RPS BKH Consulting Engineers
A MEMBER OF RPS GROUP PLC
environmental, civil and sanitary engineering

EUROPEAN COMMISSION DG ENV

ENDOCRINE DISRUPTERS:

STUDY ON GATHERING INFORMATION ON 435 SUBSTANCES WITH INSUFFICIENT DATA

FINAL REPORT

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COLOPHON

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PREFACE

RPS BKH Consulting Engineers (Delft, the Netherlands) has been commissioned by the European Commission by letter of 15 November 2001 to conduct a study on endocrine disruption focusing on man-made chemicals entitled “Endocrine disrupters: Study on gathering information on 435 substances with insufficient data”. This is a follow-up study in a first step towards the establishment, by the Commission, of a priority list of substances for further evaluation of their role in endocrine disruption. The earlier study was carried out by BKH in the year 2000.

Project co-ordinators for the present project for the EC are Mrs. K. Tierney and Mrs. C. Roncancio. The project was carried out in association with DHI Danish Hydraulics Institute (Hørsholm, Denmark) and KIWA consulting (Nieuwegein, The Netherlands). The project team included Mr. P.C. Okkerman (RPS BKH), Mrs. G. Petersen (DHI) and Mrs. M. Mons (KIWA). Project co-ordinator for RPS BKH is Dr. I. van der Putte.

A kick-off meeting with the Commission involving the set-up of the project was held on 11 December 2001. A meeting with the SCTEE to discuss the preliminary approach and methodology was held on 8 January 2002. A stakeholder meeting with representatives from government and NGO’s, in which the methodology was presented, was subsequently held on 21 February 2002. A meeting with experts in the field of endocrine disruption to categorise substances was held on the 9 and 10 September 2002.

It should be noted that the results of this study will be used as a basis for consultation by the Commission. This consultation process constitutes the second step in the establishment of a priority list of substances for further evaluation of their role in endocrine disruption, as outlined in the Commission Communication to Council and European Parliament on a Community Strategy for Endocrine Disrupters COM(2001)262 of 14 June 2001.

ABBREVIATIONS

AHH	Aryl Hydrocarbon Hydroxylase
ADEPTS/AQUATOX	A Database on Environmental Properties of Toxic Substances / Aquatic Toxicity database (RWS RIZA, BKH consulting engineers and WL Delft Hydraulics)
BUA	Bundes Umwelt Amt (Germany)
CAS	Chemical Abstract Service
CEFIC	European Chemical Industry Council
CEFIC/EMSG	Endocrine Modulators Steering Group of CEFIC
COMMPS	Revised Proposal for a List of Priority Substances in the Context of the Water Framework Directive.
ED	Endocrine Disruption
EDS	Endocrine Disrupting Substances
EEA	European Environment Agency
EPA	Environmental Protection Agency
EUSES	European Union System for Evaluation of Substances (software programme to implement the TGD)
HPV	High Production Volume (> 1000 tonnes/year)
IUCLID	International Uniform Chemical Information Database
LC50	Lethal Concentration Causing 50% mortality
LH	Luteinising Hormone
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
LPV	Low Production Volume (10 – 1000 tonnes/year)
LRAT	Long Range Air Transport
NGO	Non-Governmental Organisation
NOAEL	No Observed Adverse Effect Level
NOEC	No Observed Effect Concentration
OSPAR	The Convention for the Protection of the Marine Environment of the North-East Atlantic
PEC	Predicted Environmental Concentration
PNEC	Predicted No Effect Concentrations
PPPs	Plant Protection products
QSAR	Quantitative Structure Activity Relationship
RIVM	National Institute of Public Health and the Environment, The Netherlands
RIZA/RIKZ	Institute for Inland Water- and Wastewater management / Institute for Coastal and Marine Management, The Netherlands
SANCO	Health and Consumer Protection DG (DG Santé et protection des consommateurs)
SCTEE	Scientific Committee on Toxicity, Ecotoxicity, and the Environment
SMILES	Simplified Molecular Input Line Entry System (a code for the Structure of the Chemical)
TGD	Technical Guidance Document on risk assessment for New and Existing Substances.
TSH	Thyroid Stimulating Hormone
WHO	World Health Organisation
WRc	Water Research centre (UK)

EXECUTIVE SUMMARY

In recent years an increased number of effects have been reported in animal species and human beings that were attributed to the influence of compounds interfering with hormonal systems. The imposed threat of such compounds, also designated as endocrine disrupters, to wildlife and human health caused considerable media attention. Parliamentary questions urged the EU Commission to come up with a strategy regarding substances associated with endocrine disruptive behaviour. In December 1999, the European Commission published a Community Strategy for Endocrine Disrupters (COM(1999)706) in which it announced its intention to establish a priority list of substances for further evaluation of their role in endocrine disruption.

The Commission has adopted in its strategy short-, medium and long term actions taking into account the current concern on the basis of the precautionary principle. On the long term it is necessary for the Commission to envisage the adaptation and/or amendment of the present EU legislative instruments which cover chemicals as well as consumer, health and environmental protection in order to take account of endocrine disrupting effects. Short- and medium-term strategies of the Commission focus on substance data gathering concerning endocrine disruption, priority setting for further evaluation, and research and development activities in this field. This study together with an earlier study (BKH 2000) forms part of the short-term strategy on endocrine disruption proposed by the EU. For a more detailed account of the context the reader is referred to Commission document COM(2001)262 of 14 June 2001 on the implementation of the Community Strategy for Endocrine Disrupters.

The BKH 2000 study entitled “Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption” identifies 118 HPV or persistent man-made chemicals out of a candidate list of 553 substances, showing scientific evidence of endocrine disruption or potential endocrine disruption. A number of 109 substances was already subject to bans or restrictions or was being addressed under existing Community legislation, although for reasons not necessarily related to endocrine disruption. Priority has been given in the short-term to 9 substances which are neither restricted not currently being addressed under existing community legislation and for which more in depth studies were necessary (WRc Study). In addition 3 natural and/or synthetic hormones, oestrone, ethinylestradiol and oestradiol will be evaluated in order to gather up-to-date evidence of environmental exposure and effects related to these substances. The original number of substances on the candidate list was 564. However, a number of 11 substances was excluded from the candidate list at the ED expert meeting of 1999, as there was no scientific basis for inclusion.

The activities of the present study have strongly built upon and are partly a follow-up of the BKH 2000 report. The present study focuses on the remaining 435 compounds from the initial candidate list. The study has been carried out in the period 15 November 2001 to 15 November 2002

The general objective of the present study is to define a methodology by which to investigate 435 candidate substances identified in the BKH Report 2000 with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption.
Associated objectives are:

– To gather data/information on 435 substances, in accordance with the methodology defined.
– To define an iterative mechanism by which new substances may be included or existing substances removed from the candidate list of substances as new evidence comes to light.

To reach the objectives the following four tasks have been formulated and executed:

Task 1 *Review work done, in the context of the Community Strategy for Endocrine Disrupters, leading to the identification of the 435 candidate substances.*

The execution of this task was carried out based on the following activities:
- Review of the comments and recommendations from the existing documents
- Contacts with experts and stakeholders (industry, institutes, universities, non-governmental organisations).
- Preliminary definition of inputs for a methodology to be developed under Task 2

Task 2 *Define a methodology by which to investigate the 435 candidate substances identified in the BKH 2000 Report with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption*

The proposed methodology results from the multi-step approach described in the BKH Report 2000. This approach, however, is amended by the recommendations made respectively by the SCTEE and stakeholders, elements of an "alternative" methodology proposed by CEFIC/EMSG, and other relevant procedures used in similar work. A preliminary consultation with SCTEE and stakeholders on the methodology has been taken up. For the approach used in the present study, various new elements have been incorporated, including test reliability, dose response relationships, comparison with systemic toxicity, ED potency and occurrence in the environment.

Task 3 *In accordance with the methodology: further selection, inventory and evaluation of the group of 435 chemicals*

<u>Selection, inventory, evaluation and categorisation:</u>
With the objective of establishing priorities for further evaluation of the role of these 435 chemicals three selection steps were applied, using different criteria and expert evaluations.

An important activity in this task was the inventory of data and the development of an interactive database that contain details as well as an overview of ED effects and systemic toxicity of the selected substances. This interactive database was applied as a tool for the evaluations made by the ED experts in the second step. The three consecutive steps were:

1 A first selection of substances was made by applying criteria on production volume and persistence. In this first step selection criteria were:
   - persistency criteria, The cut-off values on biodegradation as selected in the OSPAR DYNAMEC group were used (biodegradation probability of <0.5 and ultimate biodegradability of < 2.2 instead of <0.1 and <1.0, respectively).
   - production data, Low Production Volume pesticides with a production volume of more than 10 tonnes per year were also included.
   - consumption/use patterns and monitored environmental concentrations (COMMPS).

A second selection step was made on the basis of scientific evidence for Endocrine Disruption.
In this selection step in which the substances were evaluated by ED-experts the following categories were distinguished:

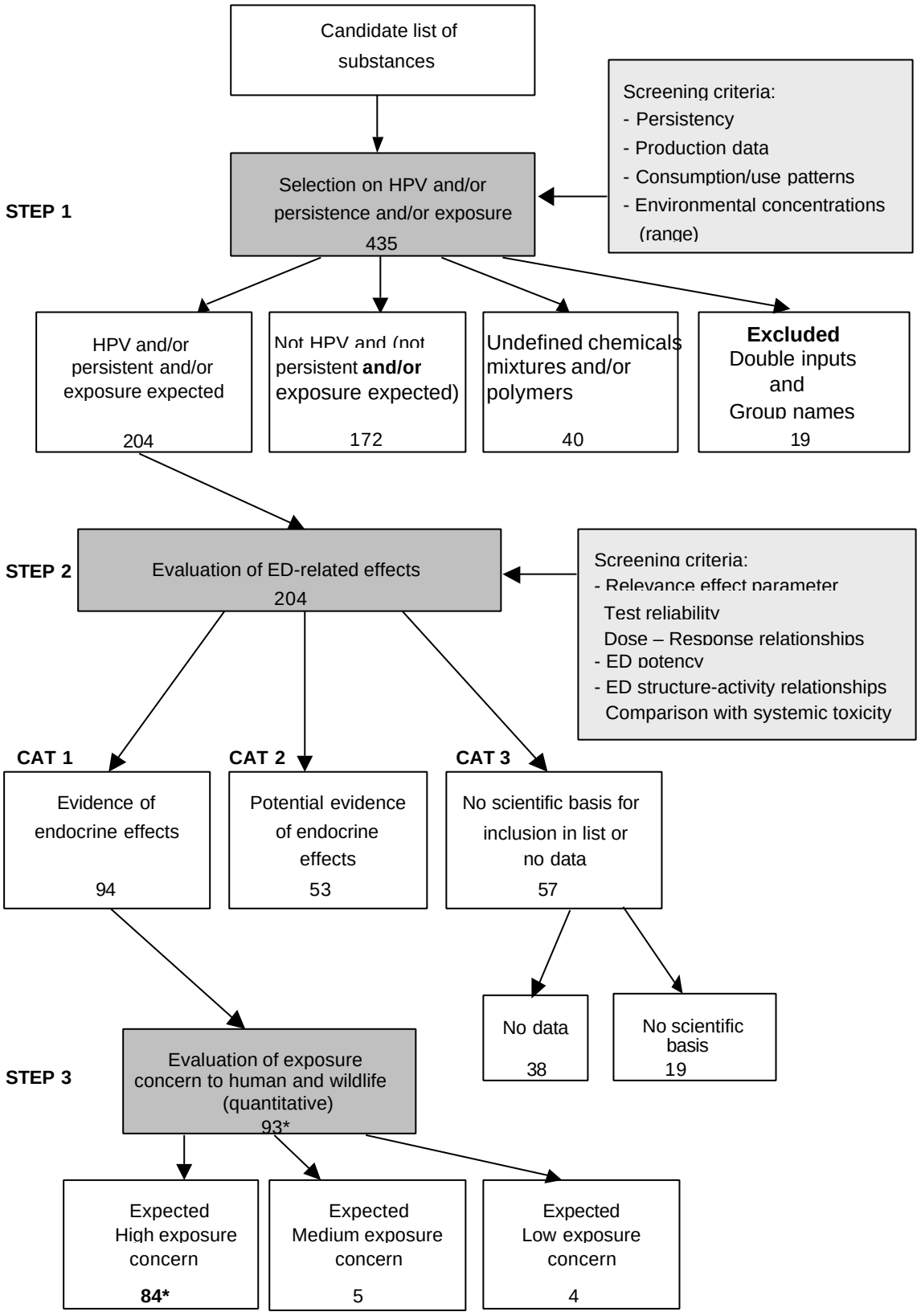
Category 1.	At least one study providing evidence of endocrine disruption in an intact organism. Not a formal weight of evidence approach.
Category 2.	Potential for endocrine disruption. In vitro data indicating potential for endocrine disruption in intact organisms. Also includes effects in-vivo that may, or may not, be ED-mediated. May include structural analyses and metabolic considerations
Category 3a.	No scientific basis for inclusion in list (ED studies available but no indications on ED effects)
Category 3b.	Substances with no or insufficient data gathered.

