1996). CL 92,100 (Terbufos/15G): Total CL 92,199-Related Residues in Sugar Beets after Treatment with Counter 15G Insecticide Applied Post-emergence (ID; 1994). American Cyanamid Company, NJ, USA. Report Norse 95-046. [TE-724-035]

York, C. (1997). CL 92,100 (Terbufos/15G): Total CL 92,100-Related Residues in Corn Grain after Treatment with COUNTER 15G Insecticide Applied Post emergence (IA, 1995). Report RES-96-021. American Cyanamid Company. Unpublished. [TE-730-030]

York, C. (1997). CL 92,100 (Terbufos 15G): Total CL 92,100-Related Residues in Corn Grain after Treatment with COUNTER 15G Insecticide Applied Post emergence (Nebraska). Report RES 96-022. American Cyanamid Company. Unpublished. [TE-730-031]

Zheng, S. Gross, J. (1989). Freezer Storage Stabilities of Total CL 92,100-Related Residues in Whole Banana and Banana Pulp. Report RES 99-070. [TE-326-015]

Zheng, S and Gross, J. (1998). Terbufos (CL 92,100): Independent Laboratory Validation of GC Method M3072 for the Determination of Total Terbufos –Related Residues in Whole Banana and Banana Pulp. American Cyanamid. [TE-244-057]

Zulalian J. (1990), Terbufos (CL 92,100): Metabolic Fate of Carbon-14 CL 92,100 in Milk and Tissues of Lactating Goats, (Princeton). [TE-440-002]

Zulalian J. (1992). Terbufos (CL 92,100): Metabolic Fate of Carbon-14 CL 92,100 in Milk

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TERBUFOS

First draft prepared by
K. L. Hamernik
Office of Science Coordination and Policy,
United States Environmental Protection Agency
Washington DC, USA

Explanation

Terbufos is an organophosphorus compound, classified as a systemic insecticide and nematocide, and was last evaluated by the JMPR in 1989, when an ADI of 0–0.0002 mg/kg bw was established. Terbufos was considered by the present Meeting within the periodic review programme of the Codex Committee on Pesticide Residues.

Evaluation for acceptable daily intake

1. Biochemical aspects

1.1 Absorption, distribution and excretion

Rats

In an study of metabolism, 16 male Royal Hart Wistar rats were given a single dose of [^{14}C]terbufos (purity, uncertain; specific activity of 26.4 µCi/mg labelled at the carbon atom of the thiomethyl portion of the parent molecule (or methylene carbon) in ethanol and water (1 : 1) at 0.8 mg/kg bw by gavage. Animals were housed individually in metabolism cages. Urine was collected on dry ice at 6, 12, 24, 48, 72, 96, 120, and 168 h after dosing, and faeces were collected and frozen at 12, 48, 72, 96, 120, and 168 h after dosing. After thawing, urine samples were pooled for each time interval. Groups of three animals were terminated at 6, 12, 24, and 48 h after dosing and the final group of four animals was terminated at 168 h after dosing. Livers, kidneys, gastrointestinal tract, muscle, skin, fat and blood were taken at these times.

Radioactivity was extracted from the urine, faeces and tissues, and metabolites in urine, faeces, liver, kidney and muscle were separated and identified. In addition, the amount of ^{14}CO2 in expired air over a 72 h period was determined in one animal that had received a dose of 0.2 mg/kg bw by gavage. There was no indication of overt toxicity. Elimination was relatively rapid and fairly complete. About 90% of the administered dose was recovered by the end of the study. Over the entire duration of the study, approximately 83% of the administered dose was found in the urine, which was thus the major route of elimination; about 72% of the administered dose was excreted by 24 h and 80% was excreted by 48 h. Over the course of the study, about 3.5% of the radiobel was found in the faeces. The recovery of the administered dose reached a peak of 31.2% in the urine by 24 h, and a peak of about 2% in the faeces by 48 h. Tissue concentrations of radiolabel reached a maximum at between 6 and 12 h after dosing. By 168 h after dosing, the concentration of radiolabel in each body tissue examined was <0.1 mg/kg. The total percentage of the administered dose recovered in tissues by 168 h was greatest in the liver (0.34%), followed by the gastrointestinal tract (0.087%), blood (0.036%), kidney (0.034%), muscle (0.024%), skin (0.017%) and fat (0.003%). No $^{14}CO_2$ was recovered during the designated interval of 72 h.

After extraction and thin-layer chromatography, metabolites that did not contain phosphorus were found to account for about 96% of the radiolabel present in urine. The predominant species appearing by 6 h after dosing was CL 202 474, with lesser amounts of CL 99 843, CL 99 844 and CL 99 875 (see Figure 1 and Table 1). Small amounts of parent compound and other species containing phosphorus accounted for most of the remainder of the radiolabel (2–3%) in the urine. Two peaks of radioactivity in urine were not definitively identified.

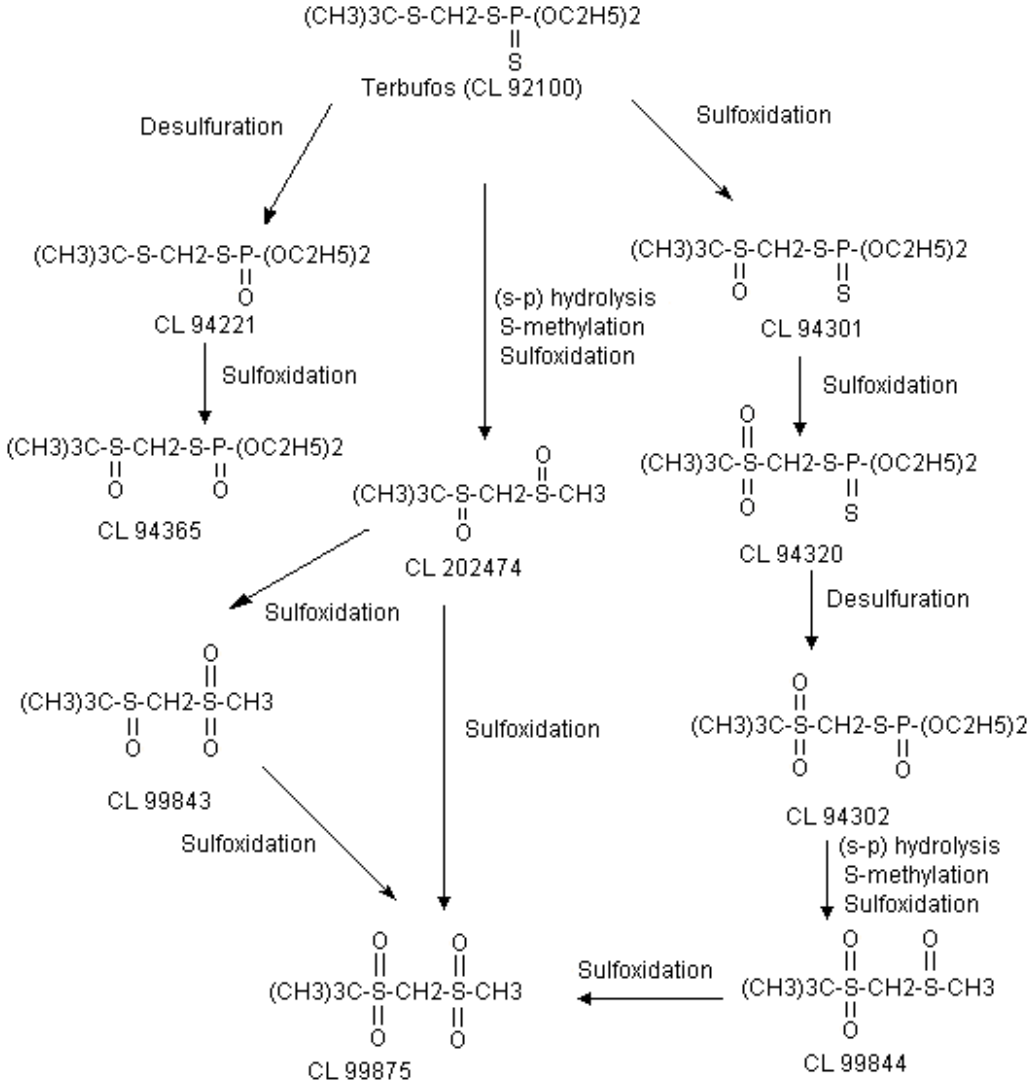

Figure 1. Proposed metabolic pathway of terbufos in rats

From Cheng (1992)

Table 1. Terbufos and its metabolites

CL No.	Chemical name	Common name
92,100	*O*,*O*-diethyl-*S*-*t*-butylthio-methylphosphorodithioate	Terbufos (parent compound)
94,301	Phosphorodithioic acid, *S*-(*t*-butylsulfinyl) methyl *O*,*O*-diethyl ester	Terbufos sulfoxide
94,320	Phosphorodithioic acid, *S*(*t*-butylsulfonyl) methyl *O*,*O*-diethyl ester	Terbufos sulfone
94,221	Phosphorothioic acid, *S*-(*t*-butylthio) methyl *O*,*O*-diethyl ester	Terbufoxon
94,302	Phosphorothioic acid, *S*-(*t*-butylsulfonyl) methyl *O*,*O*-diethyl ester	Terbufoxon sulfone
94,365	Phosphorothioic acid, *S*-(*t*-butylsulfinyl) methyl *O*,*O*-diethyl ester	Terbufoxon sulfoxide
202,474	Methane, (*t*-butylsulfinyl)(methylsulfinyl)	
99,844	Sulfoxide, (*t*-butylsulfonyl) methyl methyl	

99,843	Sulfoxide, *t*-butyl (methyl-sulfonyl) methyl	
99,875	Sulfone, *t*-butyl (methyl-sulfonyl) methyl	

From North (1973) and Cheng (1992)

In the faeces, at 12 h after dosing, about 95% of the radiolabel comprised species containing phosphorus (mostly metabolites CL 92 320 and CL 94 221, with lesser amounts of CL 94 302 and CL 94 301). At subsequent time intervals, in addition to CL 92 320, non-phosphorus-containing metabolites CL 202 474, CL 99 843, and CL 99 875 predominated. Very little parent compound was found in the faeces.

The metabolites identified in urine and faeces were also observed in tissue extracts; the types of metabolite found at detectable levels depended on the tissue and time after dosing. In liver, kidney and muscle, the approximate ratio of species not containing phosphorus (four metabolites) to those containing phosphorus (e.g. five phosphorus-containing metabolites and small amounts of parent compound) at 6 h after dosing were 2.6, 11 and 6 in liver, kidney and muscle respectively, and about 9, 23 and 7 for these same tissues at 12 h after dosing. Possible sex differences in the metabolic fate of terbufos were not addressed by this study (North, 1973). No statements of compliance with quality assurance (QA) or good laboratory practice (GLP) were provided. The study was not performed according to a specific guideline. Despite the limitations of the study some useful information can be extracted.

Radiolabelled terbufos (purity, >98%; specific activity, 61.4 mCi/g), labelled with ^{14}C at the methylene carbon position of the parent molecule, was administered in corn oil by gavage to groups of fasted male and female Crl:CD®(SD)BR rats. Groups of five male and five female rats were given single oral doses of 0.1 mg/kg bw (lowest dose) or 0.4 mg/kg bw (highest dose) and additional groups of one male and one female were similarly treated and used for collection of volatiles. In the multiple-dose segment of the study, groups of rats were given non-radiolabelled terbufos (purity, 97.8%) as single oral doses of 0.1 mg/kg bw in corn oil for 14 days, followed by a single dose of radiolabelled material of 0.1 mg/kg bw on day 15. Additional groups of one male and one female were similarly treated with terbufos at a dose of 0.1 and used for collection of volatiles. Urine and faeces for all groups were collected 0–6, 6–12, and 12–24 h after the administration of radiolabelled terbufos and daily thereafter until termination at 168 h. Cage rinses were collected as necessary. Volatiles were collected at intervals of up to 7 days after dosing. Radioactivity was extracted from urine, faeces and tissues (blood, bone, brain, fat, ovaries, testes, heart, liver, kidneys, lungs, muscle, spleen, uterus and residual carcass). Metabolites were characterized and identified only in the urine and faeces and only for the 12–24 h interval after dosing.

No toxicity was reported. In all the treated groups, total recoveries of the administered radiolabel was about 93–99% in males and 89–96% in females at 168 h after dosing. Relatively rapid elimination, primarily in the urine, indicated fairly fast and appreciable absorption via the gastrointestinal tract. Urinary excretion of radiolabel was 76% and 79% in males and females treated with single low doses of terbufos, and 79% and 69% in males and females treated with single high doses of terbufos, at 168 h after dosing. In animals receiving repeated low doses of terbufos, urinary excretion of radiolabel was 86% and 85% of the administered dose in males and females. Faecal elimination in groups of males and females treated with low and high single doses was 13–17% of the administered dose and in the groups receiving repeated doses was about 5–7% in both sexes. In males and females in all treated groups, much smaller amounts of radiolabel, as a percentage of the administered dose, were found in the tissues (about 0.09–0.15%), in the carcass (about 0.90–2%), in expired CO_2 (about 2–4%) and in volatiles (0.06–0.5%), and most of the radiolabel was eliminated in excreta by 24 h after dosing.

The highest concentrations of residues in tissues at 168 h after dosing were found in animals receiving single, high doses. For all dosing regimens, the highest tissue residues were found in the lungs of both sexes (single low doses, 0.003–0.005 mg/kg; repeated doses, 0.005–0.007 mg/kg; and single high doses, 0.018–0.022 mg/kg) and there was no indication of bioaccumulation.

Metabolites in urine and faeces were characterized only for the period between 12 and 24 h after dosing (Figure 1 and Table 1). Since appreciable amounts of radiolabel were excreted before this interval, the metabolites cannot be reliably quantified relative to percentage of administered dose. In addition, variation in the radiolabel detected in

cage rinses for individual animals (about 6–56% of the administered dose) contributed to uncertainty in metabolite quantification during the 12–24 h interval.

For all dosing regimens and for both sexes, about 70–90% of the urinary residue of radiolabel was reported to have been characterized for the 12–24 h period. Of this, about 67–80% of the residue was described as non-phosphorus-containing metabolites, about 1–4% as phosphorus-containing metabolites and about 2–9% as unknown substances (two substances). Of the non-phosphorus-containing metabolites, the major metabolite was CL 202 474; lesser amounts of CL 99 843, CL 99 844 and CL 99 875 were found. The only phosphorus-containing metabolite detected was CL 94 365; no parent compound was found. During the 12–24 h interval, for all dosing regimens and for both sexes, about 49–80% of the faecal residue of radiolabel was reported to have been characterized. Of this, about 17–34% was described as non-phosphorus-containing metabolites, about 8–44% as phosphorus-containing metabolites, and about 7–22% as unknown substances (five substances). The non-phosphorus-containing metabolites were CL 202 474, CL 99 843 and/or CL 99 844, and CL 99 875. The major phosphorus-containing entity was the parent compound (CL 92 100) with lesser amounts of CL 94 301 and CL 94 365. The proposed metabolic pathway for terbufos in rats, on the basis of the metabolites found in excreta, is depicted in Figure 1. Sulfoxidation and desulfuration of terbufos is followed by hydrolysis of the thiolophosphorus bond (S–P), enzymatic *S*-methylation and then additional *S*-oxidation.

There were no apparent sex differences in the absorption and metabolic fate of ^{14}C]terbufos in Sprague-Dawley rats on the basis of the results of this study (Cheng, 1992). Statements of compliance with QA and GLP were provided. The protocol was generally consistent with United States Environmental Protection Agency (EPA) Subdivision F Guidelines (November 1982 and revised, 1984).

1.2 Biotransformation

In a study of the biotransformation of terbufos (purity, 91%; apparently purchased from a pesticide factory in China), livers of male Wistar rats (180–220 g) were perfused in situ with 100 µl of terbufos (0.1 mol/l, dissolved in methanol and added to the perfusate reservoir) for 1 h at a flow rate of 5 ml/liver per min. Metabolic materials collected from perfusate effluent were separated with a solid-phase extraction cartridge and were characterized and quantified by gas chromatography–infrared spectrometry (GC–IR) and gas chromatography–mass spectrometry (GC–MS). The recovery of terbufos and its metabolites was expressed as a percentage of the concentration of the parent compound entering the liver. Recovery was incomplete, totaling only about 47.13%. Substances in the effluent separated into five major peaks. These were identified as terbufos (40.8%), terbufos oxon (2.13%), and three triakylphosphorothioate metabolites: metabolite I: $(C_2H_5O)_2POSCH_3$ (hydrolysate of terbufos oxon, 0.13%); metabolite II: $(C_2H_5O)_2PSSCH_3$ (hydrolysate of terbufos, 2.65%); and metabolite III: $(C_2H_5O)_2PSSC_2H_5$ (methylate of the metabolite II, 1.42%). It was suggested that metabolite III may have formed via a detoxification reaction involving *S*-adenosyl-L-methionine methyl transferase. The potential for certain trimethyl and triethyl phosphorothioates, such as metabolites I, II and III, to cause cholinergic toxicity and/or pulmonary toxicity in rats by a non-cholinergic mechanism or mechanisms was discussed. Sulfoxide and sulfone metabolites were not detected in the effluent (Li et al., 1999).

2. Toxicological studies

2.1 Acute toxicity

The acute toxicity of terbufos is summarized in Table 2.

Table 2. Acute toxicity of terbufos

Species	Strain	Sex	Route	Vehicle	LD_{50} (mg/kg bw) or LC_{50} (mg/l)	Purity (%)	Reference
Mouse	CF1 albino	Female	Oral	Corn oil	5.0	85.8	American Cyanamid

							Company A72-95 (1972a)
Mouse	CF1 albino	Female	Oral	Corn oil	9.2	96.7	Morici (1972)
Mouse	CF-1 albino	Male	Oral	Corn oil	3.5	96.7	Morici (1972)
Rat	Wistar (RH albino)	Female	Oral	Corn oil	9.0[b]	96.7	Morici (1972)
Rat	SD (Crl : CD(SD)BR)	Female	Oral	Corn oil	1.4[d]	89.7	Bradley (1996)[a]
Rat	SD (Crl:CD(SD)BR)	Male	Oral	Corn oil	3.2[d]	89.7	Bradley (1996)[a]
Rat	Wistar RH albino)	Male	Oral	Corn oil	1.6[d]	85.8	American Cyanamid Company A72-95 (1972a)
Rat	Wistar (RH albino)	Male	Oral	Corn oil	4.5[b]	96.7	Morici (1972)
Rat	SD (CD)	Female	Inhalation; 4 h, whole body	Administered as a vapour	0.0012 (1.2 µg/l)	89.6	Hoffman (1987)[6]
Rat	SD (CD)	Male	Inhalation; 4 h whole body	Administered as a vapour	0.0061 (6.1 µg/l)	89.6	Hoffman (1987)[6]
Rat	Wistar (RH albino)	Male	Inhalation; 7 h	Administered as a vapour	Could not be calculated[g]	96.7	Morici (1972)
Rabbit	New Zealand white	Female	Dermal	Report stated applied as received[c]	0.93[b]	89.6	Fischer (1985)
Rabbit	New Zealand white	Male	Dermal	Report stated applied as received[c]	0.81b	89.6	Fischer (1985)
Rabbit	Albino	Male	Dermal	Report stated applied as received[c]	1.0	85.8	American Cyanamid Company A72-95 (1972a)
Rabbit	Albino	Male	Dermal	Report stated applied as received[c]	1.1	96.7	Morici (1972)
Dog	Beagle	Female	Oral	Report stated applied as received[e]	6.3[d]	96.7	Morici (1972)
Dog	Beagle	Male	Oral	Report stated applied as received	4.5[d]	96.7	Morici (1972)

Although reports for most of these studies (except as footnoted below) were summary in nature and did not contain GLP or QA statements, protocols appeared to be generally consistent with the intent of EPA Subdivision F Guidelines (1982 or 1984, revised)

[a] Detailed report contained QA and GLP statements, but stated there was no confirmation of the concentration of test material; the protocol

was consistent with US EPA Subdivision F Guidelines (1982 or 1984, revised)

[b] Report stated that animals were not fasted

[c] Test material was a liquid

[d] Report stated that animals were fasted

[e] Test material in a gelatin capsule was administered to fasted animals

[f] Detailed report contained QA and GLP statements and protocol was consistent with US EPA Subdivision F Guidelines (1982 or 1984, revised)

[g] Ten animals were exposed for 7 h at 25°C to air that was near-saturated with product vapour at a nominal chamber concentration of 1.99 mg/l. There were two deaths, one on day 5 and the other during days 6–14 after dosing. Clinical findings described as transient irritation and discomfort were present at 0–15 min after dosing and the lung of one survivor was abscessed at necropsy. The findings of this study are inconsistent with those of Hoffman, 1987

Terbufos is of very high acute toxicity when administered by the oral, dermal, or inhalation routes. LD_{50} values for acute oral toxicity in rodents and dogs were similar, ranging from 1.4 to 9.2 mg/kg bw. The acute dermal LD_{50} was about 1 mg/kg bw in rabbits, and the acute inhalation LC_{50} in rats ranged from 0.0012 to 0.0061 mg/l. Clinical signs observed were those typical of cholinergic toxicity and, depending on the study, route and species, included tremors, salivation, exophthalmos, prostration, decreased activity, chromodacryorrhoea, diuresis, piloerection, ataxia, urogenital staining, nasal discharge, anorexia, and laboured breathing. Deaths following acute exposures occurred within minutes to hours or up to a week after administration. With regard to dermal absorption, terbufos is rapidly penetrating after dermal or ocular application.

(a) Ocular and dermal irritation

Rabbit

In a study of primary skin irritation, 0.5 ml of technical-grade terbufos (purity, 96.7%) was applied "as received" to shaved rabbit skin for 24 h under an impervious patch. The product was extremely toxic by the dermal route when administered in a single treatment; all rabbits (number not specified) died within 24 h after dosing. All animals exhibited signs of cholinesterase inhibition before death. The product (a liquid) was said to penetrate rabbit skin and mucous membranes very easily. No indications of dermal irritation or corrosion were reported (Morici, 1972).

In a second study of primary skin irritation, a single application of 0.25 ml of technical-grade terbufos (purity, 85.8%) was administered "as received" to shaved rabbit skin in a similar protocol to that of Morici (1972), with similar results. All animals died within 24 h after dosing and showed signs of cholinesterase inhibition before death. No skin irritation was reported (BASF, 1972a).