In the third and final selection step Category 1 substances were grouped as having high, medium or low exposure-concern. This last categorisation uses information on physico-chemical parameters, production, emission, use, exposure and monitoring data for the substances. Special attention was given to possible exposure of vulnerable groups e.g infants, humans suffering from certain illnesses, sensitive species or life stages. The data have been presented in summary profiles, see Annex 13. The following guidelines were used:

High exposure concern	Human exposure is expected, due to environmental concentrations and concentrations found in food or consumer products, also taking into consideration exposure of vulnerable groups *And/Or* Wildlife exposure is expected, due to use and emission patterns, and the chemical is persistent and bioaccumulative
Medium exposure concern	Human exposure is not expected *And* Wildlife exposure is expected, due to use and emission patterns, but the chemical is readily biodegradable and not bioaccumulative
Low exposure concern	No human exposure *And* No wildlife exposure

In Figure S.1 the approach, using the selection steps 1 to 3, and its outcome are presented schematically.

Figure S.1 Approach and outcome of the evaluation and categorisation (see also annex 4)



* Mestranol as synthetic contraceptive drug is excluded

Using the proposed methodology, 204 out of 435 substances were categorised as being HPV and/or persistent and/or for which exposure to different populations is expected (step 1). In subsequent steps, a number of 94 out of the 204 chemicals (or 41 clustered substances) were identified as Category 1 chemicals with evidence for endocrine disruption in a living organism (step 2). After a detailed evaluation 84 of these (or 34 clustered substances) were considered to be of high exposure concern (step 3). Categorisation of the remaining chemicals is depicted in figure S.1.

It should be noted that, in the final categorisation step 3 (evaluation of exposure concern) one substance (mestranol) was excluded because it is a synthetic hormone already studied as a part of the WRc study. In combination with the progesterone mimic norethindrone, the estrogen mestranol is used as an oral contraceptive drug better known as "the pill". In the scope of the multi-step approach of this report, mestranol, a 3-methylether derivate of 17α-ethynylestradiol, has proven to exert endocrine effects and due to its use as an oral drug it would be categorised as having high exposure concern.

Potency and toxicity considerations

As an indication of the relevance of the ED effects observed in Category 1 substances, two types of comparisons are made:

1. Comparison between ED-effect doses and effect doses, which are related to systemic toxicity for Category 1 substances.
2. A comparison between ED-effect of Category 1 substances and an ED-effect induced by the natural ligand 17-β-estradiol in vivo in rats. This results in a ratio which can be considered as a "ED potency" level of the compound related to 17-β-estradiol.

Most levels reported for ED-effects are below those reported for systemic toxicity. Considering "potency" levels, only for dioxin an ED-effect has been reported around the same concentration as 17-β-estradiol. For all other Category 1 substances ED effects are far below those induced by 17-β-estradiol. It should be emphasised, however, that a direct comparison is not conclusive due to differences in test systems, test species, life stages, effects parameters and exposure periods.

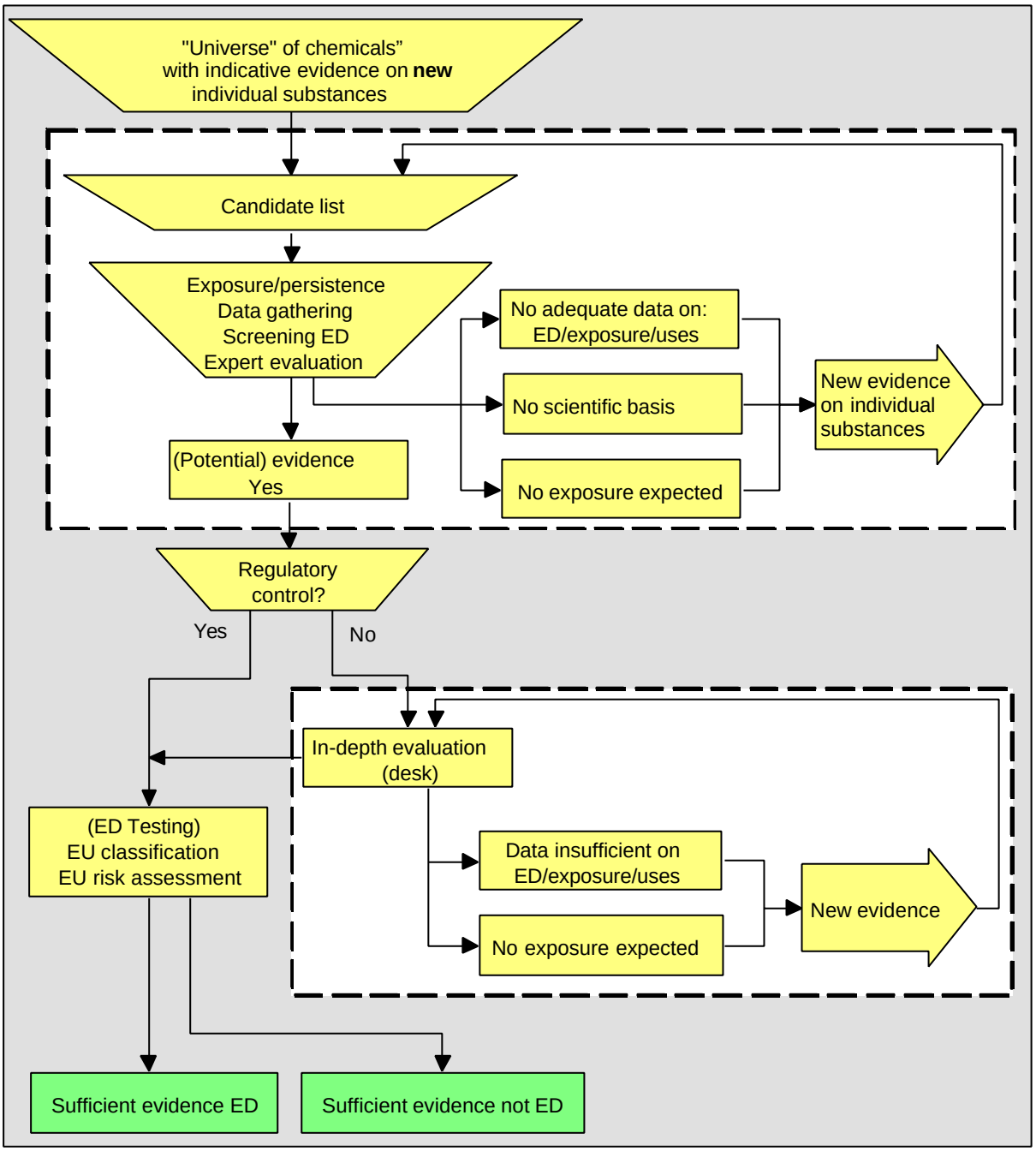
Taking into consideration the limitations and restrictions mentioned before it can be indicated that the levels reported for ED-effects are below those reported for systemic toxicity. Considering "potency" levels, only for dioxin an ED-effect has been reported around the same concentration as 17-β-estradiol. For all other Category 1 substances ED effects are far below those induced by 17-β-estradiol.

Task 4: *Define an iterative mechanism by which new substances may be included or existing substances removed from the candidate list of substances as new evidence comes to light.*

The candidate list including 435 chemicals in the present study should not be considered as final. Based on new data, other chemicals may be added to the list. For this purpose an iterative procedure has been proposed in the present study.

The proposed iterative procedure has been based on the results of the present study, experience with the BKH 2000 study, the Commission Communication to Council and European Parliament on a Community Strategy for Endocrine Disrupters COM(2001)262 of 14 June 2001 and the WRc study. It includes aspects such as new ED evidence for chemicals already on the working list and provides a way to incorporate the evaluation of new candidates. The proposed iterative procedure is depicted in Figure S.2.

Figure S.2: Iterative mechanism for screening chemicals on Endocrine Disrupting effects



1. INTRODUCTION

1.1 Background

In December 1999, the European Commission published a Community Strategy for Endocrine Disrupters (COM(1999)706) in which it announced its intention to establish a priority list of substances for further evaluation of their role in endocrine disruption.

In June 2000, BKH Consulting Engineers (NL), under contract to the Commission, prepared a report entitled "Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption – preparation of a candidate list of substances as a basis for priority-setting". The report identified a candidate list of 553[1] substances, from which evidence of endocrine disruption or potential endocrine disruption was found for 118 substances. An analysis of the legal status of these 118 substances revealed that 109 were already subject to bans or restrictions or were being addressed under existing Community legislation, although for reasons not necessarily related to endocrine disruption (Figure 1: Establishment of a priority list of substances for further evaluation of their role in Endocrine Disruption).

Following a wide consultation on the BKH report, it was decided to give priority in the short-term to an in-depth evaluation of the 9 candidate substances with evidence of endocrine disruption or potential endocrine disruption which were neither restricted nor being addressed under existing Community legislation. Before any proposals for restrictions could be envisaged, these 9 substances, together with an additional number of 3 synthetic/natural hormones present in the environment, had to be evaluated more thoroughly. This decision reflected a broad agreement among stakeholders. It also reflected the Commissions intention not to duplicate work on substances for which risk assessments were already on the way under existing Community legislation. It should however be noted that the 109 substances already regulated or being addressed under existing Community legislation do not disappear from the candidate list and may become future candidates for definitive testing once agreed test methods for endocrine disruption are available.

In addition to the in-depth evaluation of the 9+3 substances, it was decided to give equal priority to gathering data/information on persistence, production volumes and legal status on another number of 435 candidate substances, for which there was insufficient data in the 2000 BKH Report to decide on ED- or potential ED behaviour (not due to lack of data but to lack of resources to gather the data).

Thus in 2001, two studies were launched in parallel. The first, on 12 (9+3) substances, was carried out by WRc-NSF (UK). The second, on 435 substances, has been commissioned to RPS BKH Consulting Engineers (NL) and is the subject of this report.
The reader is referred to Commission document COM(2001)262 of 14 June 2001 on the implementation of the Community Strategy for Endocrine Disrupters for a more detailed account of the context of both of these studies. The reader is also reminded that the word "priority" in the context of this work does not indicate the relative importance of a substance in terms of endocrine disruption but refers rather to making the best use of available resources in the process of further evaluation of all candidate substances.

[1] The original number of substances was 564. A number of 11 substances was excluded at the ED expert meeting of 1999. This involved 7 metals or metal-compounds for which developmental- and reproductive effects have been known for a long time and are well documented in literature and 4 compounds for which no scientific evidence on endocrine disruption was found.

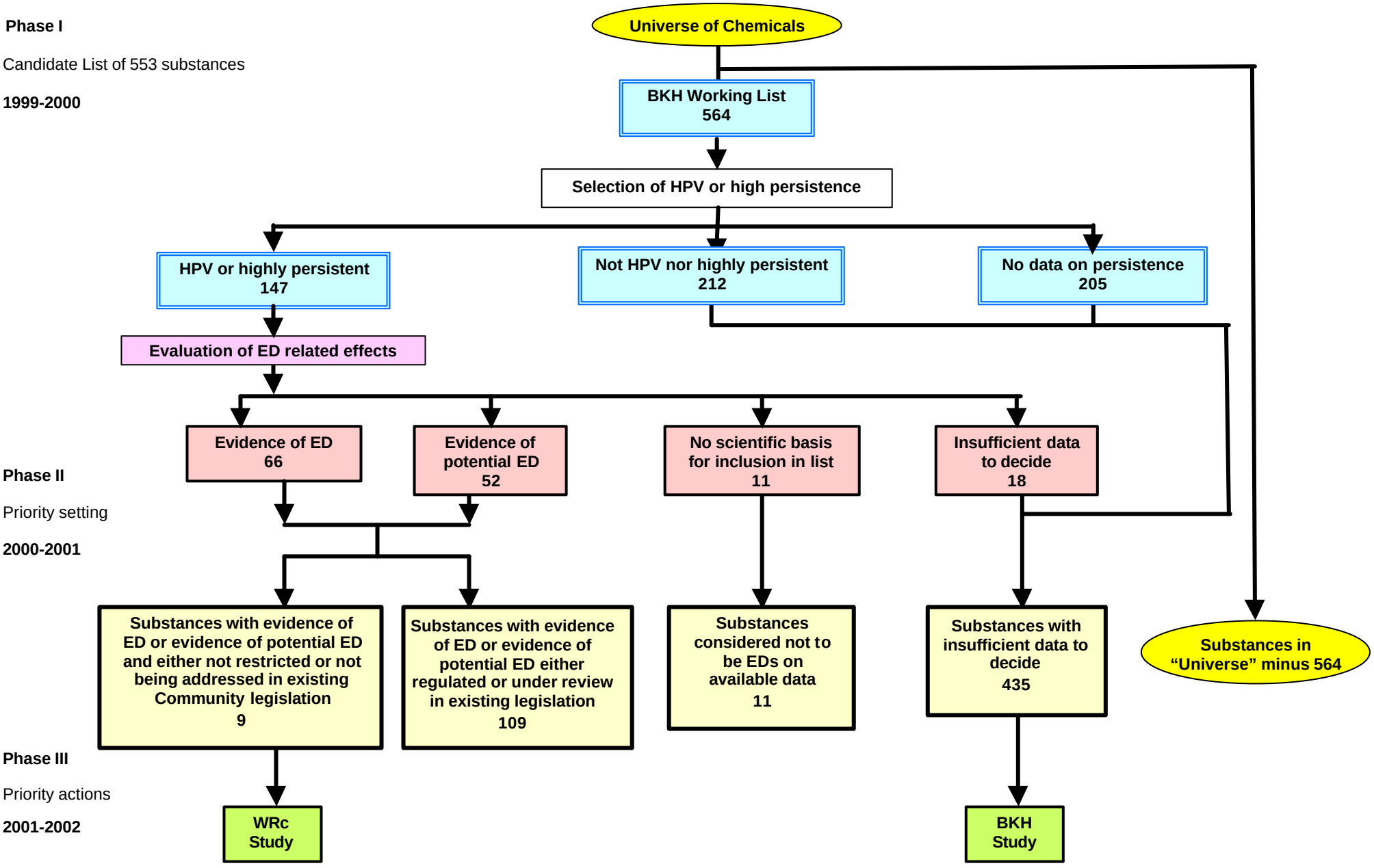


Figure 1: Establishment of a priority list of substances for further evaluation of their role in Endocrine Disruption.

1.2 Objectives and scope of the current project

The general objective of the present study is to define a methodology by which 435 candidate substances identified in the BKH Report (year 2000) are investigated in order to establish a priority list of substances needing further evaluation of their role in Endocrine disruption.
Associated objectives are:

– To gather data/information on these 435 substances, in accordance with the methodology defined.
– To define an iterative mechanism by which new substances may be included or existing substances removed from the candidate list of substances as new evidence comes to light.

The study will focus primarily on the 435 candidate substances selected from the original BKH working list as described in the BKH report of the year 2000 (also see Figure 1). The iterative mechanism, will take into consideration the wider "universe of chemicals", including substances that were not present on this original BKH working list. In future this will result in a continuous up-date of potential endocrine disruptive candidates.

The Commission, in consultation with the Member States and other stakeholders, will use the outcome of this study to provide input in discussions at European level about possible risk reduction measures. When agreed methods are available, selected priority substances will have to be submitted to screening and testing on endocrine disruption.

The following *working* definitions of endocrine disrupters or suspected endocrine disrupters served as a basis for the project:

- An endocrine disrupter is an exogenous substance or mixture that alters function(s) of the endocrine system, and consequently, causes adverse health effects in an intact organism, or its progeny, or (sub)populations (IPCS);

- A potential endocrine disrupter is an exogenous substance or mixture that possesses properties that might be expected to lead to endocrine disruption in an intact organism, or its progeny, or (sub)populations (IPCS).

Two classes of endocrine disrupters can be distinguished:

1. *'Natural' hormones* which include oestrogen, progesterone and testosterone found naturally in the body of humans and animals, and phytoestrogens, substances contained in some plants such as alfalfa, sprouts and Soya beans which display oestrogen-like activity when ingested by the body;

2 Man-made substances which include
   A) Synthetically-produced hormones, including those hormones which are identical to natural hormones, such as oral contraceptives, hormone replacement treatment and some animal feed additives, which have been designed intentionally to interfere with and modulate the endocrine system; and
   B) Man-made chemicals designed for uses in industry such as in some industrial cleaning agents, in agriculture such as in some pesticides, and in consumer goods such as in some plastic additives. It also includes chemicals produced as a by-product of industrial processes such as dioxins, which are suspected of interfering with the endocrine systems of humans and wildlife.

The present project predominantly involves the 435 substances originating from the original BKH working list (BKH report 2000) , which are man-made chemicals.

1.3 Study approach

In the framework of the present study, four main tasks have been identified to accomplish the objectives proposed:

Task 1 *Review work done, in the context of the Community Strategy for Endocrine Disrupters, leading to the identification of the 435 candidate substances.*

The execution of this task was carried out based on the following activities:
- Review of the comments and recommendations from the existing documents;
- Contacts with experts and stakeholders (industry, institutes, universities, non-governmental organisations);
- Preliminary definition of inputs for a methodology to be developed under Task 2.

Task 2 *Define a methodology by which to investigate the 435 candidate substances identified in the BKH 2000 Report with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption*

The proposed methodology to establish priorities of candidate substances in Endocrine Disruption results from the multi-step approach described in the BKH Report year 2000. This approach, however, is amended by the recommendations made by the SCTEE and stakeholders, elements of an "alternative" methodology proposed by CEFIC/EMSG, and other relevant procedures used in similar work. A preliminary consultation with SCTEE and stakeholders on the methodology has been taken up. For the approach used in the present study various new elements have been incorporated, including test reliability, dose response relationships, comparison with systemic toxicity, ED potency and occurrence in the environment.

Task 3 *In accordance with the methodology: further selection, inventory and evaluation of the group of 435 chemicals*

A multi-step approach was followed applying different selection criteria and expert evaluations. In consultation with stakeholders, a first selection was made applying criteria on production volume, persistence and probability of exposure in different populations. A second selection was made after consultation of, and evaluation by experts in the field of endocrine disruption. Substances were selected on the basis of scientific evidence. The third and last selection was based on criteria related to exposure of vulnerable groups, environmental behaviour and monitoring data.

One of the main outputs of this task was the inventory of data and the development of an interactive database, which includes ED effects as well as systemic toxicity of the selected substances. Endocrine effects on human health range from for example effects on the weight of sex-organs, effects on sperm development, vaginal opening to altered hormone levels, synthesis or -binding. Endocrine effects observed in wildlife included aspects such as reduced fertility, masculisation/feminisation, skewed sex ratios, sex reversal as well as altered levels, synthesis or binding of hormones. The developed interactive database was applied as a tool for the evaluations made by the ED experts.

Task 4 *Define an iterative mechanism by which new substances may be included or existing substances removed from the candidate list of substances as new evidence comes to light.*

The iterative mechanism has been proposed based on the results of the present study, experience with the BKH 2000 study, the Commission Communication to Council and European Parliament on a Community Strategy for Endocrine Disrupters COM(2001)262 of 14 June 2001 and the WRc study.

The iterative mechanism includes aspects such as new ED evidence for chemicals already on the working list and a mechanism to incorporate the evaluation of new candidates not yet on the list.

2. REVIEW EARLIER WORK (TASK 1)

The following reports and documents have been reviewed:

- Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption – preparation of a candidate list of substances as a basis for priority setting, June 2000 (the "BKH Report 2000");
- Opinion of Scientific Committee for Toxicity, Ecotoxicity and the Environment on the BKH Report, 5 September 2000 ("SCTEE Opinion");
- Comments from stakeholders on the BKH Report, September 2000;
- Towards the establishment of a weight of evidence approach to prioritising action in relation to endocrine disruption, CEFIC-EMSG working paper, August 2000;
- Report of informal stakeholder consultation meeting, 8-9 November 2000, Brussels.

The BKH Report of the year 2000 was designed to be a starting point in a priority-setting exercise. A total of 553 candidate substances was identified and subsequently grouped according to available information. The selection criteria used in the BKH 2000 Report for the first cut of substances, which were chosen in consultation with stakeholders, were as follows:

- Production volume;
- Persistence in the environment;
- Evidence of endocrine disruption from scientific literature, and
- Exposure considerations.

A description and evaluation of the BKH 2000 report with comments of the stakeholders is given in Annex 1. An evaluation of the alternative approach of CEFIC/EMSG is given in Annex 2.

In general it was concluded that the BKH study can be used as a first step in developing the priority list. The approach taken and described in the report is reasonable for a first cut of the data.

The SCTEE Opinion made several recommendations for improvement of the BKH approach concerning, inter-alia, dose-response relationships, potency considerations, environmental concentrations and comparison with systemic toxicity, synthetic hormones, quantitative exposure assessment as well as cut-off points for production volume and persistence criteria.
Stakeholders made additional recommendations concerning, inter-alia, QSAR data, effect parameters, risk assessment for vulnerable groups, substances which are no longer manufactured or marketed in the EU, and pharmaceutical and veterinary medicines.
In addition, CEFIC/EMSG has presented a weight of evidence approach to prioritising action in relation to endocrine disruption which it describes as "an alternative to the approach used by BKH".

In the present study the following important issues have been taken into consideration in order to improve the methodology[1]:

- Consumer exposure to LPV (Low Production Volume) chemicals has been taken into account, because for some specific uses exposure to LPV chemicals might be more important than the contribution of HPV chemicals. Considering possible effects in humans and the environment, exposure (and not only persistency) is important. Therefore, persistency and production volume should not be the only selection criteria in the first selection step. People and the environment may be continuously exposed although a substance is degradable. Hence, knowledge about environmental occurrence and/or use patterns should be included at this stage as well. Special reference was made to LPV plant protection products.
- The list of SMILES notations was completed as far as possible as it was strongly recommended to obtain SMILES notations for all listed chemicals. SMILES notations are used for further selection in the ED evaluation process;

[1] ED-structure activity relationships have only been considered as a potential approach
Although commercially available programmes can be purchased on the market, this approach has not been applied.

- Cut-off values for biodegradation as selected in the DYNAMEC group (OSPAR) have been used (biodegradation probability of <0.5 and ultimate biodegradability of < 2.2 instead of <0.1 and <1.0, respectively as applied in the BKH 2000 study).
- Grouping of certain substances has been introduced. This requires careful consideration as not all members of the group may have similar potency (e.g. PBBs, chlorinated paraffins).
- On the basis of the precautionary approach, substances with insufficient evidence, but chemically closely related to category 1 substances, have been categorised as category 1;
- A category of chemicals has been added for which it might be decided that no scientific basis for inclusion is available;
- For assessing the action of endocrine disrupters, dose-response and potency aspects have been considered;
- A comparison of endocrine disruption with other toxic effects has been made;
- Potency considerations and quantification of exposure (physical-chemical characteristics, use, production and dispersion patterns have been included early in the process;
- In step 4 (Preliminary evaluation of exposure to humans and wildlife) exposure is handled in a more quantitative way;
- As far as possible unpublished information available on Plant Protection Products has been incorporated in this report;
- An important requirement in the evaluation on ED chemicals is the quality of data especially referred to in the CEFIC/EMSG alternative approach. For this purpose relevance of test parameters and test reliability have been taken up as an important evaluation parameters.