In a study of primary eye irritation, 0.1 ml of technical-grade terbufos (purity, 96.7%) was applied "as received" to the conjunctival sacs of six rabbits. The product was extremely toxic by the ocular route when administered in a single treatment; all animals died on the day of dosing and were observed to exhibit signs of cholinesterase inhibition before death. The product (a liquid) was said to penetrate rabbit skin and mucous membranes very easily. No indications of ocular irritation were reported (Morici, 1972).

In a second study of primary eye irritation, a single application of 0.1 ml of technical-grade terbufos (purity, 85.8%) was introduced "as received" into the conjunctival sacs of six rabbits in a protocol similar to that of Morici (1972), with similar results. All animals died 2–3 h after dosing and were observed to exhibit signs of cholinesterase inhibition before death. No ocular irritation was reported (BASF, 1972a). Although the reports for most of these studies were summary in nature and did not contain statements of compliance with GLP or QA, protocols appeared to be generally consistent with the intent of EPA Subdivision F Guidelines (1982 or 1984, revised).

(b) Dermal sensitization

A study of skin sensitization of technical grade terbufos was not performed owing to the severe toxicity observed in the studies of primary skin and eye irritation.

2.2 Short-term studies of toxicity

(a) Oral administration

Mice

In a preliminary study, groups of 10 male and 10 female albino CF1 mice were given diets containing technical-grade terbufos (CL 92 100; purity, 96.7%) at a nominal concentration of 0, 1.0, 4.0 or 16 mg/kg (nominally equivalent to 0, 0.218, 0.911 and 3.30 mg/kg bw per day in males and 0, 0.286; 0.988 and 3.70 mg/kg bw per day in females) for 31 days. Data on analysis of concentrations of test material in the diet were not provided, so test material intake and stability in the feed could not be confirmed. Very few parameters were evaluated. Cholinesterase activity was not assessed. Six females at the highest dose were found dead between days 5 and 14 and one female at the lowest dose was found dead on day 9. Autolysis prevented attempts to determine the cause of death. Mortality was, however, only notable in females receiving the highest dose (60%), therefore it is possible that the increase in mortality was related to treatment. Decreases in body weight and food consumption were reported in males and females at the highest dose. Weights of the two organs examined (liver and kidney) in four to five animals of each sex per group treated with terbufos were not statistically significantly different from those of respective control groups. For the parameters examined, no effects were observed in other groups. It was reported that upon gross pathological examination of four to five animals of each sex per group at study termination, no gross lesions were found that were attributed to treatment (gross pathology data were not provided). The no-observed-adverse-effect level (NOAEL) in males and females was nominally 4.0 mg/kg (nominally equivalent to 0.911 mg/kg bw per day in males and 0.988 mg/kg bw per day in females; intake of test material could not be confirmed) on the basis of decreases in body weight and food consumption in both sexes and mortality of 60% at the dose above in females only (Morici, 1972). No statements of compliance with QA or GLP were provided and the study was not performed to address a specific guideline.

Rats

In a short-term feeding study, groups of five male and five female Sprague-Dawley rats (aged 4 weeks at study initiation) were given diets containing technical-grade terbufos (CL 92 100; purity, 90.1%), prepared in a vehicle of corn oil and methylene chloride (1 : 1), at a concentration of active ingredient of 0, 0.125, 0.250, 0.500, 1.00, 3.00 or 6.00 mg/kg per day (equal to 0, 0.020, 0.039, 0.080, 0.16, 0.49, and 0.77 mg/kg bw per day in males and 0.017, 0.033, 0.066, 0.132, 0.409 and 0.750 mg/kg bw per day in females, respectively) for 14 days. The parameters evaluated were limited, including observations for mortality, morbidity and clinical signs of toxicity (data for individual animals were not provided for signs), measurement of body weight and food consumption, organ weight determinations (liver and kidney only) and a gross examination at study termination. Plasma and erythrocyte cholinesterase activity was assessed before treatment and on days, 1, 4, 7, and 14 in the control groups and in groups of males and females receiving the four lowest doses (i.e. 0.020, 0.039, 0.080 and 0.16 mg/kg bw per day). Cholinesterase inhibition was determined relative to the value for the appropriate concurrent control group. Brain cholinesterase activity was not measured, and clinical chemistry, haematological, urine and histopathological examinations were not conducted in this study.

There were two deaths; two females in the group receiving the highest dose (6.00 mg/kg) died or were sacrificed in a moribund condition on days 11 and 13 from treatment-related causes, respectively. Before death, the animals exhibited severe tremors, salivation and prostration. Clinical signs of toxicity in males and females were reported to start on day 2 and last until termination in the group receiving the highest dose (6.00 mg/kg) and included, initially, ataxia, tremors and miosis. From day 7 on, more severe tremors developed and exophthalmos and piloerection were also observed. At 3.00 mg/kg, clinical signs (slight tremors) were also noted in both sexes from day 4 until the end of the study. Signs of toxicity were considered to be treatment-related and were not observed at lower doses. Changes in body weight and/or food consumption seen at the two highest doses were also considered to be related to treatment. Statistically significant decreases in body weight and body-weight gain relative to respective control groups were observed in both sexes (being more severe in females) at 6.00 mg/kg during both weeks. Food consumption was also statistically significantly decreased in males and females at the highest dose in weeks 1 and 2. At 3.00 mg/kg, body weight was reduced (statistically significantly in males) during the first week only in both sexes, while food consumption did not appear to be affected. Statistically significant decreases in liver and kidney absolute weights and weights relative to body weight were observed in both sexes at 6.00 mg/kg, but terminal body weights were also reduced. At gross necropsy, there were no findings that were attributed to treatment with the test material in any group.

At 1.00 mg/kg (the highest dose assessed), plasma cholinesterase activity was statistically significantly inhibited by 21–37% at all time-points during treatment in males, and by 27–38% on days 4, 7, and 14 in females. At 0.500 mg/kg, plasma cholinesterase was statistically significantly inhibited on day 4 in males (15%) and on days 4 and 7 in females (23%), but no significant inhibition was observed on day 14 in either sex. Erythrocyte cholinesterase was statistically significantly inhibited at 1.00 mg/kg (the highest dose assessed) in males by 51–61% and in females by 40–52%, on days 4, 7 and 14. At 0.500 mg/kg, a statistically significant reduction in erythrocyte cholinesterase activity was noted on these same days, ranging from 22% to 25%, in males. In females at this dose, a significant decrease in erythrocyte cholinesterase activity of only 16% was seen on day 4. This finding in females was not considered to be of toxicological relevance, although the study authors considered that the decreases in erythrocyte cholinesterase activity in both sexes at this dose were associated with administration of the test material. If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, and considering that brain cholinesterase activity was not measured in this study, the NOAEL was 0.250 mg/kg (equal to 0.0039 mg/kg bw per day) in males and 0.5 mg/kg (equal to 0.066 mg/kg bw per day) in females on the basis of statistically significant inhibition of erythrocyte cholinesterase activity (Fischer, 1978).

A statement of compliance with QA, but not with GLP, was provided. The study was preliminary in nature and was not conducted to fulfil a particular guideline.

In a preliminary study performed to aid in selection of doses for a study of subchronic neurotoxicity, groups of five male and five female albino rats (outbred) (Crl : CD®(SD)IGS BR VAF/Plus®) (aged 6 weeks at study initiation) were given diets containing technical-grade terbufos (AC92100; purity, 89.7%) (dissolved in acetone, mixed with a GRIT-O'Cobs® carrier) at a concentration (adjusted for purity) of 0 (acetone and carrier), 1.0, 5.0 or 6.0 mg/kg in males (equal to 0, 0.11, 0.55 and 0.67 mg/kg bw per day, respectively) and of 0 (acetone and carrier), 0.5, 3.0 or 4.0 mg/kg in females (equal to 0, 0.06, 0.33, and 0.43 mg/kg bw per day, respectively) for at least 21 days. Diets were made available to animals until termination on day 22. The number of parameters evaluated was limited and included observations for general condition, mortality and clinical signs of toxicity, and measurement of body weight and food consumption. Plasma, erythrocyte and brain (one-half homogenate) cholinesterase activities were measured from samples obtained and processed on day 22 at study termination and stored frozen at -70 C until analysis. Cholinesterase inhibition was determined relative to the value for the appropriate concurrent control group. Clinical chemistry, haematological, urine, organ weight, and gross and histopathological evaluations were not conducted in this study.

No animals died and no clinical signs of toxicity were observed. Statistically significant decreases in body-weight gain relative to respective control groups, considered to be treatment-related, were noted during each of the 4 weeks in males at the highest dose (6.0 mg/kg) and during weeks 1 and 2 in females at the highest dose (4.0 mg/kg). Food consumption was statistically significantly decreased only in males at the highest dose during the first week of the study. Treatment-related decreases in blood and brain cholinesterase activities were observed in males and females at the two higher doses. In males at 5.0 mg/kg and 6.0 mg/kg, plasma cholinesterase activity was statistically significantly inhibited by 73% and 85%, respectively. In females, plasma cholinesterase activity was inhibited at 3.0 mg/kg and 4.0 mg/kg by 84% (not statistically significant) and 94% (statistically significant), respectively. Erythrocyte cholinesterase activity was statistically significantly inhibited by 98% and 99% in at 5.0 mg/kg and 6.0 mg/kg, respectively. A smaller inhibition of erythrocyte cholinesterase of about 35% was noted in males at 1.0 mg/kg. In the study report, the finding was not considered to be associated with the administration of test material, as it was not statistically significant and there were no reductions in either plasma or brain cholinesterase activity in males at this dose. It may, however, have been related to treatment as the values for cholinesterase activity for four of the five animals in this group fell below those in the control group in replicate assays. In females, at 3.0 mg/kg and 4.0 mg/kg, respectively, erythrocyte cholinesterase was inhibited by 99% to 100%. Statistically significant decreases in brain cholinesterase of 64% and 81% were observed at 5.0 mg/kg and 6.0 mg/kg in males, respectively, as were statistically significant decreases in females at 3.0 mg/kg and 4.0 mg/kg, of 68% and 84%, respectively.

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect and brain (not erythrocyte) cholinesterase inhibition and clinical signs of toxicity are considered to be relevant effects for terbufos, the NOAEL was 1.0 mg/kg in males (equal to 0.11 mg/kg bw per day) and 3.0 mg/kg in females (equal to 0.06 mg/kg bw per day) on the basis of statistically significant inhibition of brain cholinesterase inhibiton at the next highest dose (Mandella, 1999). Statements of compliance with QA and GLP were provided. This study was preliminary in nature and was not conducted to fulfil a particular guideline.

In a preliminary feeding study, groups of 10 male and 10 female albino RH Wistar rats were given diets containing technical-grade terbufos (CL 92 100; purity, 96.7%) at a nominal concentration of 0, 0.125, 0.5 or 2.0 mg/kg (nominally equivalent to 0, 0.012, 0.069 and 0.299 mg/kg bw per day in males and 0, 0.012, 0.053, and 0.212 mg/kg bw per day in females) for 31 days. Data on analysis of test material levels in the diet were not provided so test material intake and stability in the feed could not be confirmed. Study parameters examined included observations for appearance, mortality, and measurement of body weight and food consumption. In five animals of each sex per group (when possible), haematological and limited clinical chemistry evaluations (glucose, urea nitrogen and glutamic-pyruvic transaminase), liver and kidney weight measurements and a gross examination were conducted. At the end of the study, blood (from fasted animals) and brain samples (one-half of the cerebrum) were taken from five animals of each sex per group for determination of cholinesterase activity. Brain samples were stored frozen until analysis, and assays were conducted on homogenates. Inhibition of cholinesterase activity was determined relative to the value for the appropriate concurrent control group.

There were many deaths in the study; four males at the highest dose died on day 3, 17, 31 or 31, one male at the intermediate dose died on day 12, and one male at the lowest dose died on day 31. One female at the highest dose was terminated in a moribund condition on day 24, two females at the intermediate dose died on day 9 or 24 and one control female died on day 31. The deaths of five unspecified animals were thought to be the result of a respiratory infection, and autolysis prevented attempts to determine the cause of death in the remainder (again, unspecified). Therefore, it was not possible to ascertain whether any of the deaths were related to treatment. There was no apparent effect of treatment on body weight, food consumption, on measured haematological and clinical chemistry parameters, or on organ weights in any group treated with terbufos. Cholinesterase activity was statistically significantly inhibited only at the highest dose in both sexes. Statistically significant inhibition of cholinesterase activity in plasma (57%), erythrocytes (36%) and brain (28%) was noted in males at the highest dose, as was (mostly) a statistically significant inhibition in plasma (68%), erythrocytes (37%; not statistically significant), and brain (53%) in females at the highest dose. These decreases were attributed to treatment. There was also a decrease of 29% in erythrocyte cholinesterase activity in males at the intermediate dose; although not statistically significant, this was considered to be a possible result of treatment owing to the magnitude of the decrease. It was reported that upon gross pathological examination of four to five animals of each sex per group at study termination, no gross lesions were found that were attributed to treatment (gross pathology data were not provided). An overall NOAEL could not be identified in this study because insufficient information was provided about the mortality that occurred at all doses in males and at the intermediate and highest dose in females. There were a number of unspecified deaths that were judged likely to be the result of infection in the animal facility. In addition, intake of test material could not be confirmed (Morici, 1972). No statements of compliance with QA or GLP were provided. This study was not performed according to a specific guideline.

In a feeding study, groups of 20 male and 20 female Sprague-Dawley rats were given diets containing technical-grade terbufos (purity, 90.1%; prepared in corn oil and methylene chloride, 1 : 1) at a concentration (adjusted for purity) of 0 (vehicle), 0.125, 0.250, 0.500 or 1.000 mg/kg (equal to mean intakes of test substance of 0, 0.011, 0.021, 0.041, and 0.082 mg/kg bw per day in males and 0, 0.012, 0.023, 0.048 and 0.095 mg/kg bw per day in females) for 3 months. Parameters evaluated included observations for mortality and clinical signs of toxicity, assessments of body weight, food intake and food efficiency, ophthalmoscopic, haematological, and clinical chemistry evaluations, urine analysis, organ weight determinations, a macroscopic examination in all animals and a microscopic evaluation of organs and tissues in animals at the highest dose and in the control group only. The heart, liver, and kidney, any gross lesions or masses, and any other tissues, as indicated by findings at the highest dose, were examined microscopically in all animals. Plasma and erythrocyte cholinesterase activities were measured on day 1, and at weeks 1 and 2 and months 1, 2 and 3 in 10 animals of each sex per group. Brain cholinesterase activity was measured in 10 animals of each sex per group at study termination. Inhibition of cholinesterase activity was determined relative to the value for the appropriate concurrent control group.

One female at 0.5 mg/kg was mistakenly sexed as male until week 4, when the animal was put with other females in the group. All animals survived until the end of the study, except for one female and one male at 0.5 mg/kg, which died of accidental causes on days 8 and 51. No clinical signs of toxicity were observed and there were no obvious effects of treatment on body weight, food consumption, food efficiency, haematological, clinical chemistry, or urine analysis parameters at any dose. Slight statistically significant increases in liver weight to body weight ratios but not absolute weights in females at the two highest doses were not considered to be of biological relevance. Plasma cholinesterase activity was statistically significantly decreased only at the highest dose, at which activity was

inhibited throughout the study in both sexes. At study termination, decreases in activity at the highest dose were 33% in males and 52% in females. Erythrocyte cholinesterase and brain cholinesterase activities were not affected by treatment. The macroscopic examination was not remarkable. Upon microscopic examination of tissues and organs, increases were observed in the incidence of mandibular lymph node hyperplasia at the highest dose in males (20%) and females (70%) compared with that in male control animals (6.25%) and female control animals (32%). Also, the incidence of mesenteric lymph node hyperplasia was increased in females at the highest dose (50% compared with 25% in the control group), but not in males at the highest dose (25% compared with 30% in the control group). There was no clear association with treatment for these or other histopathology findings in the study. In the study report, the mesenteric lymph node lesions were considered to be related to nematodiasis. Other groups treated with terbufos were not examined for the incidence of either mandibular or mesenteric lymph node hyperplasia. Some respiratory tract lesions that occurred with similar frequency in control groups and in groups treated with terbufos were ascribed to chronic murine pneumonia (said to be a common finding in rodent colonies). If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, the NOAEL was ≥1.00 mg/kg (the highest dose tested) in males and females (equal to 0.082 mg/kg bw per day in males and 0.092 mg/kg bw per day in females) (Daly & Knezevich, 1979). A statement of compliance with QA, but no GLP statement, was provided. The protocol was generally consistent with US EPA Subdivision F Guidelines (November 1982 and 1984, revised).

In a study of toxicity, groups of 30 male and 30 female CD® (Sprague-Dawley derived) COBS® rats were given diets containing technical-grade terbufos (AC 92 100; purity, 89.6%) (prepared in corn oil and methylene chloride, 1 : 1) at a concentration of 0 (vehicle only), 0.125, 0.5, or 1.0 mg/kg (equal to 0, 0.007, 0.028, and 0.055 mg/kg bw per day for males and 0, 0.009, 0.036, and 0.071 mg/kg bw per day for females) for 1 year. Parameters assessed included observations for general health and mortality, clinical signs of toxicity, measurement of food consumption and body-weight changes, haematological and clinical chemistry determinations, urine analysis, organ weight measurements and ophthalmoloscopic and macro- and microscopic pathology examinations. Plasma and erythrocyte cholinesterase activities were assessed in 10 animals of each sex per group at week 6, months 3 and 6, and at study termination. Brain cholinesterase activity was determined at study termination. Inhibition of cholinesterase activity was calculated relative to values for values for concurrent controls.

There were six deaths in the study; two control animals (one male on day 306 and one female on day 271) and two animals at the intermediate dose (one male on day 351 and one female on day 262) were terminated in a moribund condition. One male at the intermediate dose was found dead on day 310 and one female at the highest dose died accidently on day 97. There was no obvious pattern in the deaths in the animals treated with terbufos that would suggest a relationship with administration of the test material. There was no clear relationship with treatment for the slight increases observed mostly during the last half of the study in the group of females at the highest dose in the incidence of excess lacrimation, chromodacryorrhoea and alopecia compared with the control and other treated groups. As similar increases were noted at lower doses in males, the findings in females were considered to be likely to be caused by random variation. There were no clear effects of treatment on body weight. Variation was noted among groups in food consumption over the course of the study, but there was no consistent pattern of findings that would clearly indicate an effect of treatment in groups of males or females treated with terbufos. There was no evidence that the results of the urine analyses or those of the ophthalmoscopic and haematological examinations were related to treatment. Statistically significant decreases, of small magnitude, in blood urea nitrogen and bilirubin at termination in females at the highest dose were not considered to be clearly of adverse significance in the absence of other findings. Clinical chemistry evaluations were otherwise not remarkable. Slight, statistically significant reductions were observed at the highest dose in the absolute weight and weight relative to brain weight (but not relative to body weight) of male testes, and slight statistically significant decreases in the absolute weight and weight relative to brain weight (but not relative to body weight) of the kidney were noted in females at the intermediate and highest doses. These organ-weight changes were not clearly adverse in the absence of other supporting indications of toxicity. No obvious effect of treatment was indicated by the results of the gross and microscopic examinations. There was no evidence of carcinogenity.

Decreases in cholinesterase activity that could be clearly related to treatment were observed only at the highest dose in both sexes. Plasma cholinesterase activity was statistically significantly inhibited in males at the highest dose by 25% and 29%, respectively, at 6 and 12 months. Statistically significant inhibition of plasma cholinesterase activity (33–51%) was noted at all time-points in females at the highest dose. Erythrocyte cholinesterase activity was not statistically significantly inhibited at any dose or time-point in either sex. Brain cholinesterase activity in males was

decreased relative to control values at the lowest, intermediate and highest dose, respectively by 4% (statistically significant), 3% (not statistically significant) and 8% (statistically significant). On the basis of the magnitude and pattern of the response, inhibition at the lowest dose was not considered to be related to treatment. In females, brain cholinesterase activity was statistically significantly inhibited only at the highest dose. Virtually no changes relative to the control group was observed at the lowest and intermediate doses. Although the decrease observed at the highest dose in males and females may have been related to treatment, because of the relatively low magnitude of the response and the absence of clinical signs at this dose, it was not considered to be toxicologically relevant.

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect and inhibition of brain cholinesterase activity of 8–10% is not considered to be toxicologically relevant, the NOAEL was 1.0 mg/kg (equal to 0.055 mg/kg bw per day in males and 0.071 mg/kg bw per day in females), the highest dose tested (Daly, 1987). This study complied with QA and GLP and was consistent with US EPA Subdivision F Guidelines.

Dogs

In a short-term study to assess cholinesterase activity, groups of four male and four female beagle dogs (except at the highest dose, where two dogs of each sex were used) were given technical-grade terbufos (AC 92 100; purity, 89.6%) at a dose (adjusted for purity) of 0 (vehicle), 1.25, 2.5, 5.0, or 15.0 µg/kg bw per day, administered orally in corn oil in gelatin capsules, once daily in the morning for 29 days. Originally planned for 28 days, dosing was extended by 1 day through a protocol amendment. The number of parameters evaluated was limited and included observations for mortality, morbidity and clinical signs of toxicity, and measurement of body weight and food consumption. Plasma and erythrocyte cholinesterase activities were assessed before dosing and after 1, 2, and 4 weeks of treatment from blood samples collected before dosing on the given day. Brain cholinesterase activity was determined at study termination in samples from the cerebrum and cerebellum obtained 20– 24 h after administration of the last dose. In the study report, cholinesterase inhibition in the plasma and erythrocytes was determined and statistically analysed relative to values obtained before the start of dosing. Inhibition of cholinesterase activity in the brain was determined relative to the value for the appropriate concurrent control group. Clinical chemistry, haematological, urine, organ weight and gross and microscopic histopathological evaluations were not performed in this study.