3. METHODOLOGY (Task 2)

"To define a methodology by which to investigate the 435 candidate substances identified in the BKH Report with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption".

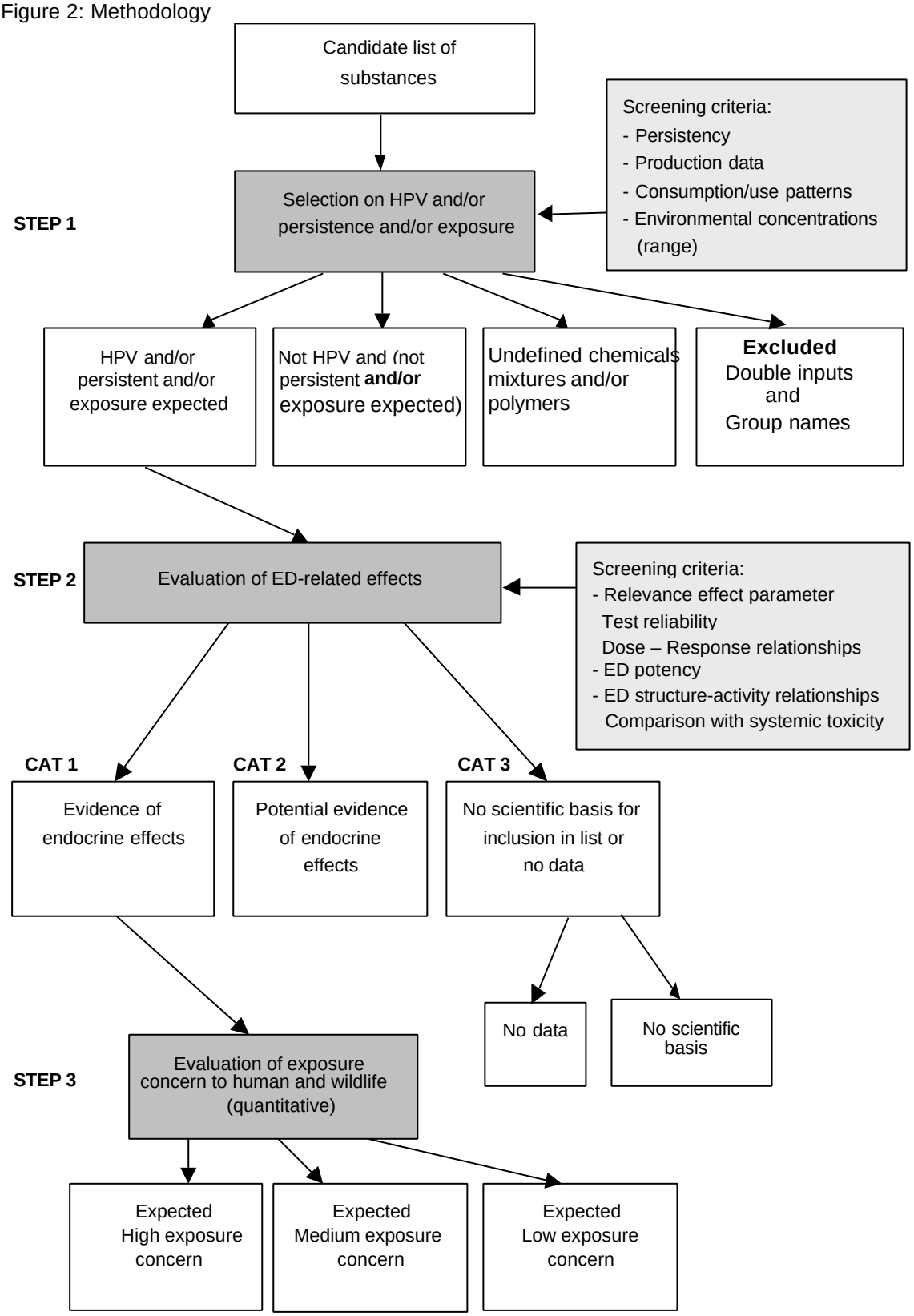
The proposed methodology to establish priorities of candidate substances in Endocrine Disruption results from the multi-step approach described in the BKH Report year 2000. This approach, however, is amended by the recommendations made by the SCTEE and stakeholders, elements of an “alternative” methodology proposed by CEFIC/EMSG, and other relevant procedures used in similar work. The approach used in the present study incorporates various new elements, including test reliability, dose response relationships, comparison with systemic toxicity, ED potency and occurrence in the environment (see chapter 2).

A preliminary consultation with SCTEE on the methodology took place. On the basis of recommendations and discussions the methodology has been decided to consist of the following 3 steps:
1: Selection of a second cut of substances,
2: Review of the data on ED for the selected substances,
3: Evaluation resulting in expected exposure concern levels.

In the developed methodology the following "New" elements were incorporated:
- Use of a quality assurance scheme for the evaluation of Key ED studies by experts;
- Comparison of the ED evidence against systemic toxicity and ED potency (if available);
- Identification of certain "groups" of substances with an overall ED categorisation on the basis of reference substances;
- A more quantitative approach for the evaluation of expected exposure concern.

It should be noted that all substances on the working list should be evaluated following the methodology described below. The set-up of the methodology is depicted in Figure 2.

Figure 2: Methodology



3.1 Step 1: Selection on HPV and/or persistence and/or exposure

In Step 1 a second cut of substances was made on the basis of:

- screening the existing list for lacking basic data (CASno., SMILES notations etc.);
- persistency criteria, limits used by updated TGD and/or in OSPAR/COMMPS[2] work (QSAR calculations, adaptation of the criteria to the recommendations of the stakeholders and experimental data on biodegradation);
- production data, and including Low Production Volume pesticides with a production volume of more than 10 tonnes per year (ECB non-exhaustive list of biocidal substances with possible existing active substances (BAS2000[3])) (See additional information in Annex 3);
- consumption/use patterns (data from industry, internet sources, open literature);
- environmental concentrations (range) (COMMPS).

Additionally data on biodegradation and consumption patterns were requested from institutions of the EC, National Authorities, industry and NGO's. Sources were IUCLID and the ECB for the substances with lower production volumes. Information on environmental concentrations was derived from the COMMPS project on the prioritisation of substances in the context of the Water Framework Directive and through contact with the European Environment Agency (EEA) for environmental monitoring data.

The cut-off values on biodegradation as selected in the DYNAMEC group were used. The rate or probability of aerobic biodegradability is assessed on the basis of Structure Activity Relationships developed by Syracuse. Using CAS numbers and SMILES notations as the entrance, molecular fragments are defined. These fragments have been given a specific value based on multiple linear regression analysis and expert judgements.
The linear regression method results in classes of probability. Substances with a probability of rapid biodegradation > 0.5 are expected to biodegrade rapidly. Substances with a probability of <0.5 are expected to biodegrade slowly.
In addition the programme includes a model that predicts the time for ultimate degradation (complete mineralisation) of a substance. This model is based upon a survey of 17 biodegradation experts that were asked to evaluate 200 chemicals in terms of the time required to achieve ultimate biodegradation. The substances were rated to time units: 5 = hours; 4 = days; 3 = weeks; 2 = months; 1 = more than months. The results were averaged per substance and formulated to 36 fragments and molecular weight parameter like the probability estimation on linear regression. As persistent chemicals are those that need months or more than months (<2.2) this property based on the expert judgement was combined with a low probability for rapid biodegradation (probability in linear regression model < 0.5).

[2] COMMPS Procedure, 1999. Revised Proposal for a List of Priority Substances in the Context of the Water Framework Directive. Fraunhofer-Institut, Final Report.

[3] BAS2000: The Biocidal Active Substances list 2000, derived from ECB, is an non exhaustive list of possible existing Biocides Active Substances (including High and Low Production Volume Plant Protection Products and carriers) draft version

3.2 STEP 2: Evaluation of ED-related effects

In Step 2 the selected second cut of data were reviewed for evidence on endocrine disruptive effects.
This step consisted of:
1. Gathering information on ED and systemic toxicity;
2. Incorporation of all gathered information in a database;
3. Evaluation by experts.

1a. Gathering information on endocrine disruption:
- Information was requested from EC, National Authorities, and Non Governmental Organisations (NGO's).
- Background documents used in the BKH 2000 report were used as basis for information.
- The collection of literature data through experts, review documents and a literature search to include the most recent references not covered by the review documents. In review documents (such as WHO- Environmental Health Criteria reports) all literature on certain chemicals is collected and in most cases also evaluated.
- Review documents were used for backtracking and retrieving primary literature sources, such as WHO: Environmental Health Criteria and EU risk assessments. Furthermore databases like IUCLID, ADEPTS/AQUATOX were used as sources of information.
- A literature search to retrieve references, not yet covered by the review documents was carried out for almost all chemicals in on-line databases like DIMDI-TOXCAS, TOXNET, TOXLINE, TOXBIO, IPA. The search was based on the CAS number or, if not available, on the chemical name.

1b. Gathering information on systemic toxicity
- Data for standard toxicity such as NOECs/LOECs, L(E)C50s NOAELs/LOAELs were retrieved from the same sources presented above plus those from RTECS, ECOTOX (formerly named AQUIRE), DOSE and Verschueren databases.

2. Incorporation of data in a EDS database
The EDS database compiles information on Human health and Wildlife relevant data concerning both Endocrine Disrupting effects and systemic toxicity and might be used for further research. It resulted from two studies on identification of Endocrine Disrupters (BKH 2000 and present study), conducted by RPS BKH Consulting Engineers in 1999-2000 and 2002. Furthermore the categorisation results are included prepared by experts at two separate EU Expert meetings on endocrine disrupters held on 27-28 September 1999 and 9-10 September 2002. See EDS database.

Two versions of the EDS database have been prepared: the view version gives the opportunity to select (groups of) chemicals, view and print all available effects data, identified key-studies, categorisations and qualifying remarks given by experts. The evaluation version additionally makes it possible to add and edit data in the database.

3. Evaluation by experts
Starting point of the evaluation by the experts was the EDS database containing Human Health relevant and Wildlife relevant data. Experts with different fields of expertise were requested to evaluate the data and categorise chemicals considering ED effects data.

As the number of chemicals is relatively high, with a considerable amount of information, it was decided to use 9 groups of experts for the evaluation. The chemicals and data were divided among the groups of experts in such a way that the amount of work was evenly distributed. Chemicals from specific chemical families (e.g. PCBs) were allocated to one evaluation group of experts to categorise groups of chemicals on the basis of "reference" chemicals.

Experts were assigned to evaluation groups of 2-3 persons. All experts within an evaluation group evaluated a number of chemicals and discussed their evaluation results with the other expert(s) in the evaluation group at the EDS Expert Meeting held at 9-10 September 2002. The conclusions

of the discussions per substance were added to the database, printed in a hardcopy at the expert meeting and subsequently signed by the experts.

The evaluation by experts consisted of four parts: Identification of key studies; evaluation of the data quality of key studies, and ED categorisation of the selected chemicals and adding qualifying remarks and additional remarks by comparing the ED information with ED potency and systemic toxicity data (if available).

Part 1: Identification of key studies from the database
Key studies are those studies, which determine the categorisation of a chemical. Experts could select one up to three studies if available. Selected key studies might hold either positive or negative evidence on endocrine disruption. In case the expert decided that no key studies were available in the database, the substance was categorised as CAT3a or CAT3b (explanation, see Part 3). Another option was that the experts added key studies themselves, under the condition that a hard copy of the study (or at least the summary and main results) was made available at or after the expert meeting.