There were no deaths in the study and no clinical findings were observed that could be ascribed to treatment in any group. One instance of vomiting was observed in each of two dogs at the lowest dose only. There were no appreciable differences in body weights or food consumption among groups of either sex during the study. Statistically significant decreases in plasma cholinesterase activity ranging from 33% to 37% were noted at the highest dose in both sexes at all time-points and were ascribed to treatment. Inhibition of plasma cholinesterase activity of 20–21% was observed at 5.0 µg/kg bw per day in males after 2 and 4 weeks of treatment and in females at all time-points; these values were not statistically significantly from those for the respective groups of pre-treatment controls and were considered to be of marginal biological relevance in the study report. If inhibition of plasma cholinesterase activity was determined relative to values for the appropriate concurrent controls instead of pre-treatment values (as in the study report), there was not much difference in the magnitude of the decreases calculated by either procedure for either sex at any week or dose, except in females at 2.5 and 5.0 µg/kg bw per day. In these groups, slightly greater decreases in plasma cholinesterase activity were measured relative to values for concurrent controls at all time-points (28–30% at 5.0 µg/kg bw per day, and 18–23% at 2.5 µg/kg bw per day) than relative to pre-treatment values (20–21% at at 5.0 µg/kg bw per day, and 10–18% at 2.5 µg/kg bw per day). Under the conditions of the study, there was no effect of treatment in either sex or at any dose on erythrocyte cholinesterase activity (relative to pre-treatment values or to values for the appropriate concurrent controls) or on brain cholinesterase activity relative to the values for the appropriate concurrent controls. If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, the NOAEL was 15 µg/kg bw per day (the highest dose tested) in males and females (Shellenberger, 1987). Statements of compliance with QA and GLP were provided. This was a special study that was not conducted to comply with a particular guideline.

In a preliminary feeding study, groups of two male and two female beagle dogs (aged 8–12 months) were given diets containing technical-grade terbufos (CL 92 100; purity, 96.7%) (prepared in a vehicle of corn oil) at a nominal dose of 0, 0.01, 0.05, or 0.25 mg/kg bw per day administered daily for 30 consecutive days. Food consumption was estimated by visual inspection and many animals did not always consume all the food offered. In addition, data on the analysis of concentrations of test material in the diet were not provided, so intake of test material could not be

determined with any degree of confidence, and stability of the test material in the feed could not be confirmed. Parameters assessed included observations for appearance, mortality and measurement of body weight and food consumption, haematological and limited clinical chemistry evaluations (plasma glucose, glutamic-oxalacetic transaminase and glutamic-pyruvic transaminase, and urea nitrogen), liver and kidney organ weight measurements and gross examination of all animals. Plasma and erythrocyte cholinesterase activities were assessed before the start of dosing, at week 2 and at study termination in fasted animals. Brain cholinesterase activity was measured at study termination in homogenates of samples taken from the cerebrum. Cerebrum tissue was stored frozen until analysis. Inhibition of cholinesterase activity was determined relative to the values for the appropriate control group.

There were no deaths in the study and no clinical signs of toxicity were observed. On the basis of the estimated food refusal (%) during the study, received doses were as much as 20–35% lower than nominal doses in most animals at the lowest and intermediate doses, and by as much as 35–50% at the highest dose. Over the course of the study, males at the highest dose failed to gain weight and females at the highest dose and one female at the intermediate dose lost weight; these findings were statistically significant for the groups receiving the highest dose. There was no apparent effect of treatment on organ weights, or on the haematological and clinical chemistry parameters measured. No treatment-related findings were observed during the gross examination. As values for cholinesterase activity were similar in males and females at the same dose, data were pooled for statistical analysis. By week 4, statistically significant decreases in plasma cholinesterase activity of 68% and 84%, and in erythrocyte cholinesterase activity of 35% and 80% were observed at the lowest and intermediate doses, respectively. Brain (cerebrum) cholinesterase activity was statistically significantly inhibited only at the highest dose (by 66%). An overall NOAEL could not be identified because intake of test material could not be reliably estimated (Morici, 1972). No statements of compliance with QA or GLP were provided. This study was not performed to comply with a specific guideline.

In a feeding study, groups of four male and four female beagle dogs (aged 10–14 months, i.e. somewhat older than the age recommended in the guidelines) were given terbufos (AC 92,100; purity not specified) at a nominal concentration of 0 (vehicle only), 2.5, 10.0, or 40.0 mg/l (nominally equivalent to 0, 2.5, 10, and 40 µg/kg bw per day) in corn oil, administered daily for 6 days per week, for 6 months. One ml of the test material in the vehicle was injected via a syringe on top of each dog's daily food ration (kibbled dog chow). Doses were adjusted weekly for each individual animal's body weight. A set amount of treated food (apparently totalling 3300 g per week) was offered for 1 h each day and any food not consumed in that time was removed and weighed in order to measure food consumption and estimate intake of test material. Neither dosing solutions nor treated diets were analysed to confirm content or stability of the test material. Parameters examined included mortality and clinical signs of toxicity, assessments of body weight and food intake, ophthalmoscopic, haematological, and limited clinical chemistry (alkaline phosphatase, blood urea nitrogen, fasting blood sugar, and serum glutamic-pyruvic transaminase) evaluations, urine analysis, weights of selected organs (adrenals, gonads, kidneys, heart and liver), and macroscopic and microscopic examinations. Plasma and erythrocyte cholinesterase activities were measured before the start of dosing and at weeks 0, 4, 12 and 26. Brain cholinesterase activity was assessed at week 26. Although data on cholinesterase activity were provided for individual animals, in the study report data from both sexes were combined for statistical analysis (*t*-test) for each dose and type of cholinesterase activity, as differences between the sexes were not considered to be remarkable. Data on cholinesterase activity from groups treated with terbufos were compared with data for the combined concurrent control group.

Test material intake could not be reliably determined. In addition to a lack of analytical information on the purity, dietary content and stability of the test substance, some animals did not always consume all their food. Since the solution containing the test material was placed on top of the daily food ration, it is not clear how much of the test material was ingested by animals that did not consume the daily food allotment. Female dogs had a greater tendency not to consume the entire meal. The approximate percentage of unfinished meals over the course of the study for all females at each dose was 36% in the control group, 38% at the lowest dose, 40% at the intermediate dose and 23% at the highest dose. Over the duration of the study, some females received only about 80–90% of the intended dose of terbufos. The situation was less severe in males; the approximate percentage of all unfinished meals over the duration of the study for all males at each dose was 31% for the control group, 5% at the lowest dose, <1% at the intermediate dose and 2% at the highest dose. Also, initial body weights varied more than might be desirable (20% difference between some animals of the same sex).

One male in the control group was terminated in a moribund condition and was found to have a colon obstruction and peritonitis. Clinical signs of toxicity were not observed in any animals (individual animal or summary data was not included in the report).

With regard to general condition, one male at the lowest dose, one male at the highest dose, three females in the control group, one female at the highest dose, and possibly one female at the lowest dose and one female at the intermediate dose, had histopathological indications of bronchopneumonia. Body-weight loss (measured over the duration of the study) was noted at termination at week 26 in individual animals in all groups except females at the highest dose. The incidence of weight loss (and average body-weight change) during the study was: in males, 2 (-0.55 kg), 3 (-0.45 kg), 3 (-1.8 kg), and 3 (-0.4 kg), respectively; and in females, 1 (0.35 kg), 1 (0.075 kg), 1 (0.15 kg) and 0 (0.425 kg), in the control group and at the lowest, intermediate and highest dose, respectively. There was no obvious dose-related pattern in these findings. The greater weight loss in the group of males at the intermediate dose was due to one animal that was the heaviest animal in the group at initiation of treatment and that lost 5.7 kg in weight during the study, apparently exhibiting no clinical signs or indications of toxicity, and no unusual findings with regard to food consumption or other parameters examined (except for a slight elevation in erythrocyte sedimentation rate at week 26). The only gross or histopathopathological finding in this animal was diffuse mild leukocytosis in the liver, which the study report stated could, along with the elevated erythrocyte sedimentation rate, have been related to an infection in this dog near the end of the study. In other animals, there was no clear effect of treatment on the haematological, biochemical, urinary parameters or organ weights assessed or in the gross or histopathological examinations.

Inconsistencies and variability were noted in the data on cholinesterase activity. In the study report, differences between sexes for a given type of cholinesterase activity and at a particular dose were considered to be minimal and data were combined for both sexes for statistical analysis. Under these conditions, there were no statistically significant differences in brain or erythrocyte cholinesterase activity at the end of the study (week 26). Plasma cholinesterase activity at week 26 was statistically significantly decreased relative to values for the combined control group, by 26% at the intermediate dose and 31% at the highest dose; the study report considered these decreases to be minimal but treatment-related. The value for plasma cholinesterase activity from the control male that was terminated in a moribund condition was not included in the calculation, although it was not an outlying value compared with those for the rest of the animals in the group. Data for individual animals were provided. When plasma cholinesterase activity was calculated for each sex separately at week 26, without statistical evaluation, there was no clear effect on plasma cholinesterase activity in males relative to that of the control group, either with the inclusion of the terminated control male (no decrease at the lowest dose, decrease of 35% at the intermediate dose, decrease of 15% at the highest dose) or without it (decrease of 9% at the lowest dose, decrease of 47% at the intermediate dose, decrease of 31% at the highest dose) owing to the lack of a clear dose–response relationship at the intermediate and highest doses. In females at week 26, decreases in plasma cholinesterase activity relative to that of the control group were noted at the intermediate dose (19%) and highest dose (32%), indicating a possible, small effect of treatment, particularly at the highest dose. Erythrocyte cholinesterase activity at the highest and intermediate doses was decreased by 26% and 6%, respectively, when data for males were taken separately (as compared with reduction of 17% and 13% (neither statistically significant) at the highest and intermediate doses, respectively, when data from both sexes were combined), suggesting a possible minimal, but certainly not clear, effect of treatment at the highest dose.

There were no clear adverse findings associated with treatment in this study, but because nominal concentrations of test material in the diet could not be confirmed, intake of test material could not be reliably estimated and underconsumption of diets containing terbufos was noted, especially in females, a NOAEL could not be identified (Morgareidge, 1973). Statements of compliance with QA and GLP were not provided. The protocol and study conduct were considered to be inadequate according to current standards.

Subsequent to the 6-month feeding study in dogs (Morgareidge, 1973), a study was conducted to attempt to address questions about the 6-days-per-week dosing regimen used in that study, and to determine whether a 7-days-per-week regimen would influence cholinesterase activity, particularly in erythrocytes. Groups of two male and two female beagle dogs (aged 9.5–12 months) were given diets containing technical-grade terbufos (purity, 88%) at a dose of 50 µg/kg bw daily, for (1) 7 days per week for 28 days; or (2) 6 days per week (basal food given on day 7) for 28 days, followed in both groups by a 28 day recovery period without treatment. Five out of the eight dogs in the study had previously been exposed to dichlorvos, another cholinesterase-inhibiting chemical, 4–7 months before

their arrival in the testing facility. No other details were provided. A concurrent control group was not included in the study. The test material was prepared as a solution in corn oil, added to a fixed amount of food via a syringe at the rate of 1 ml/kg bw, and given to each dog individually in the morning. If treated food was not eaten within 1 h, it was removed and weighed. It was stated that any food treated with terbufos that was not consumed in the morning was re-administered to the animal in the afternoon (regular feed of plain dog chow), such that any remaining test substance was eaten. Erythrocyte and plasma cholinesterase activities were measured before treatment on days -7 and -6, on days 1, 3, 7, 10, 14, 18, 21 and 28, and after treatment on days 29, 31, 35, 38, 42, 49 and 56. Average cholinesterase inhibition for each group (both sexes combined) was calculated relative to the respective average value before treatment (sexes combined) at each time-point, but apparently these comparisons were not analysed statistically. Statistical analysis was performed for each time-point (both sexes combined) to determine whether there was a significant difference between the 6-day treatment regimen and the 7-day treatment regimen. Animals were observed for general condition, signs of toxicity and body-weight changes during treatment. After the first treatment phase of the study was concluded, a 28-day crossover phase was performed in which the group of animals dosed for 7 days per week were dosed for 6 days per week for 28 days and the group of animals dosed for 6 days per week were dosed for 7 days per week for 28 days. Erythrocyte and plasma cholinesterase activities were assessed before treatment and on days 1, 3, 7, 10, 14, 18, 21, 25, and 28. There was no recovery period. Brain cholinesterase activity was not assessed in either the first phase or the cross-over phase.

Dosing solutions were analysed four times during the first phase of the study and found to contain 87.6–98.8% of the target amounts (average, about 92%). All animals survived both study phases and no clinic signs of toxicity were observed. In the first phase, initial body weights in some dogs varied considerably; a difference of about 40–50% was noted between some animals in the 7- or 6-day dosing group. Three out of four dogs in both the 7- and 6-day feeding groups lost weight during at least part of the first phase of treatment; this may have been related to treatment, but there were no control groups available for comparison. Some weight gain was noted in most animals in both groups during the recovery period. Recorded weekly food intakes for individual animals in the first phase were fairly variable week-by-week and between individuals in dogs fed the test material for 7 days per week; it is thus not clear whether all animals in that group ate all the treated food offered. Far less variability was observed in dogs fed test material for 6 days per week, as apparent weekly maximums of 2400 g of food per dog were commonly consumed.

Owing to the small sample size and variability in the data, it was difficult to determine whether there was a sex difference in cholinesterase activity measurements. In the study report, it was assumed that there were no sex differences and group means from data from both sexes combined were compared. In the first phase of the study, on day 28, although data were apparently not analysed statistically, erythrocyte and plasma cholinesterase activities decreased by 14% and 68%, respectively, in the group fed test material for 7 days per week, and by 4% and 40%, respectively, in the group fed test-material for 6 days per week relative to values before treatment (there was no concurrent control group). The difference between the groups treated for 7 days per week and for 6 days per week was not statistically significant with regard to erythrocyte cholinesterase activity at any time-point, either during or after treatment. Differences in plasma cholinesterase activity between the groups treated for 7 days per week and for 6 days per week were statistically significant at weeks 7, 21 and 28. Based on the data provided, recovery to pre-treatment or almost pre-treatment levels was noted during the recovery phase with both dosing regimens, but progress appeared to be a little more rapid on the 6-day regimen and plasma cholinesterase activity seemed to recover more rapidly than erythrocyte cholinesterase activity on either regimen.

In the cross-over phase of the study, after 28 days of treatment, erythrocyte and plasma cholinesterase activities decreased by 18% and 55%, respectively, in the cross-over group fed test material for 7 days per week and by 28% and 52%, respectively, in the cross-over group fed test material 6 days per week, relative to values before treatment. No statistically significant differences were found between the groups on the 6- and 7-day feeding regimens at any time-point assessed. Body-weight losses and variable food intakes were noted with both groups. The study authors concluded that the decrease in cholinesterase activity noted was reversible after cessation of treatment. They also concluded that there were no cumulative adverse effects in erythrocyte or plasma cholinesterase activity on either regimen. In the first phase, however, there did appear to be a slightly larger effect on cholinesterase activity on the 7-day regimen compared with the 6-day regimen, and in the second phase a stronger effect on erythrocyte activity was observed relative to the first phase, possibly implying some carry-over influence between treatments. Owing to the small sample size, the limited protocol (no assessment of brain cholinesterase activity), the lack of a concurrent control group, the use of only one dose, questions about the intake of test material based on food consumption data,

the variability in data for individual animals and other uncertainties (e.g. previous treatment of test animals with dichlorvos), this study is not suitable for the identification of a NOAEL or for performing regulatory toxicology assessments for terbufos. No statements of compliance with QA or GLP were provided and the study was not performed to comply with a particular guideline (Berger, 1977).

In a 1-year study, groups of male and female beagle dogs were fed gelatin capsules containing technical-grade terbufos (AC 92,100; purity, 89.6%) at an initial dose (not adjusted for purity) of 0 (vehicle only), 15, 60, 240 or 480 µg/kg bw per day in corn oil for 1 year. Owing to toxicity that resulted in mortality, the dose of 480 µg/kg bw per day was reduced to 120 µg/kg bw per day 1 day before the start of week 6, and the dose of 240 µg/kg bw per day was decreased to 90 µg/kg bw per day 2 days after the beginning of week 8. Eight animals of each sex were assigned to the vehicle control group and six animals of each sex were assigned to each of the groups receiving terbufos. During weeks 3 and 4, an error occurred and the doses administered were only 5.2% of those intended. Administration of the test material continued until 20–24 h before termination, and animals were terminated during the 5 days following the 1-year period of treatment. Parameters assessed included general condition, mortality, morbidity and clinical signs of toxicity, measurement of body weight and food consumption, and clinical chemistry, haematology, urine analysis, ophthalmoscopy, organ weight, and gross and microscopic evaluations in all animals. Plasma and erythrocyte cholinesterase activity in fasted animals was assessed before treatment, at months 3 and 6 and at study termination. Brain cholinesterase activity in samples from the cerebrum and cerebellum was measured from tissues taken at study termination and stored frozen until analysis. Inhibition of cholinesterase activity was determined relative to the value for the appropriate concurrent control group.

There were three deaths attributable to treatment-related causes. One male and one female at the highest dose died during week 6, while the dose of 480 µg/kg bw per day was being administered. Clinical signs observed in these animals included vomiting, slight tremors and inactivity in the male and tremors, diarrhoea, weak hind legs and excessive salivation in the female. Decreased body weight and food consumption were noted in both dogs. One female at 240/90 µg/kg bw died during week 7, also from causes related to treatment, while receiving the dose of 240 µg/kg bw per day. Clinical findings in this animal included tremors that increased in severity, inactive behaviour, red-tinged faeces, excessive salivation, dehydration, listless behaviour, rough hair coat and decreased body weight and food consumption. One other female at the highest dose was sacrificed in a moribund condition at the start of week 31, owing to causes unrelated to treatment (prolapsed vagina).

Clinical signs of toxicity noted in surviving males at 480 µg/kg bw per day included tremors (slight to more severe) and inactivity. In males at 240 µg/kg bw per day, clinical signs of toxicity included excessive salivation, dehydration, red-tinged faeces, listlessness and inactivity. Symptoms in females were generally more severe than in males at these doses and included tremors (slight to more severe), inactivity, excess salivation, red-tinged faeces, vomiting and weak hind legs at the highest dose (480 µg/kg bw per day), and slight tremors, inactive behaviour, excessive salivation, weak hind legs, diarrhoea, and red-tinged faeces at the lowest dose (240 µg/kg bw per day). Decreases in body weight and food consumption were noted in males at both 480 µg/kg bw per day and 240 µg/kg bw per day and to a greater extent in females at these doses during the early weeks of the study before and just after the decrease in dose. During this time, body-weight decreases reached statistical significance in females at the highest dose, and statistically significant decreases in food consumption were noted for males and females at the highest dose and for females at 240 µg/kg bw per day. Shortly after the two higher doses were lowered to 120 and 90 µg/kg bw per day, respectively, and for the remainder of the study, there was no apparent effect of treatment with terbufos on body weights or food consumption at any dose.

After the two higher doses were reduced, the only clinical findings noted during the remainder of the study, for which an association with treatment could not be dismissed, were two instances of severe convulsions in one female at 120 µg/kg bw per day during weeks 46 and 47. There were no obvious effects of treatment on the ophthalmoscopic, clinical chemistry or urinary parameters assessed or on organ weights after doses of terbufos of ≤120 µg/kg bw per day. In males, at month 3, slight statistically significant decreases were found in erythrocyte counts at 90 and 120 µg/kg bw per day, and in haemoglobin, erythrocyte volume fraction, and mean corpuscular haemoglobin concentration at 120 µg/kg bw per day. Numbers of platelets were also slightly increased (statistically significantly) in males at 90 and 120 µg/kg bw per day. Slight, statistically significant decreases in haemoglobin and erythrocyte volume fraction were noted at month 3 in females at 120 µg/kg bw per day. These perturbations were transient and had resolved by the next assessment at month 6. They may have been related to treatment at these doses or may have been residual effects from previous dosing at 240 and 480 µg/kg bw per day.

Data on cholinesterase activity reported in this study were difficult to interpret owing to variability in the values for individual animals and because of generally inconsistent or sometimes shallow dose–response relationships. Data were apparently not analysed statistically. Plasma cholinesterase activity was inhibited by about 40% or more in all groups receiving terbufos at all time-points in both sexes. At study termination (week 52), plasma cholinesterase activity was inhibited at the lowest, low intermediate, high intermediate and highest doses by 44%, 66%, 67% (shallow dose–response relationship) and 68%, respectively, in males, and by 45%, 68%, 67% (shallow dose–response relationship) and 74%, respectively, in females. Owing to the magnitude of the relative decreases, a relationship to treatment could not be excluded at any dose. At study termination (week 52), erythrocyte cholinesterase activity was lower than the control value at the lowest, lower intermediate, higher intermediate and highest doses in males by 4%, 13%, 18% and 19%, respectively. Similar patterns were found at earlier time-points. The decreases at week 52 were considered to be marginal and the changes of slightly higher magnitude at the two higher doses were considered to be of no toxicological significance. In females, inhibition of erythrocyte cholinesterase activity varied little from control values at the lowest and lower intermediate doses, and ranged from 18% to 28% at the higher intermediate dose and 27% to 35% at the highest dose, at all time-points. At study termination (week 52), erythrocyte cholinesterase activity was lower than the control value in the lowest, lower intermediate, higher intermediate and highest doses in females by 6%, 15%, 20% and 27%, respectively. The magnitude and consistency over time of the change at the highest dose was such that a relationship to treatment could not be dismissed. At week 52, cerebellum cholinesterase activity was not inhibited at any dose (values were 98% to 125% of those of the controls) in males. Cerebrum cholinesterase activity in males was lower than the control value at the lowest, low intermediate, higher intermediate and highest dose by 5%, 10%, 22%, and 22%, respectively. Despite the lack of a dose–response relationship at the two higher doses and the large variability in the data, the magnitude of the response in the brain at the two higher doses was such that a relationship to treatment could not be dismissed. For the same doses, inhibition of cholinesterase activity in the cerebellum in females was 3%, 3%, 12% and 21%, respectively. The magnitude of inhibition in the brain at the two higher doses could not be ignored as a possible effect of treatment; however, the decrease of 12% was not considered to be toxicologically relevant. At the lowest and highest doses, cholinesterase activity in the cerebrum of females was similar to that in controls (although activity fell below the mean for controls by 18% and 24% at the two intermediate doses). Owing to the lack of a dose–response relationship, a treatment-related effect was not readily supported.