Part 2: Evaluation of the Data Quality of the Key studies:
On the basis of the information available in the database and/or on basis of the publications available at the expert meeting, the Data quality of the Key studies was determined. For the evaluation of the ED data experts applied screening criteria such as depicted in Table 1:

Table 1: Screening criteria used by experts in the evaluation of Endocrine Disruption

Screening criteria	**Description**
Relevance of the effect parameter:	with aspects such as relation ED effects with mechanistic cause
Test reliability:	- Use of validated protocols (analysis, test procedure); - Experimental design: controls, concentration range; - Test species: suitability, health, life stage; - Analysis of results: statistics; - Dose – Response relationship
Qualifying remarks	Coherence of the results of ED related tests
Additional considerations	Data availability (other ED tests); Comparison with systemic toxicity; ED potency:

The result of the evaluation to distinguish 4 levels of data quality:
DQ1: good data quality, fulfilling all (important) criteria;
DQ2: sufficient data quality, study fulfilling most of the (important) criteria;
DQ3: insufficient data quality, study cannot be used for identification;
DQ4: not evaluated;

Part 3: Categorisation of the chemicals plus qualifying remarks
On basis of the identified Key studies and their Data quality chemicals were categorised into the different categories. For this the following definitions were used:

Category 1. At least one study providing evidence of endocrine disruption in an intact organism. Not a formal weight of evidence approach.

Category 2. Potential for endocrine disruption. In vitro data indicating potential for endocrine disruption in intact organisms. Also includes effects in-vivo that may, or may not, be ED-mediated. May include structural analyses and metabolic considerations

Category 3a. No scientific basis for inclusion in list
(ED studies available but no indications on ED effects)

Category 3b. Substances with no or insufficient data gathered.

The former category 3 of the BKH report 2000 has been divided into two sub-categories, category 3a Substances with no scientific basis for inclusion *and* category 3b Substances with no or insufficient data gathered. It should be emphasised that none of the substances in category 3a or 3b are excluded.

To the categorisation in the database the experts added additional “Qualifying remarks”. This is a free field and refers to the coherence of the ED information in the database. Possible remarks are for example:
- ‘other ED evidence is supporting’;
- ‘other evidence is lacking’;
- ‘other evidence is contradicting’.

Qualifying remarks also concerns the identification of certain "families" of substances with an overall ED categorisation on the basis of reference substances.

Part 4: Additional considerations taking into account potency and systemic toxicity.
This Part includes a field of free remarks. The experts could use this field to explain their reasoning why this substance is categorised as it is. Possible items were:
- The amount of ED evidence
- ED Potency
- Comparison with systemic toxicity

3.3 STEP 3: Evaluation of exposure concern to human and wildlife

In Step 3 the identification of expected exposure concern levels was carried out only for the in step 2 identified Category 1 chemicals. For these Category 1 chemicals a separate analysis was made distinguishing between industrial chemicals, waste chemicals and pesticides.
The analysis is also based on EU risk assessment reports, applying EUSES, as far as these are available. For other chemicals reference was made to environmental concentrations.

It should be noted that direct emissions of pesticides and biocides to agricultural soil, as well as processing of pesticides and biocides are outside the scope of EUSES. For pesticides data available on risk assessments from SANCO were used.

As in most of the cases ED effects are assessed via different test systems and test species than than tests to assess systemic toxicity, direct comparison between systemic toxicity and ED effects was made only on a case by case basis.

The following guidelines were used:

High exposure concern	Human exposure is expected, due to environmental concentrations and those in food or consumer products, also taking into consideration exposure of vulnerable groups *And/Or* Wildlife exposure is expected, due to use and emission patterns, and the chemical is persistent and bioaccumulative
Medium exposure concern	Human exposure is not expected *And* Wildlife exposure is expected, due to use and emission patterns, but the chemical is readily biodegradable and not bioaccumulative
Low exposure concern	No human exposure *And* No wildlife exposure

4. Results of the Data inventory and evaluation (Task 3)

4.1 STEP 1: Selection on HPV and/or persistency and/or exposure

At the stakeholder meeting of March 2002, it was decided to prepare a second selection of substances from the working list to be evaluated by the experts. It was recommended to use production volume and/or persistence and expected exposure as selection criteria. An overview of the results of this step with reference to the number of substances is given in Table 2

Table 2: Selection of chemicals from the list of 435 substances

Selection criteria*	**No. substances**
Persistent chemicals: widened QSAR criteria	136
Production volume: plant protection products (PPP), biocides and others on ECB list HPV (chlorinated paraffins)	 20 3
Substances reported upon the first or second inquiry for monitoring data February/July 1998. Derived from Annex 1 of the COMMPS report (1999)	14
PPP under evaluation for directive 91/414/EEC (SANCO list)	13
HPV or persistent substances with insufficient data (derived from the BKH 2000 report)	18
Subtotal: second cut substances	***204***
- Undefined chemicals and mixtures - Polymers - Remaining not HPV, not persistent substances	14 26 172
Subtotal: substances that did not meet step 1 selection criteria	***212***
- Excluded double inputs, substances that were two times in the list - Excluded group names - Excluded phytoestrogens	4 13 2
Subtotal: excluded substances	***19***
Total	***435***

* Grouping of chemicals is depicted in annex 4 and annex 5, excluded chemicals are listed in annex 10

The 204 evaluated substances from the list of 435 consisted of 186 newly selected substances plus 18 substances (with insufficient data) selected from the BKH 2000 study. Most of the substances were pesticides (114), others were industrial chemicals or by-products (90).

Considering the expected exposure, LPV plant protection products were included in the list. This criterion has not been used for LPV industrial chemicals.

The group of 212 substances that did not meet step 1 selection criteria were not further investigated on ED-effects and exposure concern. However, this group contains at least 34 chemicals that are closely related to substances that in the second selection step were classified as category 1. Due to their similarity to Category 1 substances, these 34 chemicals might also exert endocrine disruptive effects. The latter symbolises the need for further investigation on ED effects of the entire group of 212 substances that did not meet the step 1 selection criteria.

The group of undefined chemicals includes chemicals from which the names could not be retrieved through CAS No or which are complex (reaction)mixtures.

4.2 STEP 2: Evaluation of ED-related effects

Data gathering

Literature and a number of other sources as well as industry were consulted to obtain information on Endocrine disruption Effects and systemic toxicity. Eventually, industry provided information on 6 substances. All information from these sources was evaluated and incorporated in the EDS database. The complete EDS database contains a total of 2,839 records on Human Health relevant effects data of which 1,257 records are ED related. For Wildlife relevant effects a total of 1,218 records are available in the database of which 327 records are ED related.

For the 204 substances evaluated in this report Human health ED-related data are available on 150 substances, whereas Wildlife ED-related data are available on 37 substances. When systemic toxicity data are included then Human health relevant and Wildlife relevant data are available for 174 and 120 substances, respectively. Endocrine effects on human health range from for example effects on the weight of sex-organs, effects on sperm development and vaginal opening to altered hormone levels, synthesis or -binding. Endocrine effects observed in wildlife included aspects like reduced fertility, masculisation/feminisation, skewed sex ratios, sex reversal as well as altered levels, synthesis or binding of hormones.

Results of EDS Expert Meeting of 9-10 September 2002

A two-days meeting on which participants contributed with their expertise on endocrine disruption, was held to evaluate the scientific data available. During the meeting experts pointed out that several important references on the endocrine disrupting behaviour of different substances on the candidate list were missing. To complete information on the ED-effects of the compounds involved, experts agreed on providing RPS BKH Consulting Engineers with the lacking references. This "additional evidence" on endocrine disruption was also incorporated in the database. A summary of all Human Health and Wildlife relevant endocrine disruption effects data (included in the database) on substances evaluated by the experts, is presented in Annex 6 and 7. A reference list of ED relevant publications and reports in the database is given in Annex 8. In Annex 9 the results of categorisation and qualifying remarks in the expert meeting are presented. In Table 3 a summary of these results is presented.

Table 3 The summarised results of the EDS Expert Meeting 2002 (EM 2002) and combined results: number of substances in category 1, 2 or 3 (a or b).

Category	Definition	EM 2002	Overall*
CAT1	At least one study providing evidence of endocrine disruption in an intact organism. Not a formal weight of evidence approach.	94	160
CAT2	Potential for endocrine disruption. In vitro data indicating potential for endocrine disruption in intact organisms. Also includes effects in-vivo that may, or may not, be ED-mediated. May include structural analyses and metabolic considerations	53	105
CAT3a	No scientific basis for inclusion in list	19	19
CAT3(b)	Substances with no or insufficient data gathered.	38	250*
Total		***204***	***534****

* Includes 212 substances that did not meet step 1 selection criteria and hence were not subject to further investigation.

**:19 out of the total of 553 chemicals were excluded, as these entries on the list were referring to group names of chemicals already on the list (see Annex 10).

As a result of the expert meeting 94 substances were classified as Category 1 chemicals. Eventually these were combined into 41 groups each containing 1 up to 28 chemicals (31 groups solely contain 1 chemical, 10 groups contain more than 1 chemical). The larger groups in this respect were PCBs (28 chemicals), DDT and derivatives (18 chemicals) and Polycyclic Aromatic Hydrocarbons (5 chemicals).

During the 2002 expert meeting the following remarks were made:

- The experts emphasized that the observation of thyroid tumours in a test is not sufficient for classifying a substance in Category 1. If no additional data exist, the substance was placed in Category 3b.
- Several working parties questioned the presence of benomyl on the list, due to the fact that its mechanism of action is already known (male reproductive toxicity).

- The presence of the oral contraceptive drug mestranol on the list was questioned. In a later stage, information obtained from the pharmaceutical industry indicated that mestranol is in fact the active ingredient of the contraceptive drug and as such has already been dealt with in the WRc report 2002.
- Human health experts selected category 1 substances on a wide range of endocrine disrupting effects as presented in Table 4.4a. The main effects were effects on uterus-, testes- or other sex organ weights, effects on sperm development, vaginal opening and effects on thyroid hormone levels or synthesis.
- Information on Wildlife ED effects was relatively scarce. An overview of the identified key ED effects are presented in Table 4.4b.
- For some substances epidemiological studies have been used as evidence such as dibromoethane, 2,4-DB, PCB138 and PCB180.
- It was put forward that industry did not provide existing ED-related information on for example polyethoxylates.

Table 4a Examples of Endocrine Disruptive effects observed of Category 1 substances, Human Health relevant data

CASno	NAME	ED EFFECT
63-25-2	Carbaryl	affected spermatocytes; increased estral cycle; decreased thyroid function; inhibition of acetylcholine esterase; prolonged estrus cycle; changes pituitary & thyroid
789-02-6	o,p'-DDT	uterine expression of progesterone and lactoferrin receptors
53-19-0	o,p'-DDD	paternal effects - spermatogenesis (incl. genetic material, sperm morphology, motility, and count)
72-54-8	p,p'-DDD	uterine expression of progesterone and lactoferrin receptors
72-55-9	p,p'-DDE	altering expression of androgen-dependent genes
14835-94-0	o,p'-DDMU	increased uterine glycogen content
2971-22-4	1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane	increased uterine glycogen content
32809-16-8	Procymidon	reduction in ano-genital distance; altered reproductive development.
72-43-5	Methoxychlor	accelerated maturation
52918-63-5	Deltamethrin	decreased weights of testis and pituitary. decreased weight of genital organs; increase in percentage dead and abnormal spermatozoa; decreased plasma testosterone concentration and fertility
10453-86-8	Resmethrin	reduced prostate weight; thyroid changes
60168-88-9	Fenarimol	decreased mounting
8018-01-7	Mancozeb	decreased bodyweight, organ toxicity; thyroid hypertrophy
9006-42-2	Metiram (Metiram-complex)	decreased T3 and T4; increased thyroid weights; thyroid follicular cell hyperplasia
21087-64-9	Metribuzin	enlarged thyroids
87-86-5	Pentachlorophenol (PCP)	decreased plasma T4 and T3 levels. decreased concentrations free T3 and T4 plus T4/T3 quotient.
122-14-5	Fenitrothion	weights of accessory glands
91465-08-6	Cyhalothrin (@Karate)	significant suppression T3 and T4; concomitant stimulation of TSH
82657-04-3	Bifenthrin (@Talstar)	significant suppression T3 and T4; concomitant stimulation of TSH
65277-42-1	Ketoconazol	suppression of sex steroids and lowering of testosterone levels
1689-83-4	Ioxynil	reduced body weight gain, liver (hypertrophy and enzyme induction). thyroid hyperactivity.
106-93-4	Dibromoethane (EDB)	decreased sperm velocity and semen volume; decreases percentage motility and amplitude of lateral head displacement
94-82-6	2,4-dichlorophenoxy-	increased cancer of the testicle, thyroid, other endocrine

CASno	NAME	ED EFFECT
	butyric acid = 2,4-DB	glands, nose and nasal cavity
106-89-8	Epichlorohydrin (1-chloro 2,3-epoxypropane)	induced antifertility effects; % fertilised ova; reduced number of sperm heads
1918-02-1	Picloram	induced thyroid tumours; increased number of neoplasms in endocrine organs, thyroid gland, pituitary, mammary glands and reproductive organs; increased atrophy of the testes
886-50-0	Terbutryn	stimulation of T3 synthesis, inhibition of T4 synthesis, increased synthesis of LH in the hypophysis and decreased secretion of LH in the serum
12002-48-1	Trichlorobenzene	histological changes in thyroid of male rats
608-93-5	Pentachlorobenzene	decreased levels of plasma T3 and T4
85535-84-8	Short chain chlorinated paraffins	increased incidence of thyroid follicular cell adenomas and carcinomas; thyroid hypertrophy and increased activity of thyroxine-UDPG-glucuronosyltransferase
85535-85-9	Intermediate chain chlorinated paraffins	reduction in plasma T4 levels and increase in plasma TSH levels; decreased hepatic vitamin A levels and histopathological changes in thyroid
84-61-7	Dicyclohexyl phthalate	testicular damage
84-66-2	Diethyl phthalate (DEP)	decreased sperm concentration and number of live pups per litter; decrease in live pups per litter and decrease in sperm concentration (F1 generation); fertility/reproductive performance
84-66-2	p-Benzylphenol	increased uterine glycogen content
No CAS 087	PCB138 2,2',3,4,4',5'-hexachlorobiphenyl	association blood concentrations of PCB's with thyroid hormone status as part of exposure to a toxic waste incineration plant
No CAS 088	PCB180 2,2',3,4,4',5,5'-heptachlorobiphenyl	association blood concentrations of PCB's with thyroid hormone status as part of exposure to a toxic waste incineration plant
7012-37-5	PCB 28 (2,4,4'-trichlorobiphenyl)	decreased serum T4 levels at weaning; histological changes in thyroid and liver
2971-36-0	1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (HPTE)	binding to the androgen receptor
8068-44-8	Clophen A50	delayed vaginal opening in females and decreased testis weight
12642-23-8	PCT Aroclor 5442	increased uterus glycogen content
56614-97-2	3,9-Dihydroxybenz(a)-anthracene	increased uterus weight
7099-43-6	5,6-Cyclopento-1,2-benzanthracene	cornification of vaginal epithelium
50-32-8	Benzo[a]pyrene	cornification of vaginal epithelium
56-49-5	3-Methylcholanthrene	reproductive maternal effects ogenesis
57-97-6	7,12-Dimethyl-1,2-benz(a)anthracene	"reproductive effects on newborn live birth index reproductive effects on newborn germ cell effects"
118174-38-2	6-Methyl-1,3,8-trichlorodibenzofuran	decreased estrogen & progesterone receptors content in uterus
50585-41-6	2,3,7,8-TeBDD	increased relative testis weight; reduced thyroid hormone concentrations; affected spermatogenesis; defective or necrotic spermatocytes in epididymis
72-33-3	Mestranol	reproductive fertility other measures of fertility

Table 4b Examples of Endocrine Disrupting effects observed of Category 1 substances Wildlife relevant data

CASno	NAME	ED EFFECT
5103-73-1	Cis-Nonachlor	*turtles*: sex reversal
39765-80-5	Trans-Nonachlor	*turtles*: sex ratio, affect circulating steroid hormone concentration; Sex reversal
789-02-6	o,p'-DDT	*fish*: stimulated vitellogenin synthesis; *gulls:* feminized males
72-55-9	p,p'-DDE	*gulls*: feminized males
319-85-7	Beta-HCH	*fish:* induced vitellogenesis, excessive vitellogenin production and hermaphrodites
72-43-5	Methoxychlor	*fish:* fecundity and vitellogenin induction *gulls:* feminized males;

In Annex 11/12 an overview is given of the systemic toxicity data and ED effects data of category 1 substances.

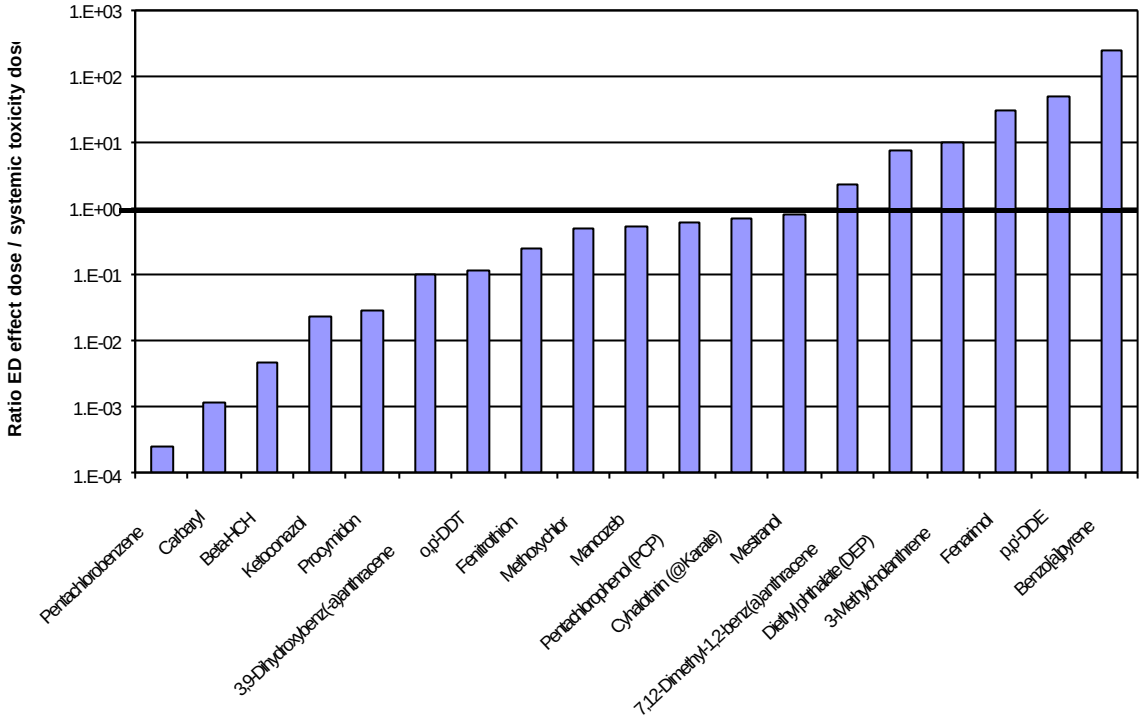
As an indication of the relevance of the ED effects observed in Category 1 substances, two types of comparisons are made:

1. Comparison between ED-effect doses and effect doses, which are related to systemic toxicity for Category 1 substances.
2. A comparison between ED-effect of Category 1 substances and an ED-effect induced by the natural ligand 17-β-estradiol in vivo in rats. This results in a ratio which can be considered as a "ED potency" level of the compound related to 17-β-estradiol.

For this purpose in both cases effect doses/concentrations were converted to (Molar) concentrations in food applying standardised bodyweights and intake values.

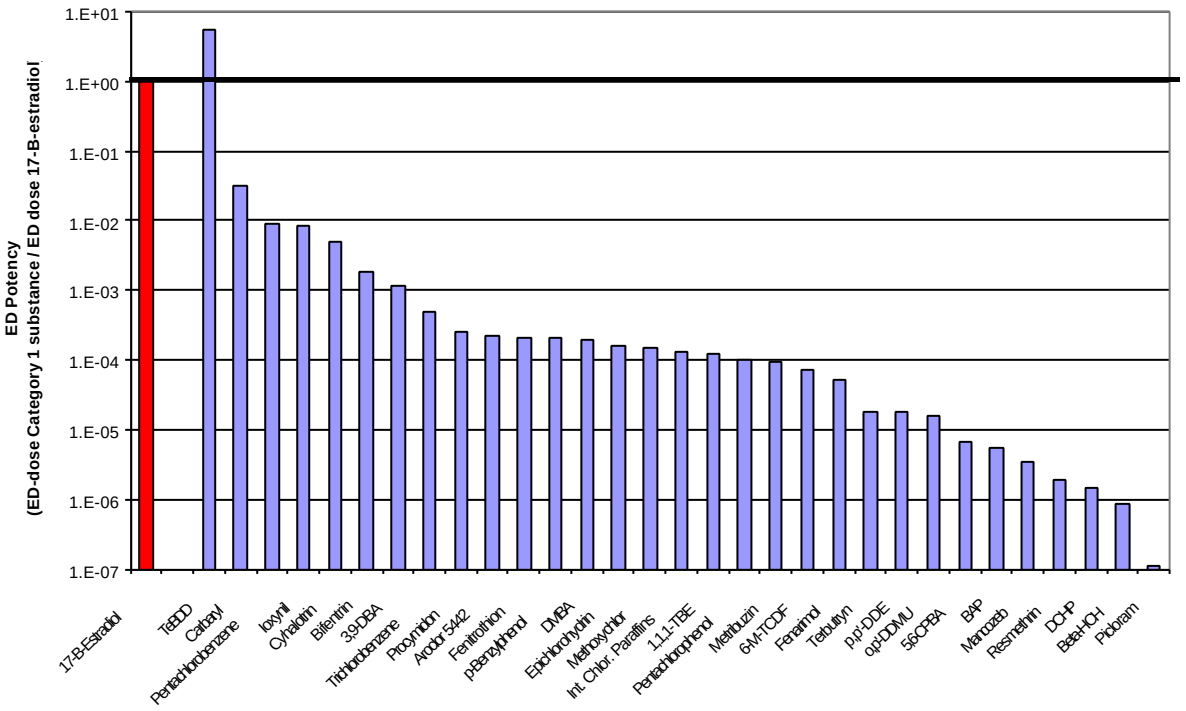
Most levels reported for ED-effects are below those reported for systemic toxicity (figure 3)

Figure 3: Ratio between ED-effect dose and systemic toxicity for Category 1 substances (based on human health relevant data).



Considering "potency" levels, only for dioxin ED-effects have been reported around the same concentration as 17-β-estradiol. For all other Category 1 substances ED effects are far below those induced by 17-β-estradiol. It should be emphasised, however, that a direct comparison is not conclusive due to differences in test systems, test species, life stages, effects parameters and exposure periods (Figure 4).

Figure 4 Potency of category 1 substances in relation to the effect observed for 17-β-estradiol



4.3 STEP 3: Evaluation of exposure concern to human and wildlife

The category 1 chemical groups (40 excluding mestranol, which is evaluated in the WRc report) with evidence for endocrine disrupting effects were evaluated in greater detail concerning exposure. Closely related substances were handled together in one summary profile. The summary profiles give an overview of the physical and chemical properties, bioaccumulating potential and degradation in the environment, as well as an overview of the use, production volumes, emissions and monitoring data. Based on this information a conclusion is given on the exposure concern this chemical group presents. The summary documents are given in Annex 13. In Table 5 the results of the detailed evaluation is summarised.