Gross lesions seen in the intestinal tracts of animals that died during weeks 6 and 7 had non-neoplastic microscopic correlates. On histopathological examination, the male at 480 µg/kg bw per day that was found dead at week 6 had diffuse congestion of the duodenum, jejunum, ileum and colon, congestion of the lungs, kidneys and liver and fibrinous thrombi in the pulmonary vessels of the lungs and in the arteries of the pancreatic mesentery. Microscopic findings in the female at the highest dose found dead at week 6 were marked haemorrhage and congestion in the mucosa and muscularis of the jejunum and areas of necrosis in the muscularis, mucosa and Peyer patches of the ileum (possibly secondary to intussusception). The female at 240 µg/kg bw per day found dead at week 7 had congestion of the muscularis and mucosa of the jejunum on microscopic examination. The study authors considered that these findings were likely to be related to treatment. Other gross and microscopic findings in the study were considered to be incidental and not related to treatment.

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, and inhibition of brain (not erythrocyte) cholinesterase activity is considered to be a relevant effect for terbufos, the NOAEL was 60 µg/kg bw per day in males on the basis of a decrease (22%) in cerebral cholinesterase activity for which a relationship to treatment could not be excluded, and 90 µg/kg bw per day in females on the basis of a decrease in cerebellar cholinesterase activity of 21% and instances of severe convulsions in one female for which an association with treatment could not be dismissed (Shellenberger & Billups, 1986). Statements of compliance with QA and GLP were provided and the protocol was consistent with US EPA Subdivision F Guidelines (November 1982 and 1984, revised).

Sheep

In a feeding study, groups of three wethers (males) were given diets containing technical-grade terbufos (purity, 89.8%; in corn oil, diluted with an equal volume of methylene chloride) at a concentration (not adjusted for purity) of 0 (with vehicle only), 0.01, 0.1 or 1.0 mg/kg (equal to 0, 0.0003, 0.0023, and 0.0245 mg/kg bw per day) administered daily in two portions (half in the morning and half in the afternoon) for 42 days. Parameters assessed included mortality and clinical signs of toxicity, measurement of body-weight changes and food consumption,

ophthalmoscopic examination, haematological and clinical chemistry determinations, urine analysis, and measurement of heart and respiratory rate. Necropsies were not conducted at study termination. Erythrocyte cholinesterase activity was determined before the start of treatment and on days 1, 3, 7, 14, 21 and 42. Erythrocytes were stored frozen for an unspecified period of time before analysis. Erythrocyte cholinesterase activity in groups treated with terbufos was compared with that for the appropriate concurrent controls at each time-point. Brain cholinesterase activity was not measured. The study report stated that the blood plasma of sheep had little or no cholinesterase activity and therefore was not assessed.

No deaths occurred during the study and no clinical signs of toxicity were observed. There was no obvious effect of treatment with terbufos on any parameter examined, including erythrocyte cholinesterase activity. It is not known whether storage conditions before assay had any effect on the cholinesterase activity of the erythrocytes. Brain cholinesterase activity was not assessed. The NOAEL in males (the only sex tested) was ≥1.00 mg/kg (equal to 0.0245 mg/kg bw per day) (the highest dose tested) (Garces et al., 1977). No statements of compliance with QA or GLP were provided. The study report stated that the facility in which the animals were maintained was fully accredited by the American Association for Accreditation of Laboratory Animal Care.

(b) Exposure by inhalation

In a short-term study of whole-body inhalation, groups of 10 male and 10 female Sprague-Dawley rats were given technical-grade terbufos (AC 92,100; purity, 90.1%) at a target concentration of 0, 0.005, 0.01, 0.05 or 0.10 mg/m^3 (not adjusted for purity) as a vapour for 8 h per day, for 5 days per week over a period of 3 weeks, for a total of 15 exposures, followed by a 2-week recovery period. A 2-week treatment period had originally been planned, but during week 1 of exposure, analytical chamber concentrations were only about 2–44% of target concentrations. During exposure weeks 2 and 3, when vaporization flasks were heated slightly, analytical concentrations were much closer to those targeted, however, the range of daily means varied widely suggesting chamber concentrations were not well maintained. Mean daily analytical chamber concentrations and the range of daily means for exposure weeks 2 and 3 corresponding to the control, 0.005, 0.01, 0.05 and 0.10 mg/m^3 groups were, respectively, for males 0, 0.0117 (range, 0.0003–0.0380), 0.0243 (range, 0.0066–0.05669), 0.0458 (range, 0.0098–0.0763) and 0.0946 (range, 0.0394–0.1523) mg/m^3, and for females 0, 0.0112 (range, 0.0003–0.0380), 0.0256 (range, 0.0066–0.0569), 0.0468 (range, 0.0098–0.0763), and 0.1001 (range, 0.0448–0.01523) mg/m^3. Estimated inhalation doses on a mg of active ingredient/kg bw per day basis for the control group and at thes lower intermediate, higher intermediate and highest dose over the last 2 weeks of exposure, assuming a retained dose of inhaled material of 50%, were: males, 0, 0.0030, 0.0065, 0.0122 and 0.0246 mg/kg bw per day; and females, 0, 0.0041, 0.0097, 0.0175 and 0.039 mg/kg bw per day, according to the study report. Possible contributions to exposure via the dermal and oral routes (i.e. from grooming) were not discussed. Owing to mortality, exposure of females at the highest dose was stopped early, on day 18. The study was terminated for half the animals in all groups at the end of the exposure period on day 21 and for the other half at the end of the recovery period on day 37. Parameters evaluated for both the treatment and recovery phases of the study included observations for mortality, clinical signs of toxicity, measurement of body weight and food consumption, haematological and clinical chemistry determinations (in five animals of each sex per group), urine analysis, selected organ weight measurements (adrenals, heart, kidneys, liver, and lungs) and an examination for gross pathology. Plasma and erythrocyte cholinesterase activities were measured in five animals of each sex per group before testing, on days 1, 5, 8, 13 for all groups, on day 18 for surviving females at the highest dose and five control animals, and on days 21 and 37 for all groups. Brain cholinesterase activity was measured in five animals of each sex per group on days 21 and day 37. Cholinesterase inhibition was calculated relative to the appropriate concurrent control group.

All animals survived except for one male at 0.0117 mg/m^3 that died accidently on day 8 and two females at the highest dose that died on days 17 and 19 from treatment-related causes. The only clinical findings ascribed to treatment in the study were observed during the treatment period in the group of females at the highest dose and included body tremors, body coldness, and rapid or laboured breathing. Body weights were statistically significantly depressed in females at the highest dose, as was food consumption, particularly towards the end of the period of exposure. Haematological and clinical chemistry findings, which were generally statistically significantly different from the respective control group and which may have been related to treatment, were noted primarily during week 3. These included decreased haemoglobin, erythrocyte volume fraction and erythrocyte counts and an elevated clotting time in females at the highest dose, and decreased blood glucose concentrations in males at the highest

dose. The results of urine analysis were not remarkable, although there were some low level increases in ketones, bilirubin and occult blood in males at the highest dose at the end of the recovery period. The only remarkable organ weight change was a slight increase in the adrenal : body weight ratio of males at the highest dose (0.03580) relative to the control group (0.0272) at the end of week 3. No gross necropsy findings were considered to be related to treatment.

There were some inconsistencies observed in the data on cholinesterase activity, which sometimes made interpretation difficult, but it appeared that by the end of the exposure period (day 18 for females at the highest dose and day 21 for all the other groups), the following changes in blood cholinesterase activity were related to treatment: statistically significant inhibition of erythrocyte cholinesterase activity of 28% and 33% in females at the intermediate and highest doses; reduced erythrocyte cholinesterase activity of 22% in males at the highest dose with statistically significant reductions of 33% and 24% seen at the two previous time-points, respectively (days 13 and 8); statistically significant decreases in plasma cholinesterase activity of 30% and 61% in females at the intermediate and highest doses, respectively, and of 12% and 21%, respectively, in males at the intermediate and highest doses. Blood cholinesterase activity values were not statistically significant at the end of the recovery period. On day 21, brain cholinesterase activity was statistically significantly inhibited in females at the highest dose (based on data from three animals) by about 45% and in males by about 15% decreases that were considered to be associated with treatment (although the decrease in males was not considered to be toxicologically relevant). At the end of the recovery phase, brain enzyme activity values were not significantly different from those of controls, but statistically significant inhibition of 29% was observed in males at the highest dose, possibly indicating a lack of recovery. However, this interpretation of the data was questionable because statistically significant inhibition of 35% was also noted in brain cholinesterase activity at 0.0243 mg/m^3, but not at the next highest dose of 0.048 mg/m^3.

No other remarkable findings in other parameters, except as already noted, were reported for the recovery period. If plasma cholinesterase inhibition is not considered to be an adverse effect of treatment and toxicologically significant brain (not erythrocyte) cholinesterase inhibition and clinical signs of toxicity are considered to be relevant effects for terbufos, the NOAEL was 0.0458 (range, 0.0098–0.0763) mg/m^3 (reflecting mean daily analytical chamber concentrations over the 3-week period of exposure and the range of daily means) in males and females on the basis of a statistically significant decrease and increase, respectively in blood glucose concentration and the adrenal to body weight ratio at the next highest dose in males, and mortality, clinical signs of toxicity, decreases in body weight and food consumption, and haematological changes in females at the next highest dose (Whitney, 1980). A statement of compliance with QA, but not for GLP, was provided. The protocol was not done to satisfy a particular guideline but was generally satisfactory for the intended purpose of the study.

2.3 Long-term studies of toxicity and carcinogenicity

Mice

In a combined long-term study of toxicity and carcinogenicity, groups of 65 male and 65 female CD-1 mice were given technical-grade terbufos (AC 92,100; purity, 89.6%; prepared in a 1 : 1 solution of corn oil and methylene chloride) at a concentration (adjusted for purity) of 0 (vehicle), 3, 6, or 12 mg/kg equivalent to 0 (vehicle only), 0.45, 0.9 and 1.8 mg/kg bw per day for males and females for 18 months. Ten animals of each sex per group were scheduled for interim termination at 12 months (week 53) and the remaining 55 animals of each sex per group for termination at 18 months (week 80). The rationale for dose selection was not provided. Parameters assessed included observations for general health and mortality, clinical signs of toxicity, measurement of food consumption and body-weight changes, haematological determinations, organ weight measurements and macro-and microscopic pathology examinations. Cholinesterase activities were not assessed in this study.

Mortality was greater at the highest dose in both sexes relative to at the other doses at both interim and final termination. At week 53, mortality in the control group, and at the lowest, intermediate and highest dose was 3.6%, 0%, 1.8% and 12.7% for males, and 7.2%, 1.8%, 7.3% and 12.7% for females, respectively. At week 80, mortality in these same groups was 12.7%, 9%, 5.5% and 27.2% for males and 27.2%, 14.5%, 21.8% and 34.5% for females, respectively. A relationship to treatment for the decreased survival at the highest dose could not be dismissed (although the study report did not come to this conclusion). There were no clinical findings in the study that were

obviously related to treatment. Body weight was statistically significantly decreased in both sexes relative to respective control groups at most weekly measurement time-points throughout the study. At week 54 and study termination, statistically significant reductions of about 8% were noted in males and of 10% and 11%, respectively, in females. At the intermediate dose, during the first 4–5 weeks of treatment, but not thereafter, statistically significant decreases in body weight of up to about 5% in males and up to about 8% in females were observed. These changes may have been related to treatment as they were not clearly associated with decreases in food consumption that might have indicated a palatability problem. Group mean body-weight gains over the entire study were reduced at the highest dose by 10% in males and 20% in females relative to respective control groups (statistical significance was not assessed) while group mean body-weight gains at the intermediate and lowest dose in both sexes exceeded those observed in animals in the control group. Statistically significant decreases in food consumption associated with treatment occurred at various times throughout the study at the highest dose in both sexes, with females somewhat more affected than males. Food consumption was not clearly affected by treatment at in the intermediate and lowest doses. There were no remarkable findings in the haematological, organ weight, or gross pathology assessments for any group treated with terbufos. With regard to non-neoplasic findings noted microscopically, slight increases in total occurrences of fatty metamorphosis in the liver were observed in test material-treated groups of males and females. For males in the control group and at the lowest, intermediate and highest doses, respectively, the incidence was 13%, 13%, 25% and 28% and for females in these same groups, the incidence was 30%, 38%, 34% and 48%, respectively. In the absence of other associated findings (e.g. organ weights or other histopathological lesions), the increased instances were considered to be of a spontaneous nature and not related to treatment (there were no historical control data available for comparison). Other microscopic findings in the study had no obvious relationship with treatment. The NOAEL for systemic toxicity was 3 mg/kg, equivalent to 0.45 mg/kg bw per day in males and females, on the basis of statistically significant decreases in body weights in both sexes during the first 4–5 weeks of the study that were not clearly associated with decreased food consumption at the next highest dose. There was no evidence of carcinogenicity (Silverman et al., 1986). Statements of compliance with QA and GLP were provided. The protocol was consistent with US EPA Subdivision F Guidelines (November 1982 and revised, 1984).

Rats

In a combined long-term study of toxicity and carcinogenicity, groups of male and female Long Evans rats were given diets containing terbufos (AC 92,100; purity not specified) at a nominal concentration of 0.25, 1.00 or initially 2.00 mg/kg (nominally to 0.0125, 0.05, and 0.1 mg/kg bw per day) for 2 years. For both sexes, the highest dose was raised to 4 mg/kg (nominally 0.2 mg/kg bw per day) at the beginning of week 6 (day 35), raised again to 8 mg/kg (nominally 0.4 mg/kg bw per day) at the beginning of week 12 (day 77), and lowered again for females only to 4 mg/kg (nominally 0.2 mg/kg bw per day) during week 16 (around day 105). Two concurrent control groups of males and females were included in the study. Diets containing terbufos were prepared by adding a premix nominally containing 100 mg/kg of feed (0.01%) of active ingredient to lab chow to achieve the desired nominal concentrations. Diets were apparently not analysed for test material content, homogeneity or stability (no supporting data or information were provided in the study report), and intake of test material was estimated based on nominal dose and food consumption data. Animals in the control group were given lab chow only. The study was initiated with 60 animals of each sex per group. A subset of this group (five animals of each sex in the control group and 10 animals of each sex in each group treated with terbufos) was terminated at 3 months. The remaining 55 animals of each sex per group in the control group and 50 animals of each sex per group in each group treated with terbufos continued into the long-term portion of the study, which terminated at 24 months. During both parts of the study, all animals were monitored for mortality, clinical signs of toxicity, body-weight changes and food consumption. Also, during the 3- and 24-month portions of the study, urine analysis, and haematological and limited clinical chemistry examinations (serum glutamic-pyruvic transaminase, alkaline phosphatase, fasting glucose and blood urea nitrogen concentrations) were performed on three control animals of each sex per group and six animals of each sex in groups treated with terbufos. At study termination, a gross examination was performed on five control animals of each sex per group and on 10 animals of each sex in groups treated with terbufos at 3 months, on all survivors at 24 months and on all animals terminated in a moribund condition or found dead.

At 3 and 24 months, selected organ weights were measured (heart, kidney, liver and thyroid) in five control animals of each sex per group and on 10 animals of each sex in each group treated with terbufos and a histopathological examination was conducted on five control animals of each sex per group and on 10 animals of each sex treated with terbufos at the highest dose. Lung, liver, kidneys and heart were evaluated microscopically in a similar number

of animals at the lowest and intermediate doses at 3 and 24 months. Tissues from other animals in the 24-month study were stored. Subsequent to the release of the original study report, tissues from all rats that were not previously processed were examined microscopically and the results of the 24 month exposure study were re-evaluated on this basis. Ophthalmoscopic examinations were performed only at 24-months. In three animals of each sex per control group and six animals of each sex in each group treated with terbufos, plasma and erythrocyte cholinesterase activities were determined for both sexes at 3, 6, 12 and 18 months, and brain cholinesterase activity was determined at 3 and 24 months. Inhibition of cholinesterase activity was assessed relative to values for the appropriate concurrent control groups.

There did not appear to be any deaths in the first 3 months of the study. At the intermediate dose, one animal, which was mis-sexed as a male, was placed with other females of that group, resulting in 59 males and 61 females. When the animals terminated at 3 months were not included in the calculations, mortality compared with that in the combined concurrent control groups was statistical significantly increased at the highest dose over the first 12 months of the study in males (28% in treated compared with 6.4% in the combined controls) and in females (28% compared with 0% in combined controls) and was statistically significantly increased over the 24 months at the intermediate and highest doses in males (57.1% and 62%, respectively, compared with 38.2% in combined controls) and in females at the highest dose (60% compared with 32.7%, respectively, in combined controls). Although a relationship of mortality rate and treatment could not be dismissed, the pathology report indicated illness existed among the test animals such as endemic bronchopneumonia (associated with bacterial infection) and pulmonary disease (said to be associated with the inhalation of food particles) and suggested that these conditions could have compromised animal well-being to a certain extent in some animals and/or contributed to the demise of others.

Neither individual nor summary data were provided in the study report for clinical findings or clinical signs of toxicity. According to the discussion in the study report, signs consistent with inhibition of cholinesterase activity (muscle tremors, excessive salivation, hyperactivity, hyperpnoea and tachycardia) were first noted in females at the highest dose during administration of the diet containing terbufos at 8 mg/kg (weeks 12–15). After the dose was lowered, the signs reportedly decreased in incidence in females at the highest dose and were not observed from months 18 until the end of the study. Some females at the intermediate dose reportedly exhibited some of the clinical signs (not specified) during months 5 and 6. Muscle tremors were reported in eight males at the highest dose during study months 22–24. Starting at around the time when females at the highest dose were placed on the die containing terbufos at 8 mg/kg, exophthalmos was noted in this group. Eventually, the condition manifested itself in all other groups of females including the controls and was said to persist until about month 15. The etiology of this condition was not clear. Ophthalmoscopic examination at the end of the study revealed an increase in corneal scarring and cataracts in males and females, but particularly in females, at the highest dose. Statistically significant decreases in body weight and food consumption compared with respective control values were observed in males and females at the highest dose throughout much or most of the 2-year study. At 24 months, there was no obvious effect of treatment on haematological, clinical chemistry or urine parameters examined. The significance, at 3 months, of small magnitude perturbations in concentrations of glucose and blood urea nitrogen in females at the highest dose was difficult to judge due to the changing doses. Small magnitude perturbations at the highest dose in relative or absolute weights at 3 months (kidney, heart, liver) and at 24 months (liver, kidney, and heart) may have been related to decreases in terminal body weights noted in this group.

Despite some variability in the magnitude and consistency of response among the various time-points measured, patterns of cholinesterase inhibition were noted for which an association with treatment could not be dismissed. Erythrocyte cholinesterase activity was statistically significantly inhibited at months 3, 6, 12, 18 and 24 at the highest dose in males (42–70%) and in females (35–80%). At the intermediate dose, statistically significant inhibition of erythrocyte cholinesterase activity was observed in males at months 6, 18 and 24 (32–40%) and in females at months 3 and 24 (43–46%). Brain cholinesterase activity was inhibited in males only at the highest dose at both 3 and 24 months (62–63%) and in females at the highest dose at 3 months (25%) and 24 months (58%) and marginally at the intermediate dose, 10% at 3 months (not statistically significant) and statistically significantly by 12% at 24 months. Inhibition of brain cholinesterase activity in females at the intermediate dose was not considered to be toxicologically relevant. Plasma cholinesterase was statistically significantly inhibited in females at the highest dose at months 3, 6, 18 and 24 by 54 to 70% and marginally in males (statistically significant inhibition of about 40% only at months 12 and 18). Plasma cholinesterase data showed a remarkable degree of variability with time and dose.

Because an insufficient number of animals had originally been evaluated for pathology, a re-evaluation of the 24-month exposure period was conducted. Apparently, most of the tissues and masses from animals not previously processed for microscopic examination were available for examination. The total number of rats whose tissues were re-evaluated histopathologically out of the original numbers started on test (60) were for (males/females): control group I, 54/55; control group II, 53/55; at the lowest dose, 50/50; at the intermediate dose, 44/50; and at the highest dose, 47/49. Animals terminated after 3 months were not included.

A new gross examination could not be re-conducted, but the previous report was said to have been used, as far as was possible, to make correlations with regard to gross and microscopic examinations.

With regard to the microscopic examination, the re-evaluation report for the 24-month treatment period discussed a number of non-neoplastic findings in both males and females. Inflammatory lesions in the lung were associated with two conditions. One was the endemic bronchial pneumonia (thought to be related to bacterial infection) found in increased incidence in the group at the highest dose. There was also a higher incidence at the highest dose of a second type of pneumonia (granulomatous) attributed to the inhalation of food particles containing plant fibres which were said to act as foreign bodies but for which treatment with test material may have been a contributing or pre-disposing factor. It was suggested that an increased incidence of oesophageal distension in animals at the highest dose may have been related to an effect of treatment on muscle contractility, but the pathology report suggested possible relationship of this finding to the bacterial infection and sequelae of the bronchopneumonia. A higher incidence at the highest dose of gastric mucosal ulceration and/or erosion was also of uncertain etiology, although a relationship to treatment could not be dismissed.

The report concluded that there was no evidence that the test material had an effect on tumorigenesis.

The study was inadequate to assess chronic toxicity owing mainly to outstanding questions involving the etiology and/or relationship to treatment and/or dose of certain non-neoplastic findings (including ocular, lung and stomach lesions), and also uncertainty associated with the variability in some of the cholinesterase measurements for which a relationship to treatment could not be dismissed, and lack of sufficient documentation of clinical signs of toxicity. Therefore, a NOAEL for chronic (systemic) toxicity was not identified.

Despite some variability and inconsistencies, there were apparent response patterns noted in the data on cholinesterase activity for which an association with treatment could not be dismissed. If inhibition of plasma cholinesterase activity is not considered to be an adverse effect and toxicologically significant inhibition of brain (but not erythrocyte) cholinesterase activity is considered to be a relevant effect for terbufos, the NOAEL for cholinesterase inhibition was 1.00 mg/kg in males and females (nominally 0.05 mg/kg bw per day) on the basis of statistically significantly decreased cholinesterase at the next highest dose.

With regard to the carcinogenicity phase of the study, information presented in the pathology re-evaluation report for the 24-month period of exposure was considered to be adequate to support the conclusion that there was no evidence of a carcinogenic response in the study, provided that the nominal intake of test material intake could be justified (Rapp, 1974). No statements of compliance with QA or GLP were provided.