Table 5 Number of substances with high, medium or low exposure concern*

	High concern Substances (groups)	Medium concern Substances (groups)	Low concern Substances (groups)
Number of chemicals/ chemical groups	84 (34)	5 (5)	4 (1)

** Mestranol is not included in this table as it is dealt with in the WRc report.*

Of the 34 chemical groups that have been categorised as having high concern for exposure, chemical groups such as chlorinated paraffins, phthalates and octylphenols are included. Other chemcial groups are PAHs, PCBs, PCTs, dioxins and furans. The largest number of groups included the plant protection products and biocides such as HCHs, pyrimidine fungicides and pyrethroids. Mestranol as synthetic contraceptive drug has been excluded from the working list. For some substances more quantitative information on exposure has been retrieved, such as calculated predictive environmental concentrations (PECs) as for chlorinated paraffins, procymidon, ioxynil, mancozeb, 2,4-dichlorophenoxy-butyric acid. In table 6 a summary of the information is categorised per chemical group with high, medium and low exposure concern.

Table 6: Information on chemical groups with high, medium and low exposure concern.

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
Bifenthrin	High		Insecticide and acaricide against foliar pests used on food crops	Workers; Food, treated crops	As a consequence of its application as a insecticide / acaricide	Poor	Readily bio-degradable	Moderately bioacumulative (fast metabolism and rapidly degraded)	No	No data	
2,2-BPPP / BADGE	High		Probably an impurity in BADGE	Production workers; Food (cans lined with BADGE coatings); Cosumer products (glue)	As a result of production and at waste stage	Moderate	Inherently bio-degradable	Not bioaccumulative	No	No data	
Carbaryl	High	LPV	Pesticide used on cotton, food crops, ornamental trees, shrubs, animals and livestock.	Workers; Contaminated air	As a conse-quence of its application as a pesticide	Good	Readily bio-degradable	Not bioaccumu-lative (Rapid biodegradation and metabolism)	Yes	In air (after spraying), water and soil due to all year use	
Chloro paraffins, interme-diate chain	High	HPV	Plasticers in PVC; Additives in paint, rubber, sealants, flame retardants and extreme pressure fluids	Various ways of exposure through presence in consumer goods	As a result of production or at waste stage	Poor	Persistent	Highly bioaccumulative	Yes	Yes, all environmental compartments	
Chloro paraffins, short chain	High	HPV	Additives in metal working fluids, sealants, rubber, textiles (as flame retardants), leather processing, paints and coatings	Various ways of exposure through presence in consumer goods	As a result of production or at waste stage	Poor	Persistent	Highly bioaccumulative	Yes	Yes, all environmental compartments	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
(Lambda)-Cyhalotrin	High		Pesticide used to control public- and animal health (parasites, flies, ticks, cockroaches etc.) but also used on food crops	Workers: Homes and workplaces during pest control; Food, treated crops	As a consequence of its application as a pesticide	Poor	Moderately persistent	Moderate bioaacumulation expected (fast metabolism and rapidly degraded)	Yes	Rarely. Levels are expected to be low considering low use pattern and low application rates Some fruits	
DCHP	High	HPV	Plasticiser in nitrocellulose, rubbers, PVC etc. Constituent of paper finishes and ink.	Various ways of exposure: Food (through packaging), toys and baby bottles, plastic incineration; Production workers	As a result of production and at waste stage	Poor	Readily bio-degradable	Hardly bioaccumulative (fast metabolism and rapidly degraded)	Yes	Rarely	Other phthalates however are frequenly reported in water, suspended matter, soil and biota)
DDT	High	zero	Insecticide against malaria forbidden in EU, USA and Japan but still used in some countries	Widespread persistence in environment, biota, mother milk and food	Widespread persistence in environment and biota	Poor	Persistent	Highly bioaccumulative	Yes	Yes	
Delta methrin	High		Pesticide used on food crops, storage protection, in public heatlth (e.g. malaria) and animal facilities (cattle infection)	Workers: Food, treated crops; Disease control	As a consequence of its application as a pesticide	Poor	Readily bio-degradabale	Moderately bioaccumulative (fast metabolism and reduced bioavailability)	Yes	Rarely	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
DEP	High	HPV	Wetting agent; Solvent in varnish, insecticidal sprays and repellants; Plasticiser in polystyrene; Fixative in perfumes; Denaturation of alcohol in desinfective soaps; Dye carrier	Various ways of exposure: Food (through packaging), toys and baby bottles, cosmetics, glue, insect repellants, plastic incineration; Production workers	As a result of production and at waste stage	Good	Readily bio-degradable	Hardly bioaccumulative (metabolised)	Yes	Yes in suspended matter, water, sediment, air and fish	
Epichlor hydrin	High	HPV	Raw material in e.g. elastomer production; Insect fumigant; Sporicide; Solvent (e.g nail varnish, paint and gums); (Heat)stabiliser in plastics and chlorine containing material.	Use of consumer goods (e.g. nail varnish and paint); Production workers	Application as insect fumigant and at production and waste stage	Very good	Readily bio-degradable	Not bioaccumulative	Yes	Solely in vincinity of production sites.	
Fenarimol	High		Fungicide against powdery mildew used on food crops, flowers, lawns and golfcourts	Workers; Food, treated crops	As a consequence of its application as a herbicide	Moderate	Persistent	Moderate Bioaccumulation expected (rapid excretion observed	No	No data, but expected to be present (persistent and accumulative)	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
Fenitrothion	High	LPV	Insecticide used on food crops and cotton as well as in public health programmes or indoor use	Workers; Food, treated crops; Indoor use (flies, cockroaches)	As a consequence of its application as a insecticide	Poor	Readily bio-degradable	Moderate bioaccumulation expected (fast metabolism and rapidly degraded)	Yes	Yes in water, sediment and soil	
HCH	High	HPV	Insecticide used on seed and soil before food crops are planted	Long range transport seen; found in fish (food)	Through wastewater at production and through application on soil and seeds	Poor	Inherently bio-degradable	Highly bioaccumulative	Yes	Yes, biota (fish), water systems	Other uses (e.g. foliar spraying) voluntarily banned in order to minimise volatalisation
Iso octylphenol	High	HPV	Raw material used in detergents, emulsifiers, wetting and dispersion agents, paints, anti-oxidants, pesticides and PVC Spermicides in contraceptive foams	Use as surfactants which are released to waste water after being used for cleaning purposes	At production and use as surfactant at the waste stage. As a result of isooctylphenol ethoxylate degradation under anaerobic conditions (sewage treatment, anaerobic sediment).	Poor	Inherently bio-degradable	Expected to bioaccumulate	yes	Yes in water, sediment, soil and biota	Biodegradation products of APEOs

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
Ketokonazol	High		Therapeutic antifungal drug applied to humans and animals (tablets, shampoo or creams)	Therapeutic drug for fungal diseases.	When washed away (shampoo, cream) or excreted in urine or faeces	Poor	Persistent	No data (Metabolisation in liver)	No	No	Solely a few procent of the administered parent compound will be excreted in faeces
Mancozeb	High		Fungicide used on food crops	Food, treated crops	At production and application (wastewater)	Poor	Degraded to metabolites e.g. ETU	Not bioaccumulative	No	No, but the metabolites ETU has been found	
Methoxychlor	High		Insecticide used on food crops, flowers, in households (spray), animal houses and dairies.	Food (treated crops) or contaminated drinking water; Household use; Workers	As a consequence of its application as a pesticide	Poor	Persistent	Highly bioaccumulative	Yes	Yes, in air, groundwater and biota	
Methoxychlor derivatives	High	zero	Formed as a result of methoxychlor degradation	Food (treated crops) or contaminated drinking water; Household use; Workers	As a consequence of methoxychlor application as a pesticide	Poor - moderate	Persistent	Highly bioaccumulative	No	No data, but expected to be rarely measured.	
Metiram	High		Fungicide used on food crops	Food, treated crops	At production and application (wastewater)	Poor	Degraded to metabolites e.g. ETU	Not bioaccumulative	No	No, but the metabolites ETU has been found	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
Metribuzin	High		Herbicide against various grasses and broad-leeved weeds used on food crops	Food (treated crops) or contaminated drinking water; Workers	As a consequence of its application as a herbicide	Very Good	Moderately persistent	Not bioaccumulative	Yes	Yes, mainly in water compartments including drink water.	
Nonyl phenol ethoxylate	High	HPV	Non ionic surfactant, detergent and wide range stabiliser (e.g. leather, textile and polymer industry, paints and wetting agents for agricultural chem.)	Emission at production- and application related waste streams	At production and application (wastewater)	Good	Low persistent	Hardly bioaccumulative (species dependent)	Yes	Yes in both water and sediment	In the EU voluntarily banned from household cleaning products
4-octyl-phenol	High	HPV	Raw material used in non ionic surfactants, as plasticiser, antioxidant, fuel oil stabiliser and as intermediate for resins, fungicides, bactercides, dyestuffs, adhesives and rubber chemicals	Use as surfactants which are released to waste water after being used for cleaning purposes	At production and use as surfactant at the waste stage. As a result of octylphenol-ethoxylate degradation under anaerobic conditions (sewage treatment, anaerobic sediment)	Poor	Inherently bio-degradable	Expected to bioaccumulate	Yes	Yes in water, sediment , soil and biota	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
PAHs	High	zero	Formed during combustion and heating processes (fossil fuels; volcanoes; wood burning; smoking; traffic; waste incineration; power plants; metal processing, foundries, tire production etc.); Biochemical research	Food, (contaminated, smoked, roasted, charbroiled); Air, (tobacco, vehicle traffic, residential heating); Workers	Exposure through industrial, natural and consumer combustion and heating processes at waste stage.	Poor	Persistent	Highly bioaccumulative	Yes	Yes, in air, water, sediment, soil and biota	DMBA + 3-MC were categorised as low concern due to their restricted use in closed systems
PCBs	High	zero	In the past used in electrical equipment, heat-transfer systems, hydraulic systems, in plastics, coats, glues, paints etc.; PCB are severely restricted and banned; still available through existing products	Food (fish) and mother milk Emission through the waste stage	Emission at production and at the waste stage	Poor	Persistent	Highly bioaccumulative	Yes	Yes in biota, humans and mother milk	Although severely restricted and banned, exposure is still expected due to persist properties and long range atmospheric transport (LRAT).
PCDDs / PCDFs	High	zero	Formed during combustion (municipal waste incineration), metal production, paper and pulp production, chlorophenols and herbicides	Exposure through emission at production and at waste stage (incineration); Food and mother milk	Exposure through emission at production and at waste stage (incineration)	Poor	Persistent	Highly bioaccumulative	Yes	Yes in food (fish, meat, dairy products) and mother milk	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
PCTs	High	zero	In the past used in fire retardants, electrical equipment, heat-transfer systems, hydraulic systems, iplastics, waxes, coatings, glues, paints, insecticides etc.; PCTs are severely restricted and banned; still available through existing products	Food (fish) and mother milk; Emission through the waste stage	Emission at production and at the waste stage	Poor	Persistent	Highly bioaccumulative	Yes	Yes in biota, humans and mother milk	Although severely restricted and banned, exposure is still expected due to persist properties and long range atmospheric transport (LRAT)
p-benzyl phenol	High		Germicide, antiseptic, preservative	Workers	As a result of production and at waste stage	Moderate	Moderately persistent	Hardly bioaccumulative	No	No data	
Penta chloro benzene	High	zero	In the past used as a fungicide, in dielectric fluids, and as an intermediate in the production of the pesticide pentachloro-nitrobenzene (PNB)		Emission at production and at the waste stage	Poor	Persistent	Highly bioaccumulative	Yes	Yes, suspended matter, sediment, soil and air	Although severely restricted exposure is still expected due to persistence and LRAT. Degradation product of persistent fungicide HCB (banned in EU but redistributed via LRAT)