2.4 Genotoxicity

The results of assays for genotoxicity with terbufos are summarized in Table 3.

Table 3. Results of studies of genotoxicity with terbufos

End-point	Test object	Concentration/dose	Purity (%)	Results	Reference
In vitro					
Reverse mutation	*S. typhimurium* TA98, TA100, TA1535, TA1537,	50–5000 µg/plate, 1000 µg/disc in DMSO, ±S9[h]	89.6	Negative	Allen (1985)[a,b]

	TA1538; *E. coli* WP2 *uvrA*$^{-}$				
Point mutation	Chinese hamster ovary cells (CHO-K_1-BH_4), *Hprt* locus	10–100 µg/ml & in DMSO, ±S9[c,i]	87.8	Negative[d]	Allen & Johnson, (1983)[a,b]
Chromosomal aberration	Chinese hamster ovary cells	2.5–100 nl/ml in DMSO, ±S9[e,i]	87.8[f] (1983)[a,b]	Negative	Thilager (1983)
Unscheduled DNA synthesis	Primary rat (male, Fischer 344) hepatocytes	0.33–33.33 µg/well in DMSO[g,i]	87.8[f]	Negative	Godek (1983)[b,n]
Mitotic gene conversion	*S. cerevisiae* strain D4 (*ade* and *trp* loci)	Apparently 0.33–33 µg/tube in DMSO, ±S9	Technical and commercial grades (purities not specified; no analytical information)	Technical-grade: positive at the *ade* locus (±S9); Commercial-grade: weakly positive at the *ade* locus (-S9)[o]	Gentile et al. (1982)
In vivo					
Dominant lethal mutation (10 mating cycles)	Crl : CD(SD)BR rats (10 male rats per group)	0, 0.1, 0.2, or 0.4 mg/kg bw per day[h,j,k] in corn oil by gavage daily for 5 days at the start of the first mating cycle[l]	89.6	Inconclusive[l]	MacKenzie (1986)[a,b]
Chromosomal aberration	Sprague-Dawley rats (20 males, 20 females per group), bone-marrow cells	Single intraperitoneal doses of 0, 0.2,0.6, 1.5 (females only)[m] or 1.8 mg/kg bw in corn oil[i]	89.6	Negative	Putnam (1986)[a,b]

DMSO, dimethyl sulfoxide

[a] Consistent with US EPA Subdivision F guidelines (1984,revised)

[b] Statements of compliance with GLP and QA were provided

[c] Cytotoxicity observed at 75 and 100 µg/ml in main study and at higher concentrations in the dose-finding study

[d] Slightly higher mutation frequencies (+S9) observed relative to the concurrent solvent control at 25 and 50 µg/ml were generally in the range of values for historical solvent controls and were attributed to unusually low mutation frequencies in concurrent controls . A repeat assay (+S9) gave negative results at concentrations of up to and including 50 µg/ml

[e] Cytotoxicity was observed at 100 nl/ml in main study and at higher concentrations in dose-finding study

[f] Purity information obtained from the sponsor

[g] Cytotoxicity observed at higher concentrations (100 µg/well and above)

[h] Dose calculations corrected for % active ingredient

[i] No correction of dose for % active ingredient

[j] No clinical signs of toxicity or effects on body weight were reported at the highest dose, but this dose was approximately one-tenth of the reported LD_{50}

[k] After treatment, each male was paired with two non-treated virgin females, 5 days per week for 10 weeks. Females were evaluated for number of implants, viable and nonviable fetuses and number of corpora lutea about 15 days after the mating period mid-point. Fertility index and implantation efficiency were calculated. The positive control used, triethylenemelamine, was administered intraperitoneally to 10 males for 5 days at a dose of 0.05 mg/5 ml saline/kg bw before the first mating cycle

[l] At mating 9, the number of viable implants at 0.4 mg/kg bw per day was reduced slightly compared with the concurrent vehicle control group (statistically significant) and with respect to the positive control group (e.g. 12 compared with 14 and 13, respectively). At mating 7, implant

efficiencies at the lowest, intermediate and highest doses (95%, 93%, and 89%, respectively) were lower (with a difference that was statistically significant at the lowest and highest doses) than that of the concurrent vehicle control group (98%) and the positive control group (97%). A slightly lower implantation efficiency (not statistically significant) relative to all other groups continued at the highest dose through the remaining three mating cycles numbers 8–10; the study report concluded that the NOAEL in males treated for 5 days was 0.2 mg/kg bw per day

[m] Evaluations of structural chromosomal aberration were conducted in five animals per group (including replacement animals) at 12, 24, and 36 h after dosing. Clinical signs of toxicity and mortality were observed after an intraperitoneal dose of 1.8 mg/kg bw in males and females and 1.5 mg/kg bw in females. Excessive mortality was observed in females at both of these doses, indicating an increased sensitivity of females to the test material. Protocol was consistent with US EPA Subdivision F guidelines (1984, revised), but only hepatocytes from males were used; hepatocytes from females should also have been assayed

[o] Results given only for the dose said to give highest recombinogenic activity. Assay protocol appeared to be generally acceptable, but no rationale for dose selection was presented. Commercial-grade terbufos gave negative results in *Zea mays* in a field plot assay for plant mutation in situ (technical grade not tested)

Most of the tests for mutagenicity with terbufos in vitro and in vivo gave negative results. However, in one acceptably performed study of dominant lethal mutation in vivo, results were inconclusive. In a paper from the open scientific literature (Gentile et al., 1982), positive results were reported in an acceptably performed assay for mitotic gene conversion in yeast cells (*ade* locus) with technical-grade terbufos in the presence or absence of a metabolic activation system, and also with a commercial grade of terbufos, without metabolic activation. However, insufficient purity and analytical data were provided in the paper for the materials tested.

Although the results of an assay for unscheduled DNA repair synthesis in cells in primary culture were negative, only male Fischer 344 rat hepatocytes were used; an optimal protocol would also have included assessment of hepatocytes from female rats.

2.5 Reproductive toxicity

(a) Multigeneration study

Rats

In a two-generation study of reproductive toxicity, four groups of 25 male and 25 female Sprague-Dawley (COBS CD) rats, F_0 generation or F_1 generation parental animals, were given diets containing technical-grade terbufos (AC 92,100; purity, 89.6%; dissolved in a 1 : 1 solution of methylene chloride and corn oil) from the pre-mating period until termination of the adults. Terbufos was administered at a dietary concentration of 0 (vehicle only), 0.5, 1.0, or 2.5 mg/kg (equal to group mean intakes for the F_0 generation during the pre-mating period of 0, 0.035, 0.07, and 0.18 mg/kg bw per day in males, and 0, 0.04, 0.085, and 0.22 mg/kg bw per day in females, and for the F_1 generation during the pre-mating period of 0, 0.0372, 0.0742, and 0.1943 mg/kg bw per day in males, and 0, 0.04, 0.089, and 0.24 mg/kg bw per day in females. An additional group of F_0 generation animals was given terbufos at a dietary concentration of 5.0 mg/kg (equal to group mean intakes of 0.42 mg/kg bw per day in males and females); this group was, however, terminated early in week 6 of the pre-mating period because of toxicity in the females.

According to a standard protocol, the F_0 and F_1 generations were mated twice to produce F_{1a} and F_{1b}, and F_{2a} and F_{2b} litters, respectively. Dosing commenced in the F_0 generation at 63 days before mating when parental animals were aged about 7 weeks and continued for about 191 days in males and 210 days in females (during the lactation period for the F_{1b} litters). Initiation of dosing for F_1 generation parental animals (from F_{1b} litters) commenced after weaning of the F_{1b} litters and continued for about 205 days in males and 220 days in females. F_1 and F_2 litters were reduced to eight pups (equal numbers of each sex, if possible) on day 4 of lactation. F_{1a}, F_{2a} and F_{2b} litters were sacrificed at or after weaning on day 21 of lactation. Pups were examined externally for abnormalities and gross malformations. One F_{1b} and F_{2b} pup of each sex per litter, as well as any dead or stillborn pups, were necropsied and any abnormal tissues found were preserved.

Assessments performed for parental animals included observations for general condition, mortality and clinical signs of toxicity, measurement of body weight and food consumption, ophthalmoscopic examinations, evaluation of reproductive performance, including mating and fertility and pregnancy rate, duration of gestation and data on

parturition, litter size and survival until day 21 of lactation, and macroscopic examination. Organ weight measurements were not made. At termination of each generation, histopathological evaluation was made of the following tissues: testes, epididymides, prostate, seminal vesicles, ovaries, uterus, vagina, pituitary and any gross lesions; this was performed only for animals receiving the highest dietary concentration (2.5 mg/kg) and for control F_0 and F_{1b} adults that had been selected for mating. Offspring parameters examined included assessment of general appearance, viability, litter sex ratio, and body weight (on days 1, 4, 7, 14, and 21 of lactation). Inhibition of plasma, erythrocyte and brain cholinesterase activities was calculated relative to the values for the appropriate concurrent control group for adult F_0 males and females (week 27) and F_{1b} adults, and for males and females at termination. Cholinesterase activity was not assessed in adult animals receiving terbufos at a dietary concentration of 5.0 mg/kg, nor in pups at any dose.

Six out of 25 females at the highest dietary concentration tested (5.0 mg/kg) died from treatment-related causes after 22–34 days. Clinical signs of toxicity, including tremors, a generally poor condition, emaciation, and unkempt appearance, were also noted in females in this group. There were no deaths among males at 5 mg/kg and few, if any, clinical signs were observed in males in this group during the same period (two males had excess salivation at pre-mating week 4). During certain periods before termination of all animals at 5.0 mg/kg at pre-mating week 6, statistically significant decreases in body weight were reported in both sexes, as were decreases in food consumption.

In the study of four groups, with 2.5 mg/kg as the highest dose, parental mortality was very low and of comparable incidence in groups treated with terbufos and respective control groups in the F_0 and F_1 generation. With the possible exception of soft stools in F_0 females at the highest dose during week 28 (12 occurrences compared with 2, 3 and 6 occurrences in the control group, and at the lowest and intermediate doses, respectively), there were no clinical findings that could definitively be associated with treatment with terbufos in either the F_0 or F_1 parents. Animals with symptoms considered in the study report to be consistent with sialodacryoadenitis viral infection (including dry eyes in females at the lowest and intermediate doses) were noticed during weeks 26 to 28 (towards the end of the F_0 generation). The study report indicated that the outcome of the study was considered not to have been affected by the presence of the virus at this stage.

There was no apparent effect of treatment on male or female body weight of parents in either the F_0 or F_1 generations, except in lactating females at 2.5 mg/kg. Over the duration of the lactation period (days 0–20) for F_{1a}, F_{1b}, and F_{2b} litters, females at the highest dose exhibited statistically significant body-weight loss relative to that in the respective control groups. Food consumption did not appear to be adversely affected in parental animals of either generation. The results of ophthalmoscopic examinations were not remarkable.

In F_0 adults, statistically significant inhibition of plasma cholinesterase activity was observed in males at the highest dose (46%) and females at the intermediate and highest doses (61% and 94%, respectively). Statistically significant reductions were noted in erythrocyte cholinesterase activity in males at the highest dose (11%) and in females at the intermediate and highest doses (7% and 15%, respectively). Brain cholinesterase activity was statistically significantly inhibited in males at 1.0 and 2.5 mg/kg (8% and 29%, respectively) and in females at 0.5, 1.0, and 2.5 mg/kg (7%, 22%, and 66%, respectively).

In F_1 adults, statistically significant inhibition of plasma cholinesterase activity was observed in males (by 20% and 53%, respectively), and in females (by 50% and 87%, respectively) at the intermediate and highest doses. Erythrocyte cholinesterase activity was statistically significantly reduced only at the highest dose in males (by 15%) and in females (by 13%). Brain cholinesterase activity was statistically significantly inhibited at the intermediate and highest doses in males (by 8% and 34%, respectively) and in females (by 21% and 59%, respectively).

Decreases in brain cholinesterase activity of 7–8% in F_0 and F_1 adults at the lowest and intermediate doses, although possibly treatment-related, were not considered to be toxicologically significant.

At 2.5 mg/kg, a treatment-related reduction in male fertility and the number of pregnant females was observed for the production of F_{1b} litters and F_{2b} litters compared with values for these parameters in the respective control

groups. In the control group, and at the lowest, intermediate and highest dose, pregnancy rates were 92%, 88%, 96% and 80% in the first generation (F_{1b}) and 86%, 92%, 82% and 63% in the second generation (F_{2b}), respectively. The corresponding male fertility index (number impregnating per number mated) for F_{1b} litters was 91%, 87%, 96% and 79% and for F_{2b} litters, 94%, 95%, 94% and 61%, respectively.

At the highest dose, there were some, generally slight, changes in several F_{1b} and F_{2a} and F_{2b} neonatal parameters (such as in mean numbers of pups, live pups or dead pups per litter and total numbers of live or dead pups per litter). When these parameters were looked at overall, they were suggestive of possible subtle treatment related decreases in pup viability, number and/or survival at 2.5 mg/kg. However, they lacked statistical significance or persistence; the only statistically significant change, a decrease in the number of live offspring in F_{1a} litters relative to that in the control group (9.8 compared with 12.8) before reduction of litter sizes on lactation day 4, was not found at later time-points).

A more concrete case for an effect of treatment with terbufos on offspring concerned pup body weights. On days 14 and 21 of lactation, decreases (about 15–17%) in the mean weight of viable pups relative to those of pups in the respective control group, were observed in F_{1a}, F_{1b}, F_{2a} (smaller decreases of 7–9%) and F_{2b} litters and were considered to be related to treatment. Decreases were statistically significant in F_{1a} litters, F_{1b} litters (a decrease of 11% was also noted on day 7), and F_{2b} litters (a decrease of 16 % was also noted on day 7).

Other parental reproductive or neonatal parameters examined were not obviously affected by treatment with terbufos. There were no obvious treatment-related findings upon gross examination of pups or adults, or upon histopathological evaluation of the adult tissues and organs selected for analysis.

The NOAEL for reproductive effects was 1.0 mg/kg for males and females (equal to 0.07–0.074 mg/kg bw per day in males and 0.0854–0.089 mg/kg bw per day in females) on the basis of decreases in male fertility and pregnancy rate, respectively. The NOAEL for parental toxicity was 2.5 mg/kg in males (equal to 0.18–0.19 mg/kg bw per day) on the basis of statistically significant decreases in body weight and decreases in food consumption at the next highest dose and 1.0 mg/kg in females (equal to 0.085–0.089 mg/kg bw per day) on the basis of statistically significant body-weight loss during lactation and an apparent increase in soft stools at the next highest dose. The NOAEL for offspring toxicity was 1.0 mg/kg (equal to 0.07–0.074 mg/kg bw per day in males and 0.085–0.089 mg/kg bw per day in females) on the basis of statistically significant decreases in the mean body weight of viable pups on days 14 and 21 of lactation in F_0 and F_1 litters.

If plasma cholinesterase inhibition is not considered to be an adverse effect and toxicologically significant brain (not erythrocyte) cholinesterase inhibition is considered to be a relevant effect for terbufos, the NOAEL for cholinesterase inhibition was 1.0 mg/kg (equal to 0.07–0.074 mg/kg bw per day) in parental males and 0.5 mg/kg (equal to 0.04– 0.044 mg/kg bw per day) in parental females on the basis of statistically significant decreases in brain cholinesterase activity in the F_0 and F_1 generations at the next highest doses (Schroeder, 1989). Statements of compliance with QA and GLP were provided. The protocol was consistent with US EPA Subdivision F guidelines (1982 and 1984, revised).

(b) Developmental toxicity

Rats

In a study of developmental toxicity, groups of Charles River albino rats were given technical-grade terbufos (AC 92,100; purity not specified) at a dose of 0 (vehicle only; 20 rats), 0.075 (20 rats) or 0.150 (21 rats) mg/kg bw per day daily on days 6–15 of gestation, inclusive, by gavage in corn oil. The study was terminated on day 20 of gestation. The basis for dose selection was not discussed. Adult animals were observed for mortality, unusual reactions, clinical signs of toxicity, and body-weight changes. Other parameters assessed were group mean numbers of corpora lutea, implantation sites, resorption sites, and viable fetuses, as well as number of fetuses, group mean fetal body weights, sex ratio and the incidence of females with one or more resorption sites. Fetuses were examined externally for effects of treatment and, where possible, approximately equal numbers of each sex were evaluated for

skeletal and internal developmental abnormalities using the Hurley method of staining with alizarin, or the Wilson and Warkany technique, respectively. Cholinesterase activity was not measured.

There were no deaths or unusual reactions in adult animals. No treatment-related effects were noted in any parameter. This study had many deficiencies, including the following: the purity of the test material and the concentration of the test material in dosing solutions could not be confirmed; it was not clear if randomization techniques were used in assigning animals to treatment groups; no data for individual adult animals or fetuses were provided in the study report; the number of dead fetuses was not indicated; maternal or fetal data were generally reported only as group means; it was not clear how fetuses were selected for examinations for developmental abnormality; fetal abnormalities were not assessed on a litter basis; the number of fetuses examined for abnormalities did not match the number of fetuses reported; complete necropsies of adult animals were not conducted. Also, animals were shipped to the laboratory on day 1 of gestation and were allowed no acclimation period. NOAELs for maternal and developmental toxicity could not be identified owing to the many deficiencies in study design and data reporting (Haley, 1972). No statements of compliance with GLP or QA were provided, the protocol was not consistent with EPA or OECD guidelines and was unacceptable by current standards; the study was conducted in 1972 (before the establishment of guidelines for GLP and EPA guidelines).

In a preliminary study of developmental toxicity, groups of five female Charles River COBS® CD® rats were given technical-grade terbufos (AC 92,100; purity, 87.8%) at a dose (adjusted for purity) of 0 (vehicle only), 0.4, 0.8, 1.4, 3, or 6 mg/kg bw per day once daily by gavage in corn oil during days 6–15 of gestation, inclusive. These doses were actually twice the amounts intended owing to an unintentional protocol error such that the volume administered was 10 ml/kg instead of 5 ml/kg. Owing to excessive toxicity and mortality in all groups treated with terbufos, the study was terminated prematurely (before day 20 of gestation) and two additional groups of five females were subsequently given the test material at a dose of 0.05 or 0.2 mg/kg bw per day administered in a volume of 5 ml/kg. This second phase was terminated as planned on day 20 of gestation. For all groups in both phases, planned evaluations in adult females included observations for general condition and clinical signs of toxicity, mortality and moribundity, body-weight changes, abortions, number of corpora lutea, and terminal necropsy. Litter and fetal assessments included number of viable and dead fetuses and fetal position in the uterus, number of implantation sites, early and late resorptions, early implant loss in uteri with no gross evidence of implantation, and postimplantation loss. No examinations were conducted of fetuses for external, visceral or skeletal abnormalities, body weight or sex ratio in either phase and cholinesterase activity was not measured.

During the first phase of the study, all animals died or were sacrificed in a moribund condition as a result of treatment at doses of ≥0.4 mg/kg bw per day. The cause of death was cardiorespiratory arrest or cerebral haemorrhage. Findings at necropsy included hepatic congestion, renal and pulmonic hyperaemia, gastric congestion and loss of epithelium, intestinal congestion and diarrhoea, and in some animals at doses of 1.4 mg/kg per day and above, haemorrhagic intestines. Deaths at 0.4 mg/kg bw per day occurred between days 10 and 16 of gestation. At higher doses, deaths or early terminations occurred on days 7–9 of gestation. Severe body-weight losses were observed in all groups treated with the test material. Clinical signs of toxicity, described as primarily yellow urogenital matting and dried red matter around the eyes and nares were noted primarily in animals given doses of 0.4 and 0.8 mg/kg per day, as survival was longest in these groups. Pregnancy rates in animals in the vehicle control group and groups treated with terbufos ranged from 80% to 100%. No abortions were reported. Uterine assessments were incomplete owing to mortality but, relative to groups receiving the highest dose, an increase in early litter resorptions was noted at necropsy at doses of 0.4 mg/kg bw per day and, to a lesser extent, at 0.8 mg/kg bw per day; this effect may have been related to maternal toxicity and day of gestation. At 0.4 mg/kg bw per day and 0.8 mg/kg bw per day, respectively, early resorptions were observed in five out of five gravid females (maternal deaths on days 10–15 of gestation in this group) and two out of four gravid females (maternal deaths on days 8 or 9 of gestation in this group), while none were reported in pregnant animals at doses of ≥1.4 mg/kg bw per day (maternal deaths on day 7 of gestation in these groups).

In the second phase of the study, the results provided indicated that doses could have, at least sometimes, been 10–15% below nominal levels. No mortality or clinical signs of toxicity were reported at 0.2 or 0.05 mg/kg bw per day. Groups treated with terbufos gained slightly less weight than did the vehicle control group during dosing (days 6–16 of gestation) and overall gestation (days 0–20 of gestation), but a statistical analysis of the data was not performed. Pregnancy rates were 100%, 80% and 100% in the vehicle control group and groups receiving the lowest and intermediate doses, respectively. A delivery early in the study on day 10 of gestation by one female at the lowest

dose was attributed to an error in the detection of mating, such that the day of parturition was assumed to be 22 on the basis of pup size and development. The results of necropsy of this and other animals in the second phase were not remarkable. There were no other premature deliveries nor were there any abortions. Litter incidence (relative to that in the vehicle control group) of viable fetuses, implantation sites and corpora lutea were similar for the three dams available for evaluation at the lowest dose and the five available at the highest dose. There were no dead fetuses or late resorptions in any group. A slightly higher postimplantation rate of 1.7 per litter at 0.05 mg/kg bw per day, associated with early resorptions, was noted compared with a value of 1.0 per litter in the control group, but the value for the group receiving the lowest dose was based on an evaluation of three animals only and the rate at 0.2 mg/kg bw per day (0.6 per litter) was lower than that for the control group. On the basis of the parameters assessed in phases one and two, the NOAEL for maternal toxicity was 0.2 mg/kg bw per day, as doses administered above this were excessively toxic. A NOAEL for developmental toxicity could not be identified owing to the small number of animals evaluated and the limited study design and assessments made (Rodwell, 1984). Statements of compliance with QA and GLP were provided. Protocol deficiencies were noted, but the study was not performed to meet a specific guideline, being a preliminary study.

In a study of developmental toxicity, groups of 25 Charles River COBS CD rats were given technical-grade terbufos (AC 92,100; purity, 87.8%) at a dose of 0 (vehicle only), 0.05, 0.10, or 0.20 mg/kg bw per day by gavage in corn oil once daily on days 6–15 of gestation, inclusive. Doses were adjusted for test material purity. The study was terminated on day 20 of gestation. Selection of doses for this main study was based on the results of a preliminary study of developmental toxicity in the same strain of rats; treatment-related mortality and clinical signs of toxicity had been reported after administration of test material at daily doses of ≥0.4 mg/kg bw per day by gavage on days 6–15 of gestation, inclusive (Rodwell, 1984). In the main study, evaluations in adult females included observations for general condition and clinical signs of toxicity, mortality and moribundity, body-weight changes, abortions, number of corpora lutea, and terminal necropsy. Litter and fetal assessments included number of viable and dead fetuses, number of implantation sites, early and late resorptions, early implant loss in uteri with no gross evidence of implantation, postimplantation loss, and fetal weight, sex, sex ratio, and uterine location. All fetuses were examined for external abnormalities. Approximately one-half of the fetuses from each litter were examined for soft tissue findings using the Wilson sectioning method, while the remainder were examined for skeletal defects using a modification of the Dawson alizarin red S staining technique and low power magnification. Cholinesterase activity was not measured.

In adult animals, no mortalities or treatment-related clinical signs of toxicity were observed during the study. Slightly lower body-weight gain was noted in groups treated with terbufos at the intermediate and highest doses, relative to the control group, during dosing (days 12–16 of gestation and during days 6–16 of gestation), and after dosing (days 16–20 of gestation). During days 12–16 of gestation, body-weight gains at the intermediate and highest doses were 7% and 10% less than that of the control group, respectively, while during days 6–16 of gestation, body-weight gains in these groups were 7% less than that of the control group. After dosing, body-weight gains at the intermediate and highest doses were 5% less than that of the control group. In the study report, the relatively lower body-weight gains at the intermediate and highest doses were considered to be related to administration of the test material. These decreases in body weight were not considered to be toxicologically significant, being of similar magnitude at the intermediate and highest doses, relatively small, and not statistically significant. In addition, there was no indication of an increase in body-weight gain after cessation of dosing.

Pregnancy rates were similar among all groups, ranging from 96% to 100%, and there were no abortions or premature deliveries.

There were no statistically significant differences in the number of corpora lutea or implantation sites in groups treated with terbufos relative to values for these parameters in the concurrent control group. Late resorptions, although not statistically significantly increased, were observed only at 0.2 mg/kg bw per day. All late resorptions (eight) and the only dead fetus reported in the study were found in the litter of one dam at the highest dose, along with one early resorption and one fetus with no remarkable findings out of a total of 11 conceptuses. At necropsy of the dam (which survived the study), abnormalities described collectively in the study report as "severe pathology" but not treatment-related, were found on gross examination of the liver (described as pale and soft with accentuation of lobular markings), spleen (described as congested enlarged and indurated) and kidney (described as pale, bilateral). Follow-up histopathology was not performed. Weight gain (50 g) in this animal during dosing (days 6–16 of gestation) was not dramatically different from the mean for the control group (57 g) or the mean for the group

receiving the highest dose (53 g); however, it was the only animal at the highest dose to lose weight (-1 g) after cessation of dosing (mean weight gain at the highest dose after cessation of dosing was 60 g). The relationship between litter/fetal findings and the pathology observed in this animal is not clear.

Early resorptions at the intermediate and highest doses of 1.2 and 1.0 per litter, respectively, were slightly elevated (not statistically significantly) relative to values for the concurrent control group (0.8 per litter) and the group receiving the lowest dose (0.5 per litter).

Fetal body weights were comparable in all groups. The number of viable fetuses at the intermediate and highest doses (13.7 and 13.6 per litter, respectively) were slightly lower, although not statistically significantly so, than those in the concurrent control group and the group receiving the lowest dose (15.0 and 14.8 per litter, respectively), and were within the range of data for historical controls for the laboratory and rodent strain used (mean, 13.9 per litter; range, 11.9–15.4). These decreases in the number of viable fetuses were attributed to slight increases (not statistically significant) in postimplantation loss at the intermediate and highest doses (1.2 and 1.3 per litter, respectively) compared with those in the respective concurrent control group and group receiving the lowest dose (0.8 and 0.5 per litter, respectively). At the intermediate dose, the increased postimplantation loss (1.2 per litter) was just inside the range for historical controls (mean, 0.6 per litter; range, 0.1–1.2) and was associated with losses due to early resorption (no early resorption data for historical controls were provided). At the highest dose, postimplantation loss (1.3 per litter) was just outside the range for historical controls and was associated with both early and late resorptions and the one fetal death. If litter/fetal data from the dam with the reported macroscopic pathology at necropsy were not considered, the changes in litter or fetal parameters at the highest dose relative to those in the control group appeared to be eliminated.

There was a statistically significant difference in the group mean fetal sex ratio in all groups treated with terbufos relative to the value for concurrent controls. This was attributed in the study report to a skewed sex ratio in the concurrent control group (male : female, about 1 : 1.4) relative to that based on the historical control data provided (calculated as male : female 1 : 1.006), although group means and ranges for historical controls were not provided in the study report. External, visceral and skeletal fetal examinations did not reveal any morphological findings associated with treatment.

The study authors did not consider any of the findings on fetal viability, resorptions, or postimplantation loss at the intermediate and highest doses to be biologically meaningful, because none of the changes were statistically significant relative to the control group. Available data for historical controls generally supported this contention at the intermediate dose and, in the case of fetal viability, at the highest dose. In addition, there was no apparent effect on postimplantation loss, fetal viability or resorptions (early or late) at the highest dose, if litter/fetal data from the female with reported pathology at the highest dose are eliminated from consideration. Although no clear maternal or developmental toxicity was considered to have occurred in this main study, mortality was seen at a dose of 0.4 mg/kg bw per day in a preliminary study (Rodwell, 1984), at just twice the highest dose used in the main study (0.2 mg/kg bw per day), thus providing support for dose selection in the main study.

The NOAEL for maternal toxicity and developmental effects was 0.2 mg/kg bw per day, the highest dose tested (Rodwell, 1985). Statements of compliance with GLP and QA were provided and the protocol was consistent with US EPA Subdivision F (1982) guidelines.

Rabbits

In a study of developmental toxicity, groups of 17 New Zealand white (Hra:(NZW)SPF) rabbits were given technical-grade terbufos (AC 92,100; purity, 89.6%) at a dose (adjusted for purity) of 0 (vehicle only), 0.05, 0.10, 0.25 or 0.50 mg/kg bw per day by gavage in corn oil, once daily during days 7–19 of gestation. The study was terminated on day 29 of gestation. Data on dose selection were not provided. Upon analysis, the range of received concentrations of test material was 87–98% of target concentrations. Evaluations in adult females included observations for general condition and clinical signs of toxicity, mortality and moribundity, body-weight changes, food consumption, abortions, premature delivery, uterine weights, number of corpora lutea, and terminal necropsy. Litter and fetal assessments included number of viable and dead fetuses, number of implantation sites, early and late resorptions, postimplantation loss, and fetal weight, sex, sex ratio and uterine location. All fetuses carried to study

termination were examined for external, visceral and skeletal abnormalities using standard techniques (including the use of alizarin red S staining). Cholinesterase activity was not measured.

There were no adult deaths and no premature deliveries. Two animals aborted, one in the group receiving the highest dose on day 21 of gestation (9 conceptuses) and the other in the group receiving a dose of 0.10 mg/kg bw per day (6 conceptuses) on day 22 of gestation. Litters were not available for analysis, presumably due to cannibalization. The study report did not attribute this litter loss to treatment, as there were no signs of toxicity or apparent gross lesions at necropsy. There was some decrease in body weight and food consumption in both animals in the days immediately before abortion. A possible relationship of abortion at the highest dose to treatment could not be discounted, as other maternal treatment-related findings occurred at that dose.

The only clinical related to treatment was a statistically significant increase in the incidence of does with soft or liquid faeces at a dose of 0.5 mg/kg bw per day. This effect, which did not occur in the vehicle control group, was observed in four rabbits on 1 or 2 days and was associated with some decrease in body weight and food consumption, but no gross lesions at necropsy. Three rabbits (one not pregnant) had occurrences during the latter part of or just outside of the dosing period during days 16–20 of gestation. Another pregnant animal had one occurrence on day 29 of gestation. Instances of soft or liquid faeces associated with transient decreases in body weight and food consumption at other doses were not considered to be related to treatment, as there was no statistically significant increase and the incidence was low (e.g. found once, on day 18, in one animal at 0.05 mg/kg per day and twice, on days 24 and 25, in one animal at 0.10 mg/kg bw per day).

Maternal body-weight gain at the two higher doses (+ 0.16 and +0.16 kg, respectively) was decreased relative to that in the vehicle control group and at the two lower doses (+0.26, +0.23 and +0.23 kg, respectively) during the time interval encompassing the dosing period (days 7–20 of gestation). Between days 16 and 20 of gestation, there was some loss of body weight in animals at the highest dose, which was not seen in other groups. Although none of the body-weight findings at the two higher doses was statistically significant, in the study report they were considered to be related to treatment. Slight decreases in food consumption relative to that of controls were only noted at the two higher doses and then only during the period after cessation of dosing (days 20–29 of gestation); the study report suggested that this could have been related to a delayed effect of treatment. The present reviewer considered that his interpretation was possible but questionable. At necropsy, two animals at the highest dose (not those with soft or liquid faeces) were found to have reddened areas in the fundic area of the stomach that were considered to be treatment-related in the study report. The results of necropsy in other animals were not remarkable.

The incidence of pregnancy in the control group and at 0.05, 0.10, 0.25 and 0.50 mg/kg bw per day was 94%, 71%, 82%, 76% and 88%, respectively. There was no apparent effect of treatment with the test material on the number of corpora lutea, implantations, or live and dead fetuses (all fetuses were reported to be alive at study termination), or on litter size, sex ratio, or uterine weights (not including data from the two females that aborted). Although incidences of early or late resorptions were comparable between groups, at the highest dose there was an increase in the incidence of does with any resorption site. For the control group and at 0.05, 0.10, 0.25 and 0.50 mg/kg bw per day, the total number (and percentage) of does with resorptions of any type was 3 (18.8%), 5 (41.7%), 5 (38.5%), 4 (30.8%) and 10 (71.4%), respectively. The increase at the highest dose was not statistically significant and was not considered to be treatment-related in the study report. However, the incidence was higher than that in the concurrent control and was outside of the range for historical controls (data provided on a percentage basis, e.g. mean, 129 (39.2%) with a range of 0 (0%) to 10 (64.3%) based on data from 329 control groups from 21 studies conducted at the test facility between 1986 and 1988; current study conducted in 1988), such that a relationship to treatment could not be dismissed. In addition, a slight decrease in the group mean fetal body-weight at the highest dose (42.48 g) relative to that of the concurrent control (44.8 g) was considered by the study authors to be an effect of treatment, although the difference was not statistically significant. Similar values were obtained when male and female fetal body weights at the highest dose were separately compared with those for the appropriate concurrent control group. No fetal external, visceral or skeletal findings were considered to be related to treatment with the test material.

With regard to maternal toxicity, although the study report suggested that there was a treatment-related effect at the intermediate dose, the evidence cited to support this contention (a relatively small body-weight decrease during the dosing period, which was not dose-dependent and was not statistically significant in a species in which body-weight variability is common; and possibly a slight decrease in food consumption after dosing) is of questionable toxicological significance in the absence of other findings. The NOAEL for maternal toxicity was 0.25 mg/kg bw

per day on the basis of an increased number of does with soft or liquid faeces, maternal body-weight loss during days 16–20 of gestation, occurrence of reddened areas in the fundic region of the stomach at necropsy, and one abortion at the next highest dose. The NOAEL was 0.25 mg/kg bw per day on the basis of decreased fetal body weights and an increase in the incidence of does with any resorption sites at the next highest dose (Hoberman, 1988a, 1988b). Statements of compliance with GLP and QA were provided and the protocol was consistent with EPA Subdivision F Guidelines (1982 or 1984, revised).

2.6 Special studies

(a) Neurotoxicity

(i) Acute delayed neurotoxicity

Technical-grade terbufos (AC 92,100; purity, 96.7%) was tested for acute delayed neurotoxicity potential in sex-link hens (aged approximately 1 year). Confirmation of the content of test material in the dosing solution was not provided in the study report. In a preliminary study to aid in dose selection for the main study, the acute oral LD_{50} in this strain of hen for technical-grade terbufos in corn oil was estimated by probit analysis to be 40 mg/kg bw (95% confidence interval (CI), 31.8–48.2 mg/kg bw). The test material was administered by gavage as single doses at 10 (one animal), 20 (one animal), 28.3 (three animals), 40 (four animals), 56.6 (four animals) or 80 mg/kg bw (two animals). The incidence of mortality in these groups respectively, was 0/1, 0/1, 1/3, 1/4, 4/4 and 2/2. There was some variability in the time to death. Mortality was observed at 22 h after dosing at 28.3 mg/kg bw, at 4.5 h after dosing at 40 mg/kg bw, at 1.5–22 h after dosing at 56.6 mg/kg bw and within 2.5 h of dosing at 80 mg/kg bw. The only clinical findings reported were observed in some animals at 28.3 and 40 mg/kg bw and consisted of wobbly gait or unsteady gait and stance at 20–24 h after dosing, and resolved by 70–72 h after treatment.

The main study consisted of two phases. In phase one, 10 hens received the test material in corn oil as a single dose of 40 mg/kg bw by gavage. Included in this group of 10 were the three surviving animals that had received a dose of 40 mg/kg bw in the preliminary study for determination of acute LD_{50}. Other groups of hens received corn oil alone (four animals) or tri-ortho-cresyl phosphate (TOCP) at 500 mg/kg bw in corn oil as the positive control (10 animals). There was no pretreatment with atropine. Hens were observed for 21 days after dosing for mortality, signs of neurotoxicity and locomotor abnormalities.

All animals surviving study phase one were entered into study phase two. This inadvertently included any animals exhibiting effects consistent with delayed neurotoxicity (e.g. animals treated with TOCP) that were originally intended for sacrifice on day 22 after dosing in phase one. In phase two (which appeared to commence about 26 days after phase one dosing), the seven terbufos-treated hens surviving phase one received a second single dose of the test material by gavage in corn oil, while the surviving three or seven hens in the vehicle and positive control groups, respectively, were similarly dosed a second time with either corn oil only or 500 mg/kg bw of TOCP. Animals treated with TOCP were pretreated with atropine. After a 21-day observation period, animals treated with TOCP (seven) and vehicle control group animals (three) were terminated on day 22 after dosing. Surviving hens (six) treated with TOCP were terminated three days after dosing in phase two (i.e. 29 days after dosing in phase one). The original study report indicated that the spinal cords of only the three animals in the vehicle control group and the six animals treated with TOCP (animals considered to display signs of (delayed) neurotoxicity) were subjected to histopathological examination. Procedures used in preparation for the examination were only described briefly in the study report. It was stated that spinal cords were fixed in situ (perfusion was not indicated) in buffered formalin for 2 days before sectioning. Although brain, spinal cord (cervical, thoracic and lumbosacral sections), and sciatic nerve tissue were taken, only lumbosacral spinal cord sections (stained with haematoxylin and eosin) were examined microscopically. The tibial nerve was not examined. The hens were not subjected to a period of forced motor activity and there was no evaluation of cholinesterase or neuropathy target esterase activities in either study phase one or two.

During phase one of the main study, one out of four control animals died on day 19 and exhibited no signs or symptoms before death. Three out of 10 animals treated with terbufos and not pretreated with atropine died; two on day 0 and one on day 12 after dosing. No clinical symptoms were reported for the animals that died on day 0. The animal that died on day 12 exhibited two instances of wobbly gait and/or wobbly stance of low severity on days 1

and 7 after dosing. On day 1 after dosing, three additional animals treated with terbufos displayed single occurrences of low severity wobbly gait and/or wobbly stance. The deaths and clinical observations in the animals receiving terbufos were attributed to cholinergic toxicity. None of the animals treated with terbufos or the vehicle control animals dying during phase one were examined histopathologically. Based on the deaths in the terbufos animals in the preliminary study and in phase one of the main study, the acute oral 50 in hens was re-estimated to be 43.5 mg/kg bw.

Animals treated with TOCP in phase one exhibited no signs of acute toxicity but did have symptoms of locomotor impairment (wobbly gait and/or wobbly stance) that started on day 11 after dosing in all animals and grew progressively worse, such that by day 21 after dosing most animals fell while walking, could only stand or walk in a squatted position or could not walk or stand at all. Three of the most severely affected hens died 26 days after dosing in phase one and were not examined histopathologically.

After dosing in phase two, signs of acute toxicity were observed in all seven animals treated with terbufos (and pretreated with atropine). The findings, which were attributed to cholinergic toxicity, lasted up to 72 h and were generally of low severity (wobbly gait and/or wobbly stance) except in the case of one animal that could not walk or stand one day after dosing only. There were no observational findings in these animals after day 3 after dosing. According to the study report, these animals were not examined histopathologically after termination on day 22 after dosing in phase two because they showed no indications of delayed neuropathy.

Of the seven hens that inadvertently received a second dose of TOCP, three (which already had severe symptoms of locomotor impairment subsequent to phase one) died on day 2 or 3. The remaining hens in this group were terminated on day 3 after dosing in phase two and the spinal cord of six of the seven hens was subjected to histopathological examination. Minimal (two hens), slight (two hens), and moderate (two hens) degrees of demyelination of spinal cord fibre tracts (white matter) were found. One animal had swollen axis cylinders (white matter) and another had gliosis, both effects being of low severity. There were no observational or histopathological findings in the three control animals carried over into phase two.

Subsequently, the spinal cords of the seven animals treated with terbufos in phase two were examined histopathologically; it is not clear how the tissues of these animals were prepared for examination. Two animals had a perivascular lymphocytic cell infiltrate of low severity in the spinal cord, which was not considered to be of any concern. No demyelination or other adverse changes were apparent in the tissues examined. There was no evidence to suggest that terbufos caused delayed neuropathy in hens under the conditions of the study (Smith, 1972, 1973). No statements of compliance with QA or GLP were provided. The protocol was generally consistent with EPA Subdivision F Guidelines (1982 and 1984, revised).

(b) Acute neurotoxicity

In an study of acute oral neurotoxicity, groups of 20 male and 20 female Sprague-Dawley-derived (outbred) Crl:CD®(SD)IGS BR VAF/Plus® rats (fasted before dosing) were given technical-grade terbufos (AC 92,100; purity, 89.7%) as a single dose (not adjusted for purity) of 0 (vehicle only) 0.15, 0.30, or 0.90 mg/kg bw by gavage in corn oil. The study was terminated on day 15, following an observation period after dosing.

The selection of doses administered in the definitive study was based on the results of a pilot study to determine time of peak effect in males and females of the same strain of rat. In this study, groups of five males and five females were given single doses of the test material at (0 (vehicle only), 0.025, 0.05, 0.15, 0.40, 1.2 or 1.6 mg/kg bw in males and 0 (vehicle only), 0.025, 0.05, 0.15, 0.30, 0.90 and 1.2 mg/kg bw in females by gavage in corn oil. Five additional females were treated with terbufos at the highest dose, in case replacements were needed. All animals were monitored for clinical signs of toxicity, and at about 6 h after dosing (designated as the time of peak effect), plasma, erythrocyte and brain cholinesterase activities were measured in five animals of each sex per group. In the pilot study, one female died from causes attributed to treatment with the test material within 5 h of treatment with a dose of 1.2 mg/kg bw. Clinical signs of toxicity consistent with inhibition of cholinesterase activity were noted at the two higher doses in males and females about 6 h after dosing; females were said to have been more severely affected. At 1.6 mg/kg bw in males, excessive salivation, irregular gait and tremors were observed in one male and irregular gait was observed in two males at 1.2 mg/kg bw group. Seven females at 1.2 mg/kg bw group exhibited irregular gait and tremors. Other findings in this group were excessive salivation and lacrimation, moist rales and

ventral surface and anogenital yellow staining in two animals, and decreased activity in one animal. At a dose of 0.9 mg/kg bw, the only clinical finding observed was ano-genital staining in one female. No clinical signs were observed in other groups. Miosis was not reported for any animals in the study. Plasma cholinesterase activity was statistically significantly inhibited in males by 45%, 90% and 88% at doses of 0.40, 1.2, and 1.6 mg/kg bw per day, respectively, and in females by 17%, 87% and 96% at 0.3, 0.9, and 1.2 mg/kg bw, respectively. Erythrocyte cholinesterase activity was inhibited at the two higher doses in both sexes: in males, by 92–94% (statistically significant); and in females, by 88–93% (not statistically significant but considered to be treatment-related). Brain cholinesterease activity was statistically significantly inhibited by 57% and 52% at 1.2 and 1.6 mg/kg bw, respectively, in males. A statistically significant decrease in brain cholinesterase activity of 67% was observed in females at 1.2 mg/kg bw, and a decrease of 41% at 0.9 mg/kg bw was considered to be treatment-related, if not statistically significant. In the pilot study, no treatment-related effects were reported in either sex at doses of <0.40 mg/kg bw in males and <0.30 mg/kg bw in females.

Before the start of the definitive study, survival was assessed in an additional group of 10 females given the test material at a dose of 0.90 mg/kg bw by gavage. The only data reported for this study were the findings for animals manifesting clinical signs of toxicity during daily observations. Signs of toxicity (first observed on the day of treatment and apparently disappearing by day 5 after dosing) were reported for six of the 10 animals and included bilateral tremors in fore and hind paws, slight to moderate anogenital staining, decreased faecal volume, fasciculation, extreme lacrimation and excessive salivation. No miosis was observed.

In the definitive study, all animals were assessed for physical condition, mortality, clinical signs of toxicity, body-weight changes and food consumption. Neurobehavioural evaluations (motor activity and functional observational battery) were conducted on 10 animals of each sex per dose pre-test, at approximately 6 h after dosing (time of peak effect) and on days 8 and 15 (study termination day). Blood was collected for plasma and erythrocyte cholinesterase activity measurements from 10 animals of each sex per dose at about 6 h after dosing, and on day 8, and in five animals of each sex per dose on day 15. Brain cholinesterase activity in one-half brain homogenates was also assessed in the same number of animals at about 6 h after dosing and on day 15. Cholinesterase inhibition was determined relative to the appropriate concurrent control group value. All animals received macroscopic examinations and selected tissues from the central and peripheral nervous system were evaluated histopathologically in five perfused animals of each sex per group.

In the definitive study, the only death attributed to treatment occurred in females at the highest dose, 5–6 h after dosing. There were no accompanying clinical findings reported for this animal, which was replaced by another female for the remainder of the study. Clinical signs of toxicity, some commencing on the day of treatment, were noted in the daily physical examinations in one surviving female at the highest dose; these included moderate to extreme ano-genital staining, lethargy, decreased faecal volume and food consumption, and oral/buccal staining. No clinical findings were reported after day 5 during daily physical observations in this female. One male at the intermediate dose exhibited a red ocular exudate on day 9, but this may have been related to orbital sinus bleeding for cholinesterase measurements. Slight statistically significant decreases in body weights observed in females at the highest dose may have been largely related to decreases noted in the one animal exhibiting clinical signs of toxicity. There were no significant changes noted in male body weights or food consumption in either sex, relative to values for the respective control groups.

There were no statistically significant differences noted in the mean value for motor activity for the group, relative to values for the respective control group, on days 1, 8 and 15. The study report mentioned that the one female at the highest dose that had clinical signs of toxicity during the daily physical examinations also exhibited decreased motor activity on days 1 and 8, but not on day 15.

Treatment-related abnormalities in the functional observational battery, attributed to cholinergic toxicity, were apparent in males and females at the intermediate and highest dose and only during the peak time assessment at day 1. Miosis, present in three males at the intermediate dose, six males at the highest dose and one female at the intermediate dose, was the only finding at these doses. A wider spectrum of findings was present in females at the highest dose. In addition to miosis in all 10 rats, females in this group exhibited tremors (seven animals), and muscle fasciculations (four animals) and, to a lesser extent, ataxic gait and slightly impaired locomotion, tip-toe gait, moderate lacrimation and soiled coat. In one animal, very low arousal state, flattened posture (in home cage), no approach response, severe lacrimation and slight salivation, no open field movement, soiled coat, and markedly

decreased forelimb and hindlimb grip strength were reported. At the next two time-points (days 8 and 15), no abnormal findings were evident in any group.

On day 1, around the time of peak effect, plasma cholinesterase activity was statistically significantly decreased in males by 31% and 69%, and in females by 20% and 90% at the intermediate and highest doses, respectively. There was no statistically significant inhibition at any dose in either sex on days 8 or 15. Erythrocyte cholinesterase activity was statistically significantly inhibited on day 1 only in males (67%) and females (90%) at the highest dose. Values continued to be decreased in females at the highest dose by about 45% on days 8 and 15. Brain cholinesterase activity was statistically significantly inhibited on day 1 only at the highest dose by 21% in males, and by 51% in females. Statistically significant depression of brain cholinesterase activity (of 13%) continued to be observed on day 15 in females at the highest dose.

Macroscopic and microscopic examinations did not reveal any findings related to treatment. Trauma related to retro-orbital sinus bleeding was considered to account for the minimal to slight focal degeneration of optic nerve fibres accompanied by minimal to slight gliosis observed in two females at the highest dose and minimal degeneration of a single sciatic nerve fibre in only one male at the highest dose was considered to be incidental in nature. It should be noted that miosis was observed during the functional observational battery in both sexes at 0.3 mg/kg bw, with no significant decrease in concurrently measured brain and erythrocyte cholinesterase activity. Only marginal (but statistically significant) concurrently measured plasma cholinesterase activity was observed at this dose in both sexes. If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, the NOAEL was 0.15 mg/kg bw in males and females on the basis of miosis in the functional observational battery in both sexes at the next highest dose (Mandella, 1998). Statements of compliance with QA and GLP were provided and the study protocol was consistent with EPA Subdivision F Guidelines (1984, revised and March 1991).

(c) Neurotoxicity after repeated doses

In a study of neurotoxicity, groups of 20 male and 20 female Sprague-Dawley derived (outbred) Crl:CD®(SD)IGS BR VAF/Plus® rats were given diets containing technical-grade terbufos (AC 92,100; purity, 89.7%; dissolved in acetone and mixed with a GRIT-O'Cobs® carrier) at a dose (adjusted for purity) of 0 (diet mixed with acetone and carrier), 0.5, 0.8, or 5.0 mg/kg in males (equal to 0, 0.036, 0.059 and 0.369 mg/kg bw per day) and of 0 (diet mixed with acetone and carrier), 0.5, 0.8 or 3.0 mg/kg in females (equal to 0, 0.042, 0.064, and 0.251 mg/kg bw per day) daily for approximately 13 weeks. Animals evaluated for potential neurobehavioural changes were treated for at least 13 weeks and animals in which cholinesterase activities were measured were treated for at least 85 days. Selection of doses was based on a 22-day preliminary study of feeding in the same strain of rat (Mandella, 1999), in which treatment-related findings were noted at doses of ≥5 mg/kg (0.55 mg/kg bw per day) in males and ≥3 mg/kg (0.33 mg/kg bw per day) in females. In the 13-week study, all animals were assessed for physical condition, mortality, clinical signs of toxicity, body-weight changes, and food consumption and received ophthalmoscopic examinations. Neurobehavioural evaluations (motor activity and functional observational battery) were conducted on 10 animals of each sex per group, before treatment and at weeks 4, 8, and 13. In animals designated for cholinesterase activity determinations (9–10 animals of each sex per group), blood samples for assessment of plasma, erythrocyte and brain (one-half homogenate) cholinesterase activities were obtained at weeks 4, 8, and 13. In animals designated for neurobehavioural examinations, blood and brain samples for measurement of cholinesterase activities were obtained from five animals of each sex per group during weeks 13 or 14. Cholinesterase inhibition was determined relative to values for the appropriate concurrent control group. At study termination (week 13 or 14), macroscopic examinations were performed on all animals and selected tissues from the central and peripheral nervous system were evaluated histopathologically in five animals of each sex per group.

One male at the lowest dose died in week 5 due to accidental causes. Otherwise, there were no deaths in the study. There were no findings during physical examinations that were considered to be treatment-related and miosis was not observed in any animal. The results of ophthalmoscopic examinations were not remarkable. Over the 13-week period, males at the highest dose gained only about 90% of the weight gained by animals in the control group; a possible effect of treatment could not be dismissed. Weight gains in males at the lowest and intermediate doses during the same period were slightly higher than those of animals in the control group. Females at the highest dose gained about 13% more weight over the duration of the study than did animals in the control group, but this was not considered to be an adverse effect. There were no changes in food consumption in either sex that could definitively be ascribed to treatment and no obvious effect of treatment with the test material on motor activity or on functional

observational battery parameters. In the macroscopic and microscopic examinations, there were no findings that were attributable to treatment.

At the highest dose, plasma cholinesterase activity in animals designated for cholinesterase measurements or neurobehavioural evaluations was statistically significantly inhibited at all time-points by 70–74% in males and by 91–92% in females. In the same groups, erythrocyte cholinesterase activity was virtually completely inhibited at all time-points (decreases of 97–100% in males and 100% in females). At the intermediate dose, erythrocyte cholinesterase activity was statistically significantly inhibited in males in the group of animals designated for cholinesterase measurement at week 8 and 13 by 48% and 37%, respectively, and by 35% at week 13 in the group designated for neurobehavioural evaluations. In both groups of females at the intermediate dose, inhibition of 33% (statistically significant) and 27% (not statistically significant) was observed at week 13. At study termination, brain cholinesterase activity was decreased only at the highest dose in animals designated for cholinesterase measurement and neurobehavioural evaluation, by 58% and 55%, respectively, in males and by 71% and 68%, respectively in females.

Table 4. Acute toxicity of metabolites and degradation products of terbufos in female mice

Metabolite	Strain	Route	Vehicle	LD_{50} (mg/kg bw)	Purity (%)	Reference
Terbufoxon sulfoxide[a]	CF1 albino	Oral	Corn oil	1.1	Not stated	American Cyanamid Company A72-35 (1972d)
Terbufos sulfoxide[b]	CF1 albino	Oral	Corn oil	3.4	Not stated	American Cyanamid Company A72-37 (1972b)
Terbufoxon sulfone[c]	CF1 albino	Oral	Corn oil	3.4	Not stated	American Cyanamid Company A72-38 (1972e)
Terbufos sulfone[d]	CF1 albino	Oral	Corn oil	14[i]	Not stated	American Cyanamid Company A72-34 (1972c)
Terbufoxon[e]	CF1 albino	Oral	Corn oil	2.2	Not stated	American Cyanamid Company A72-36 (1972f)
CL 202,135[f]	CF1 albino	Oral	Corn oil	3670[g]	Not stated	American Cyanamid Company A73-21 (1973a)
CL 202,474[h]	CF1 albino	Oral	Corn oil	>2500[j]	Not stated	American Cyanamid Company A73-122 (1973b)

Although reports for these studies were not detailed and statements of compliance with GLP or QA were not provided, protocols appeared to be generally consistent with EPA Subdivision F Guidelines (1982 or 1984, revised)

[a] Phosphorothioic acid, *S*-(*t*-butylsulfinyl) methyl *O*,*O*-diethyl ester (CL 94,365)

[b] Phosphorodithioic acid, *S*-(*t*-butylsulfinyl) methyl *O*,*O*-diethyl ester (CL 94,301)

[c] Phosphorothioic acid, *S*-(*t*-butylsulfonyl) methyl *O*,*O*-diethyl ester (CL 94,302)

[d] Phosphorodithioic acid, *S*-(*t*-butylsulfonyl) methyl *O*,*O*-diethyl ester (CL 94,320)

[e] Phosphorothioic acid, *S*-(*t*-butylthio) methyl *O*,*O*-diethyl ester (CL 94,221)

[f] Methane, bis(*t*-butylsulfonyl) (CL 202,135)

[g] Report stated that acute oral LD_{50} was calculated assuming a mortality of 9 out of 10 animals at a dose of 10 000 mg/kg of feed

[h] Methane, (*t*-butylsulfinyl)(methylsulfinyl)

[i] Report stated that acute oral LD_{50} ws calculated assuming a mortality of five out of five animals at a dose of 50 mg/kg of feed

[j] Report stated that animals were not fasted

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect and statistically significant inhibition of erythrocyte cholinesterase activity of 33–43% is not considered to be a relevant effect for terbufos, the NOAEL was 0.8 mg/kg (equal to 0.059 mg/kg bw per day in males and 0.064 mg/kg bw per day in females) on the basis of statistically significant inhibition of brain and erythrocyte (almost completely inhibited) cholinesterase

activity at the next highest dose (Mandella, 1999). Statements of compliance with QA and GLP were provided. The protocol was consistent with EPA Subdivision F Guidelines (November, 1984, revised, and March 1991).

(d) Studies on metabolites

In a study of short-tem toxicity, groups of four male beagle dogs were given gelatin capsules containing technical-grade terbufos (AC 92,100; purity, 89.6%) or one of its metabolites, terbufos sulfoxide (CL 94,301; purity, 90.0%) and terbufos sulfone (CL 94,320; purity, 92.0%), in corn oil, administered orally once daily in the morning for at least 14 days. A similarly treated control group of six animals received gelatin capsules containing corn oil only. The animals used were described as having physical impairments but not of sufficient magnitude to jeopardize study integrity. Doses administered (adjusted for purity) were: terbufos, 2.5 or 250 µg/kg bw per day; terbufos sulfoxide, 5, 15, 625, or 250 µg/kg bw per day; or terbufos sulfone, 15, 62.5, 250, and 1000 µg/kg bw per day. A limited number of parameters were assessed, including mortality, morbidity and clinical signs of toxicity, measurement of body weight and food consumption, and a gross examination at the end of the study. Plasma and erythrocyte cholinesterase activity in fasted animals was assessed twice before treatment, and on days 4, 8, 11, and 15. Brain cholinesterase activity (in homogenates of cerebellum and cerebrum) was measured from tissues taken at study termination (day 15 or 16) and stored frozen until analysis. Inhibition of cholinesterase activity was determined relative to the value for the appropriate concurrent control group. Overall, the data on brain cholinesterase activity, especially those from the cerebellum, were considered to be unreliable owing to inconsistencies, variability in the data and poor dose–response relationships. Clinical chemistry, haematological, urine analysis, organ weight and histopathological evaluations were not conducted in this study.

There were no deaths in the control group. The only clinical observations reported were occurrence of soft faeces (four animals) and one occurrence of alopecia. There were no other adverse findings.

There were no deaths in the groups of animals treated with terbufos. Clinical findings attributed to treatment at the highest dose (250 µg/kg bw per day) were instances of emesis and lacrimation, and an increased incidence of soft or soft sanguineous-looking faeces (seven occurrences) compared with the control group; treatment-related decreases in body weight and food consumption were also noted in some animals. At the highest dose, plasma cholinesterase activity was statistically significantly inhibited by 57–76% at all time-points during the study, and erythrocyte cholinesterase activity was statistically significantly inhibited by 42–79% on days 8, 11 and 15, and cerebellar and cerebral cholinesterase activities were statistically significantly inhibited by 48% and 37%, respectively. At the lowest dose, statistically significant decreases in plasma cholinesterase activity were noted on days 11 and 15, but they were of low magnitude (23–25%) and not clearly related to treatment. There were no obvious effects of treatment on erythrocyte or cerebral cholinesterase activities at the lowest dose. Cerebellar cholinesterase activity at the lowest dose was statistically significantly inhibited by 42%. As a finding of significant brain cholinesterase inhibition at this dose was inconsistent with other studies of repeated dosing with terbufos, it was considered highly unlikely to be related to treatment. A finding of dark mesenteric lymph node(s) at gross necropsy in one animal in the group treated with the lowest dose of terbufos was not clearly related to treatment.

In the groups of animals treated with terbufos sulfoxide, there were no mortalities. At the highest dose (250 µg/kg bw per day), clinical findings ascribed to treatment included ataxia, salivation, languid behaviour, salivation, miosis, no faeces, emesis, and an increased incidence relative to control of soft faeces (11 occurrences). Decreases in body weight and food consumption attributed to treatment were noted in some animals at the highest dose.

At all time-points during the study, plasma and erythrocyte cholinesterase activities were statistically significantly inhibited by 60–71% and 30–93%, respectively, at the highest dose. In groups given terbufos sulfoxide at 62.5 and 15 µg/kg bw per day, there was no clear treatment-related effect on body weights, food consumption or clinical findings. Single occurrences of emesis or sanguineous-looking emesis were noted in each of these groups, as was one instance of no faeces at 15 µg/kg bw per day. Occurrences of soft stool in the control group, and at the lowest, lower intermediate, higher intermediate and highest dose were 4, 3, 13, 6, and 11, respectively. Increases relative to the control group at the two intermediate doses did not appear to be part of an obvious pattern that might be definitively atributed to treatment. Although plasma cholinesterase activity was statistically significantly inhibited at all time-points at both intermediate doses, erythrocyte enzyme activity was not statistically significantly inhibited at any time-point at either dose. Inhibition of brain cholinesterase activity was found at the two higher doses. Cerebral cholinesterase activity was statistically significantly inhibited only at the highest dose (250 µg/kg bw per

day) by 45%. At the higher intermediate and highest doses, cerebellar cholinesterase activity was statistically significantly inhibited by 52% and 31% (not statistically significant), respectively. At the lowest dose (5.0 mg/kg bw per day), there were no obvious effects of treatment on the parameters assessed. A statistically significant decrease in plasma cholinesterase activity that was noted only on day 15 was of low magnitude (19%). Findings at gross necropsy that were reported to be related to treatment were observed in one dog at the highest dose. They were described as a dark red area in the mucosa of the jejunum mucosa, associated with dark red mesenteric lymph node(s). This animal exhibited a number of clinical signs during the study and had decreases in plasma, erythrocyte cerebellar and cerebral cholinesterase activities. Dark mesenteric lymph node(s) were also reported in one other animal at the highest dose.

In groups of animals treated with terbufos sulfone, there were three treatment-related deaths preceded by clinical signs of toxicity. Two animals were found dead on day 9 and 14 and the third was terminated in a moribund condition on day 15. Clinical findings associated with treatment in this group included tremor, languid behaviour, prostration, ataxia, emesis, salivation, dyspnoea, cold-to-touch, squint eye, miosis, no faeces, an increase in soft faeces relative to the control group, prolapsed rectum, sanguineous-appearing material in cage. Also at this dose, decreases in body weight and food consumption attributed to treatment were noted in some animals. In groups given terbufos sulfone at 250, 62.5 or 15 µg/kg bw per day, there was no clear treatment-related effect on body weights, food consumption or clinical findings. Two occurrences of lacrimation and two occurrences of soft faeces were reported at 250 µg/kg bw per day, two instances of soft or sanguineous-looking faeces and one instance of emesis were found at 62.5 µg/kg bw per day and four occurrences of soft faeces were found at the lowest dose. Plasma cholinesterase activity was statistically significantly inhibited at all time-points: by 67–77% at the highest dose, by 39–56% at 250 µg/kg bw per day, and by 24–37% at 62.5 µg/kg bw per day. At the lowest dose (15 µg/kg bw per day), statistically significant inhibition of plasma cholinesterase activity (of only 20%) was seen only on day 8 but not on day 15 and thus was not clearly related to treatment. Statistically significant decreases in erythrocyte cholinesterase activity were observed only at the highest dose where inhibition was noted at all time-points ranging from 57% to 93%. Inhibition of brain cholinesterase activity was found at the two higher doses (statistically significantly only at the highest dose, by 62%). Cerebellar cholinesterase activity was inhibited by 23% (not statistically significant) at 250 µg/kg bw per day and by 46% (not statistically significant) at the highest dose.

At gross necropsy, findings related to treatment were observed in the group receiving the highest dose: dark, red or dark red areas, intussusceptions, and/or a prolapsed anus with associated redness in the mesenteric lymph nodes were observed in the gastrointestinal tract of the animals that died. Some other gross findings at this dose were ascribed to the poor condition of the animals.

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, the NOAEL for terbufos was 2.5 µg/kg bw per day in males on the basis of clinical findings and statistically significant inhibition of erythrocyte cholinesterase activity.

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, the NOAEL for terbufos sulfoxide was 15.0 µg/kg bw per day in males on the basis of statistically significant inhibition of brain cholinesterase (cerebellum) at the dose above, for which a relationship to treatment could not be dismissed.

If inhibition of plasma cholinesterase activity is not considered to be an adverse effect, the NOAEL for terbufos sulfone was 62.5 µg/kg bw per day on the basis of inhibition of brain cholinesterase (cerebellar) activity at the dose above, for which a relationship to treatment could not be dismissed (Bailey, 1988). Statements of compliance with QA and GLP were provided. This study was not conducted to fulfil a particular guideline.

3. Observations in humans

There have been a number of reports of occupational and non-occupational poisoning incidents associated with exposure to terbufos. With regard to possible effects from terbufos manufacturing facilities, no "reportable incidents" have been noted and no other information was available.

Comments

In rats, absorption of single doses of [^{14}C]terbufos was rapid and fairly complete. Most of the radiolabel was excreted within 24–48 h. Most (about 70–80%) of the administered dose was excreted in the urine. Terbufos was extensively metabolized and little radioactivity was found in the tissues. There were no significant sex-specific differences in the toxicokinetics of terbufos.

Sulfoxidation and desulfuration of terbufos is followed by hydrolysis of the thiolophosphorus bond (S–P), enzymatic *S*-methylation and then additional *S*-oxidation. On the basis of a 14-day study of repeated dosing, terbufos showed little potential for bioaccumulation.

By analogy with other phosphorodithioate compounds, it is likely that terbufos is metabolically activated to terbufos oxon and other oxons, which cause inhibition of acetylcholinesterase activity.

Terbufos is of very high acute toxicity when administered by oral, dermal, and inhalation routes. Acute oral LD_{50} values in rodents and dogs were similar, ranging from 1.4 to 9.2 mg/kg bw. Clinical signs observed were those typical of cholinergic toxicity.

The acute dermal LD_{50} for terbufos was about 1 mg/kg bw in rabbits; a single application of undiluted terbufos to the shaved skin (0.25–0.5 ml) or into the conjunctival sac (0.1 ml) killed all animals within 24 h. The acute LC_{50} for terbufos administered by inhalation ranged from 0.0012 to 0.0061 mg/l in rats.

In studies in rats and dogs, the critical effects of repeated doses of terbufos were inhibition of brain cholinesterase activity and associated clinical signs. NOAELs for inhibition of brain cholinesterase activity in these studies ranged from about 0.04 to 0.11 mg/kg bw per day, and LOAELs ranged from about 0.085 to 0.55 mg/kg bw per day. Inhibition of brain cholinesterase activity of 7–12%, in the absence of clinical signs, was not considered to be toxicologically relevant. NOAELs and LOAELs for inhibition of erythrocyte cholinesterasese activity were not substantially different from those for inhibition of brain cholinesterase activity.

In a 1-year study in dogs given terbufos in capsules, the NOAEL was 0.060 mg/kg bw per day on the basis of inhibition of brain acetylcholinesterase activity at 0.090 mg/kg bw per day. The NOAELs for inhibition of brain acetylcholinesterase activity in other short-term studies in dogs were consistent with that of the 1-year study.

In an 18-month study in mice fed with terbufos, there was no evidence of carcinogenicity at doses considered relevant for risk assessment. Cholinesterase activities were not measured. The NOAEL was 3 mg/kg (equivalent to 0.45 mg/kg bw per day) on the basis of significant decreases in body weights at the next highest dose of 6 mg/kg (equivalent to 0.9 mg/kg bw per day).

A 2-year study of toxicity and carcinogenicity in rats had limitations that included outstanding questions involving the etiology and/or relationship to treatment of certain non-neoplastic findings, confounding by non-treatment related illness in test animals and the lack of supporting data to adequately quantify dietary intake, stability, and homogeneity. However, on the basis of inhibition of brain cholinesterase activity in animals receiving the highest dose, this study was considered to be adequate for testing for carcinogenicity. No increase in tumour incidence was observed after a histopathological re-evaluation of tissues for the assessment of carcinogenic potential. The NOAEL was 1 mg/kg (equivalent to 0.05 mg/kg bw per day) on the basis of inhibition of brain acetylcholinesterase activity at 4 mg/kg (equivalent to 0.2 mg/kg bw per day).

This conclusion was supported by a subsequent 1-year study of toxicity in rats; no significant systemic or neoplastic effects were observed. The NOAEL was 1 mg/kg (equal to 0.055 mg/kg bw per day) on the basis of the absence of significant inhibition of brain acetylcholinesterase activity at all doses.

The Meeting concluded that terbufos was not carcinogenic in mice or rats.

The genotoxic potential of terbufos was assessed in an adequate range of in vitro and in vivo tests. On the basis of the overall weight of evidence from the studies of genotoxicity, the Meeting concluded that terbufos is unlikely to pose a genotoxic risk to humans.

In view of the lack of significant genotoxicity and the absence of carcinogenicity observed, the Meeting concluded that terbufos is unlikely to pose a carcinogenic risk to humans.

In a study of reproductive toxicity in rats, mortality and clinical signs of toxicity in females, some occurrences of excess salivation in males and decreases in body weight and food consumption in both sexes were observed at 5 mg/kg (equal to 0.42 mg/kg bw per day), a treatment that was terminated prematurely. At 2.5 mg/kg, an increase in soft stools and body-weight loss was noted in lactating females. Also observed were decreases in pregnancy rate, male fertility and significant decreases in the mean body weight of viable pups on days 14 and 21 of lactation in F_0 and F_1 litters. The NOAEL for effects on reproduction and offspring was 1.0 mg/kg (equal to 0.086 mg/kg bw per day). Inhibition of brain cholinesterase activity was observed in both sexes, with a NOAEL of 0.5 mg/kg (equal to 0.043 mg/kg bw per day).

In a study of developmental toxicity in rats, the NOAEL for maternal and developmental effects was 0.2 mg/kg bw per day, the highest dose tested. Mortality was seen at a dose of 0.4 mg/kg bw per day in a preliminary study.

In a study of developmental toxicity in rabbits, the NOAEL for maternal and developmental effects was 0.25 mg/kg bw per day on the basis of clinical and systemic findings in does, an increased number of does with resorption sites and decreased fetal body weights at the next highest dose of 0.50 mg/kg bw per day.

The potential of terbufos to induce delayed polyneuropathy in hens when given as a single dose by gavage was assessed. The activity of neuropathy target esterase was not measured in this study. No significant changes in spinal cord and peripheral nerves were apparent in the group treated with terbufos. The Meeting concluded that at doses relevant to dietary exposure in humans, there was no concern for the induction of delayed polyneuropathy by terbufos.

In a study of neurotoxicity in which terbufos was given to rats as a single dose by gavage, mortality, clinical signs of toxicity, including miosis, and inhibition of brain and erythrocyte cholinesterase activities were noted at the highest dose tested of 0.90 mg/kg bw. The only finding at the intermediate dose (0.3 mg/kg bw) was miosis, which was observed in the absence of inhibition of concurrently measured brain and erythrocyte cholinesterase activities. No neurohistopathological lesions were found at any dose. The NOAEL was 0.15 mg/kg bw on the basis of findings of miosis in both sexes at the next highest dose of 0.30 mg/kg bw.

A 13-week study of neurotoxicity was conducted in rats. Other than a slight decrease in body weight and inhibition of brain and erythrocyte cholinesterase activities at the highest dose of 3.0 mg/kg (equal to 0.25 mg/kg bw per day), no effects (including miosis) were observed. The NOAEL was 0.8 mg/kg (equal to 0.059 mg/kg bw per day) on the basis of inhibition of brain acetylcholinesterase activity at 0.25 mg/kg bw per day.

The acute oral toxicity of a number of metabolites of terbufos was evaluated in female mice. LD_{50}s were as follows: 1.1 mg/kg bw (terbufoxon sulfoxide), 3.4 mg/kg bw (terbufos sulfoxide), 3.4 mg/kg bw (terbufoxon sulfone), 14 mg/kg bw (terbufos sulfone), 2.2 mg/kg bw (terbufoxon), 3670 mg/kg bw (methane, bis (*tert*-butylsulfonyl) and >2500 mg/kg bw (methane, (*tert*-butylsulfinyl)(methylsulfinyl)).

In a comparative 14-day study in dogs, terbufos given in capsules was found to be more toxic than either terbufos sulfoxide or terbufos sulfone.

There have been a number of reports of occupational and non-occupational poisoning incidents associated with exposure to terbufos. No information was available regarding possible effects from terbufos manufacturing facilities.

The Meeting concluded that the existing database on terbufos was adequate to characterize the potential hazard to fetuses, infants and children.

Toxicological evaluation

The Meeting established an ADI of 0–0.0006 mg/kg bw based on an overall NOAEL of 0.06 mg/kg bw per day and a safety factor of 100 for inhibition of brain cholinesterase activity, in the 1-year study of toxicity, the 13-week study of neurotoxicity and the two-generation study of reproduction in rats, and the 1-year study in dogs.

The Meeting established an acute reference dose (RfD) of 0.002 mg/kg bw based on a NOAEL of 0.15 mg/kg bw per day for miosis in the study of neurotoxicity in rats given a single dose of terbufos, and a 100-fold safety factor. Since only in this study was miosis observed in the absence of inhibition of cholinesterase activity, it might be possible to refine the acute RfD after better characterization of this effect.

Levels relevant to risk assessment

Species	Study	Effect	NOAEL	LOAEL
Mouse	18-month study of toxicity and carcinogenicity[a]	Toxicity	3 mg/kg of feed, equivalent to 0.45 mg/kg bw per day	6 mg/kg of feed, equivalent to 0.90 mg/kg bw per day
		Carcinogenicity	12 mg/kg of feed, equivalent to 1.8 mg/kg bw per day[d]	—
Rat	2-year study of toxicity and carcinogenicity[a]	Carcinogenicity	4 mg/kg of feed, nominally equivalent to 0.2 mg/kg bw per day[d]	—
	1-year study of toxicity[a]	Toxicity	1 mg/kg of feed, equal to 0.055 mg/kg bw per day[d]	—
	13-week study of neurotoxicity[a]	Toxicity	0.8 mg/kg of feed, equal to 0.059 mg/kg bw per day	3.0 mg/kg of feed, equal to 0.25 mg/kg bw per day
	Single-dose study of neurotoxicity[b]	Toxicity	0.15 mg/kg bw per day	0.30 mg/kg bw per day
	Multigeneration study of reproductive toxicity[a]	Parental toxicity	0.5 mg/kg of feed, equal to 0.043 mg/kg bw per day	1.0 mg/kg of feed, equal to 0.086 mg/kg bw per day
		Offspring toxicity	1.0 mg/kg of feed, equal to 0.086 mg/kg bw per day	2.5 mg/kg of feed, equal to 0.21 mg/kg bw per day
	Study of developmental toxicity[b]	Maternal toxicity	0.20 mg/kg bw per day[d]	—
		Embryo- and fetotoxicity	0.20 mg/kg bw per day[d]	—
Rabbit	Study of developmental	Maternal toxicity	0.25 mg/kg bw per day	0.50 mg/kg bw per day
		Embryo- and fetotoxicity	0.25 mg/kg bw per day	0.50 mg/kg bw per day
Dog	1-year study of toxicity[c]	Toxicity	0.06 mg/kg bw per day	0.09 mg/kg bw per day

[a] Diet
[b] Gavage
[c] Capsule
[d] Highest dose tested

Estimate of acceptable daily intake for humans

0–0.0006 mg/kg bw

Estimate of acute reference dose

0.002 mg/kg bw

Studies that would provide information useful for continued evaluation of the compound

- A study of delayed neurotoxicity with neuropathy target esterase measurements (known to be ongoing)
- Further observations in humans
- Characterization of miosis

Summary of critical end-points for terbufos

Absorption, distribution, excretion and metabolism in mammals	
Rate and extent of oral absorption	Rapid and fairly complete
Dermal absorption	No specific study; rapidly penetrating following dermal or ocular application
Distribution	Relatively rapid and fairly complete
Potential for accumulation	Little
Rate and extent of excretion	Relatively rapid and complete; most eliminated in 24–48 h; elimination in urine predominates
Metabolism in animals	Sulfoxidation and desulfuration of terbufos is followed by hydrolysis of the thiolophosphorus bond (S-P), enzymatic *S*-methylation and then additional *S*-oxidation
Toxicologically significant compounds	Terbufos Terbufos oxon Terbufos sulfoxide Terbufos sulfone Terbuoxon sulfoxide Terbuoxon sulfone
Acute toxicity	
Rat, LD_{50}, oral	1.4–9.0 mg/kg bw
Rabbit, LD_{50}, dermal	0.81–0.93 mg/kg bw
Rat, LC_{50}, inhalation	Vapour, 4-h whole body exposure: 0.0012–0.0061 mg/l
Dermal irritation	Could not be determined due to lethality, rabbit
Ocular irritation	Could not be determined due to lethality, rabbit
Skin sensitization	Not determined owing to potential for severe toxicity
Short-term studies of toxicity	
Target/critical effect	Inhibition of brain cholinesterase activity
Lowest relevant oral NOAEL	0.059 mg/kg bw per day (13-week study of neurotoxicity in rats)

Lowest relevant dermal NOAEL	Data not available
Lowest relevant inhalation NOAEC	No appropriate data available
Genotoxicity	Unlikely to be genotoxic
Long-term studies of toxicity and carcinogenicity	
Target/critical effect	Inhibition of brain cholinesterase activity
Lowest relevant NOAEL	0.055 mg/kg bw per day (1-year study in rats)
Carcinogenicity	No evidence of carcinogenicity; Unlikely to pose a risk to humans
Reproductive toxicity	
Reproduction target/critical effect	Decreases in male fertility and female pregnancy rate
Lowest relevant reproductive NOAEL	0.086 mg/kg bw per day (rats)
Developmental target/critical effect	Not teratogenic; Reduced fetal body weight
Lowest relevant developmental NOAEL	0.25 mg/kg bw per day (rabbits)
Neurotoxicity/delayed neurotoxicity	
Acute neurotoxicity	
Target/critical effect	Miosis
Relevant NOAEL	0.15 mg/kg bw (rats)
13-week study of neurotoxicity	
Target/critical effect	Inhibition of brain cholinesterase activity
Relevant NOAEL	0.059 mg/kg bw per day (rats)
Delayed neuropathy	No evidence to suggest toxicity at dietary exposures
Medical data	There have been a number of reports of occupational and non-occupational poisoning incidents associated with exposure to terbufos. No information was available regarding possible effects from terbufos manufacturing facilities.

Summary	Value	Study	Safety factor
ADI	0–0.0006 mg/kg bw	Rats and dogs, overall NOAEL for studies of repeated doses	100
Acute RfD	0.002 mg/kg bw	Rat, study of acute neurotoxicity	100

References

Allen, J.S. (1985) Bacterial/microsome reverse mutation (Ames) test on CL 92 100 COUNTER® terbufos. Unpublished report GTOX Vol. 5 No.3 (BASF RDI No. TE-435-006) from American Cyanamid Company,

Princeton, NJ, USA.

Allen, J. & Johnson, E. (1983) Mutagenicity testing of AC 92 100 in the *in vitro* CHO/HGPRT mutation assay. Unpublished report GTOX Vol. 3 No.19 (BASF RDI No. TE-435-005) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1972b) Phosphorodithioic acid, *S*-(*Tert*-butylsulfinyl) methyl *O*,*O*-diethyl ester (CL94 301): mouse oral LD_{50}. Unpublished report No. A-72-37 (BASF RDI No. TE-470-008) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1972c) Phosphorodithioic acid, *S*-(*Tert*-butylsulfonyl) methyl *O*,*O*-diethyl ester (CL94 320): mouse oral LD_{50}. Unpublished report No. A-72-34 (BASF RDI No. TE-470-005) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1972d) Phosphorothioic acid, *S*-(*Tert*-butylsulfinyl) methyl *O*,*O*-diethyl ester (CL94 365): mouse oral LD_{50}. Unpublished report No. A-72-35 (BASF RDI No. TE-470-006) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1972e) Phosphorothioic acid, *S*-(*Tert*-butylsulfonyl) methyl *O*,*O*-diethyl ester (CL94 302): mouse oral LD_{50}. Unpublished report No. A-72-38 (BASF RDI No. TE-470-009) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1972f) Phosphorothioic acid, *S*-(*Tert*-butylthio) methyl *O*,*O*-diethyl ester (CL 94 221): mouse oral LD_{50}. Unpublished report No. A-72-36 (BASF RDI No. TE-470-007) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1973a) Methane, Bis(*Tert*-butylsulfonyl) (CL 202 135): mouse oral LD_{50}. Unpublished report No. A-73-21 (BASF RDI No. TE-470-002) from American Cyanamid Company, Princeton, NJ, USA.

American Cyanamid Company (1973b) Methane (*Tert*-butylsulfinyl)(methylsulfinyl) (CL 202 474): mouse oral LD_{50}. Unpublished report No. A-73-122 (BASF RDI No. TE-470-001) from American Cyanamid Company, Princeton, NJ, USA.

Bailey, D.E. (1988) 14-Day oral toxicity study in the dog with AC 92 100 and its metabolites, CL 94 301 and CL94 320. Unpublished report on HLA Study No. 362-190 (BASF RDI No. TE-420-007) from Hazleton Laboratories America, Inc., Vienna, VA, USA.

BASF (1972a) AC 92 100 Technical: Acute rat and mouse oral, rabbit dermal, rabbit skin and eye irritation. Unpublished report No. A-72-95 (BASF RDI No. TE-410-001) from BASF, Princeton, NJ, USA.

Berger, H. (1977) Experiments L-1680 and L-1680A: Cholinesterase activity of dogs receiving COUNTER* soil insecticide in the diet for 28 days. Unpublished report No. A77-158 (BASF RDI No. TE-420-004) from American Cyanamid Company, Princeton, NJ, USA.

Bradley, D. (1996) Oral LD50 study in albino rats with AC 92 100. Unpublished report No. A96-14; toxicology study T-0899 (BASF RDI No. TE-411-004) from American Cyanamid Company, Princeton, NJ, USA.

Cheng, T. (1992) Metabolism of ^{14}C-terbufos (CL 92 100) in rats (preliminary and definitive phases). Unpublished report No. TE-440-004 from American Cyanamid, Princeton, NJ, USA.

Daly, I.W. & Knezevich, A.L. (1979) A three-month feeding study of COUNTER* terbufos insecticide in rats. Unpublished report, project No. 78-2343 (BASF RDI No. TE-425-001) from Bio/dynamics Inc., East Millstone, NJ, USA.

Daly, I.W. & ? (1987) A one-year dietary toxicity study with AC 92 100 in rats. Unpublished report, project No. 85-2964 (BASF RDI No. TE-427-003) from Bio/dynamics Inc., East Millstone, NJ, USA.

Fischer, J.E. (1978) Experiment L-1728: 14-day rat feeding study with CL 92 100 (COUNTER®). Unpublished report No. A78-129 (BASF RDI No. TE-412-003) from American Cyanamid Company, Princeton, NJ, USA.

Fischer, J.E. (1985) AC 92 100 Technical: acute dermal toxicity in rabbits. Unpublished report No. A85-54 (BASF RDI No. TE-420-006) from American Cyanamid Company, Princeton, NJ, USA.

Garces, T.R., Stryeski, V. & Clinton, J.M. (1977) Safety of COUNTER® terbufos insecticide when present in the ration of sheep. Unpublished report (BASF RDI TE-411-003) from American Cyanamid Co., Agricultural Division, Princeton, NJ.

Gentile, J.M., Gentile, G.J., Bultman, J., Sechriest, R., Wagner, E.D. & Plewa, M.J. (1982) An evaluation of the genotoxic properties of insecticides following plant and animal activation. *Mutat. Res*., **101**: 19-29.

Godek, E.G. (1983) AC 92 100: rat hepatocyte primary culture/DNA repair test. Unpublished report PH 311-AC-001-83 (BASF RDI No. TE-435-004) from Pharmakon Research International, Inc., Waverly, PA, USA.

Haley, S. (1972) Teratogenic study with AC 92 100 technical in albino rats. IBT No. B1374-(B). Unpublished report (BASF RDI TE-432-001) from Industrial Bio-Test Laboratories, Inc., Northbrook, IL, USA.

Hoberman, A.M. (1988a) A developmental toxicity (embryo-fetal toxicity/teratogenicity) study with AC 92 100 in rabbits. Unpublished report Argus protocol No. 101-003 (BASF RDI No. TE-432-006) from Argus Research Laboratories, Inc., Horsham, PA, USA.

Hoberman, A.M. (1988b) Addendum to a developmental toxicity (embryo-fetal toxicity/teratogenicity) study with AC 92, 100 in rabbits (sample identification and analysis of dosing solutions). Unpublished report No. 101-003 from Argus Research Laboratories, Inc., Horsham, PA, USA.

Hoffman, G.M. (1987) An acute inhalation toxicity study with AC 92 100 in rats. Unpublished report, Bio/dynamics Project No. 86-3128 (BASF RDI No. TE-430-002) from Bio/dynamics Inc., East Millstone, NJ, USA.

Li, J-T.L., Sheng, S-J. & Du, X-L. (1999) Metabolism of terbufos in rat liver, *J. Occup. Health*, **41**: 62-68.

MacKenzie, K.M. (1986) Dominant lethal study with AC 92 100 in rats. Unpublished report, Hazleton study No. 6123-137 (BASF RDI No. TE-435-002) from Hazleton Laboratories America, Inc., Madison, WI, USA.

Mandella, R.C. (1998) An acute neurotoxicity study with AC 92 100 in the rat via oral garage administration. Unpublished report, Huntingdon study No. 98-4525 (BASF RDI No. TE-451-002) from Huntingdon Life Sciences, East Millstone, NJ, USA.

Mandella, R.C. (1999) 13-week dietary neurotoxicity study with AC 92 100 in the rat. Unpublished report, Huntingdon study No. 98-4521 (BASF RDI No. TE-451-004) from Huntingdon Life Sciences, East Millstone, NJ, USA.

Morgareidge, K. (1973) Six-month feeding study in dogs on AC-92 100. Unpublished report, FDRL Lab. No. 1193 (BASF RDI No. TE-427-004) from Food Drug Research Laboratories Inc., Maspeth, NY, USA.

Morici, I.J. (1972) *O*,*O*-Diethyl-*S*(*Tert*-butylthiomethyl)phosphorodithioate: acute toxicity, and thirty-day repeated feeding studies to albino rats, mice and beagle dogs. Unpublished report No. 72-3 (BASF RDI No. TE-420-002) from American Cyanamid Company, Princeton, NJ, USA.

North, H. (1973) COUNTER® insecticide: rat metabolism of CL 92 100 (*O,O*-diethyl-*S*-I-butylthio-methylphosphorodithioate). Unpublished report (BASF RDI No. TE-440-001) from Princeton, NJ, USA.

Putnam, D.L. (1986) AC 92 100: the acute in vivo cytogenetics assay in rats. Unpublished report, MA study No. T4277.105002 (BASF RDI No. TE-435-007) from Microbiological Associates, Inc., Bethesda, MD, USA.

Rapp, W.R. (1974) A three and twenty-four month oral toxicity and carcinogenicity study of AC 92 100 in rats. Unpublished report, Bio/dynamics project No. 71R-725 (BASF RDI No. TE-427-001), from Bio/dynamics Inc., East Millstone, NJ, USA.

Rodwell, D.E. (1984) A range-finding teratology study with AC 92 100 in rats. Unpublished report, WIL study No. WIL-35 013 (BASF RDI No. TE-432-003), from WIL Research Laboratories, Inc., Ashland, OH, USA.

Rodwell, D.E. (1985) A teratology study with AC 92 100 in rats. Unpublished report, WIL study No. WIL35 014 (BASF RDI No. TE-432-001), from WIL Research Laboratories, Inc., Ashland, OH, USA.

Schroeder, R.E. (1989) A two-generation (two-litters) reproduction study with AC 92 100 to rats. Unpublished report, Bio/dynamics Project No. 86-3128 (BASF RDI No. TE-430-002) from Bio/dynamics Inc., East Millstone, NJ, USA.

Shellenberger, T. (1987) 28-day oral toxicity study in the dog with AC92 100. Unpublished report No. 87 019 (BASF RDI No. TE-420-003) from Tegeris Laboratories, Inc., Laurel, MD, USA.

Shellenberger, T. & Billups, L.H. (1986) One-year oral toxicity study in purebred beagle dogs with AC 92 100. Unpublished report No. 8414 (BASF RDI No. TE-427-002) from Tegeris Laboratories, Inc., Laurel, MD, USA.

Silverman, M.E.B., Shellenberger, T.E., Billups, L.H. & Tegeris, A.S. (1986) Chronic dietary toxicity and oncogenicity study with AC 92 100 in mice. Unpublished report No. 8422 (BASF RDI No. TE-428-002) from Tegeris Laboratories, Inc., Laurel, MD, USA.

Smith, J. (1972) A neurotoxicity study of AC 92 100, an organic phosphate cholinesterase inhibitor, in hens. Unpublished report, Bio/dynamics Project No. 72S-788 (BASF RDI No. TE-451-001), from Bio/dynamics Inc., East Millstone, NJ, USA.

Smith, J.M. (1973) A neurotoxicity study of AC 92 100, an organic phosphate cholinesterase inhibitor in hens: addendum I (Project No. 72S-788). Unpublished report No. BASF RDI No. TE-451-001 from Bio/dynamics, East Millstone, NJ, USA.

Thilager, A. (1983) AC 92 100: Chromosome aberrations in Chinese hamster ovary cells. Unpublished report, MA study No. T1906.337 006 (BASF RDI No. TE-435-003), from Microbiological Associates, Inc., Rockville, MD, USA.

Whitney, W.K. (1980) A two week inhalation toxicity study of technical COUNTER® terbufos in the rat. Bio/dynamics project 78-7168. Unpublished report No. TE-420-008.

See Also:
- Toxicological Abbreviations
- Terbufos (ICSC)
- Terbufos (Pesticide residues in food: 1990 evaluations Toxicology)