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
Penta chloro phenol	High	LPV	In the past used as a pesticide, wood preservative and in handling of textile and leather Severely restricted in US and EU	Workers	Waste stream of wood treating facilities, saw mills and waste incineration facilities.	Poor	Readily bio-degradable	Highly bioaccumulative	Yes	Yes, suspended matter, sediment, soil and air	
Procymidon	High		Fungicide used on food crops	Workers; Food, treated crops	As a consequence of its application as a fungicide	Poor	Persistent	Highly bioaccumulative	Yes	Yes, soil, sediment and suspended matter	
Resmethrin	High		Insecticide against pests used in agriculture horticulture, households and public health	Workers Household use (pet sprays, pet shampoos, insect control)	As a consequence of its application as an insecticide	Poor	Expected to be readily bio-degradable	Moderate bioacumulation expected (fast metabolism and rapidly degraded)	No	No data	
TBDD	High	zero	Formed during manufacturing of brominated organic chemicals e.g. flame retard-ants, pesticides and solvents	Exposure thro-ugh emission at production and at waste stage (incineration); in food and mother milk	Exposure through emission at production and at waste stage (incineration)	Poor	Persistent	Highly bioaccumulative	Yes	Yes in air, soil, and sediment but often below detection limit	
Trichloro benzene	High		Chemical interme-diate; Additive in dyes; dielectric fluids, lubricating oils and heat trans-fer media; Degrea-sing solvent; In the past used as an insecticide	Contaminated food and drinking water; Workers	Emission at production and at the waste stage	Poor	Persistent	Highly bioaccumulative	Yes	Yes in air, water, soil, fly ash and biota.	Also formed as an impurity during production of monochloro benzene

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
2,4-DB	Medium		Herbicide against broad-leaved weeds mainly used on grasslands and barley.	Workers	As a consequence of its application as a herbicide	Very good (pH = 7)	Readily bio-degradable	Not bioaccumulative (rapid biodegradation)	Yes	Rarely. Highly degradable	Due to production proces dioxin contamination is observed
EDB	Medium	HPV	In the past used as a scavenger in leaded gasoline and as a fumigant. Nowadays solely used in manufacturing of pharmaceuticals, polymers and as a solvent in resins, waxes, gums and dyes	Workers Formerly from spills of gasoline and traffic exhaust	Accidental spills from its use as a solvent.	Moderate	Moderately bio-degradable	Hardly bioaccumulative	Yes	Yes, in air and groundwater but mostly as a consequence of former use as a fumigant and in leaded fuel	Naturally produced by various algae Primary source of leaded fuels is restricted
Ioxynil	Medium		Herbicide against broad-leaved weeds used on food crops and lawns	Workers	As a consequence of its application as a herbicide	Moderate	Readily bio-degradable	Not bioaccumulative (Rapidly eliminated)	Yes	Rarely. (Rapidly degraded to benzamide and benzoic acid metabolites)	
Picloram	Medium		Herbicide against broad leaved weeds and woody plants used on grass land, forests and non-crop areas.	Workers	As a consequence of its application as a herbicide	Good	Moderately persistent	Not bioaccumulative (rapidly excreted)	Yes	Yes, both terrestrial and aquatic compartment	
Terbutryn	Medium	LPV	Herbicide against various broad leaved weeds used on food crops	Workers	As a consequence of its application as an insecticide	Poor	Readily bio-degradable	Hardly bioaccumulative	Yes	Yes in water	

Substance	Concern	HPV	Concerned use	Human exposure	Wildlife exposure	Soluble	Persistent	Bio-accumulation	Mea-sured	Observed in environment	Remark
Nonachlor	Low	zero	Constituent of the broad-spectrum insecticide chlordane (mostly non-food crops). Forbidden in US and EU		Phase out of the chemical present in immoblile sinks; no long range air transport	Poor	Persistent	Highly bioaccumulative	Yes	Yes in food (fish) and mother milk	Should be checked if nonachlor is still found in mother milk.

5. ITERATIVE MECHANISM TO INCLUDE/EXCLUDE SUBSTANCES ON / FROM THE CANDIDATE LIST (TASK 4)

The methodology defined in Task 2 has been applied to the candidate list of 435 substances. Inclusion and exclusion of chemicals from the list rely on scientific evidence on which stakeholders support to take decisions.

The work of RPS BKH concentrated on the pre-selection of substances with (potential) evidence of ED effects. In those cases where selected substances are not being addressed under existing community legislation, which (in future) is or will be linked to ED testing, an in-depth evaluation is carried out (WRc study). An iterative mechanism can be followed in case new evidence on substances comes available.

On basis of our present knowledge of the process, in future studies on endocrine disruption the following procedure is proposed (see Figure 5). This procedure can be applied in an iterative way for every new substance suspected of endocrine disruptive behaviour. This new substance can originate either from the general "universe of chemicals" or from substances already on the list for which new scientific evidence has been found. The following elements for the procedure can be taken up:

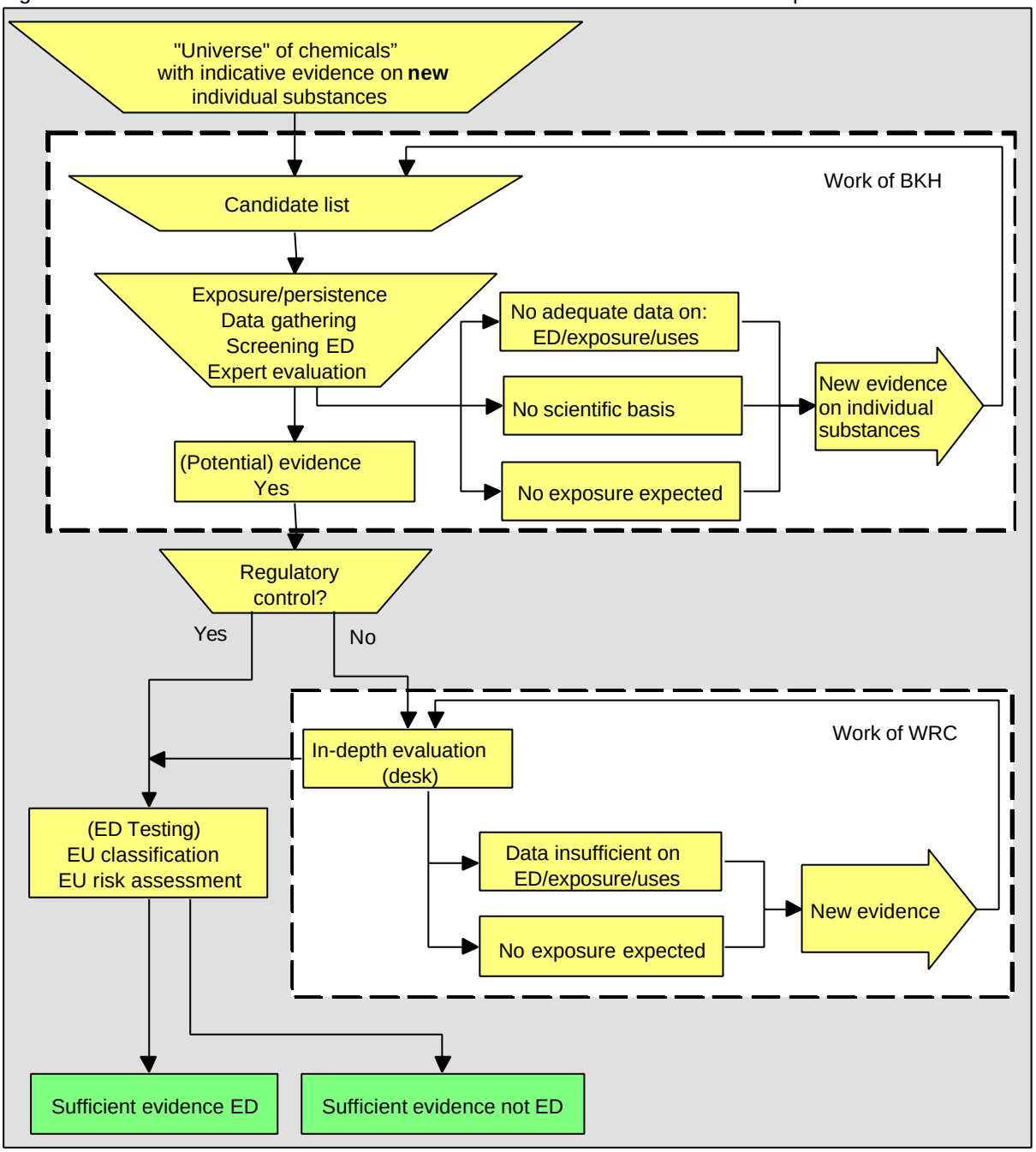
Candidate list update
Inventory of possible new substances for the candidate list and proposals for exclusion of chemicals from the list (literature search and contacts with experts).

Expert Meetings – Data evaluation
A. Prepare an expert meeting with a focus on analysing the existing candidate list;
B. Give experts / stakeholders the opportunity to send in new candidates and add existing scientific evidence;
C. Carry out an additional literature search and request for additional information from industry and other stakeholders;
D. Adapt the EDS database with scientific evidence for the selected chemicals and prepare a second expert meeting to evaluate the available ED and systemic toxicity evidence;
E. Carry out an initial assessment of the category 1 chemicals.

Regulatory control
Gathering information on regulatory control of category 1 chemicals, which (in future) is linked to ED testing.

In depth evaluation
Prepare a stakeholder meeting to discuss the results of the former steps and future activities. In this step it may be decided whether an in-depth evaluation of a chemical is obligatory.

Figure 5. Scheme for the evaluation of chemicals in relation to Endocrine Disruption.



6. CONCLUSIONS AND RECOMMENDATIONS

6.1 Conclusions

The imposed threat of compounds interfering with hormonal systems, also designated as endocrine disrupters, to various ecosystems and human health urged the EU Commission to come up with a strategy regarding substances associated with endocrine disruptive behaviour. In December 1999, the European Commission published a Community Strategy for Endocrine Disrupters (COM(1999)706) in which it announced its intention to establish a priority list of substances for further evaluation of their role in endocrine disruption.

In June 2000, BKH Consulting Engineers (NL), under contract of the Commission, prepared a report entitled "Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption". The results of this report, referred to as "BKH report 2000" identified 118 HPV man made chemicals out of a candidate list of 553 substances, showing scientific evidence associated with endocrine disruptive effects. For 109 of these high priority substances bans or restrictions measures already existed under Community legislation, whereas for the other 9 more in depth studies were necessary (WRc Study).

The activities of the present study carried out in the period 15 November 2001 to 15 November 2002 have strongly built upon and are partly a follow-up of BKH 2000 report and focuses on the remaining 435 compounds from the initial candidate list. This study is a part of the short-term strategy on endocrine disruption proposed by the EU. For a more detailed account of the context of both of these studies, the reader is referred to Commission document COM(2001)262 of 14 June 2001 on the implementation of the Community Strategy for Endocrine Disrupters. Although being a follow-up study this project is still to be considered as a first step towards the establishment by the Commission of a priority list of substances for further evaluation of their role in endocrine disruption.

The general objective of the present study has been to define a methodology by which to investigate these remaining 435 candidate substances (identified in the BKH Report 2000) with a view to establishing priorities for further evaluation of the role of these substances in endocrine disruption. In this respect the earlier work done in the context of the Community Strategy for Endocrine Disruption has been reviewed and subsequently a methodology to establish priorities has been defined. In accordance with the methodology data were gathered for the 435 substances and furthermore an iterative mechanism was developed by which new substances may be included or existing substances removed from the candidate list of substances as new evidence comes to light.

Gathered data on the 435 substances together with the data gathered in the BKH study 2000 were incorporated in the EDS database, as an interactive database. This database contains details on and gives an overview of ED effects and systemic toxicity of all substances of the candidate list. Furthermore, the EDS database was applied as a tool for evaluations (categorisation) of chemicals by experts on Endocrine Disruption as part of the developed multi-step approach. The evaluation process itself consisted of three steps. In table 7 and Figure 6 the results are given of the outcome of the various steps.

Table 7 Multi-step approach to establish a priority list of substances for further evaluation of their role in Endocrine Disruption

Step	Description		Results
1	Selection of substances from the list of 435, based on production volume and or persistence and expected exposure	204	HPV chemicals / LPV pesticides / Persistent chemicals / COMMPS chemicals / Insufficient data (BKH 2000)
2	ED and systemic toxicity; incorporation of ED information in a database and evaluation by experts	94	with evidence for endocrine disruption in a living organism
3	Preliminary evaluation of exposure to humans and wildlife	84	with expected high exposure concern

Step 1: In the study 204 chemicals of the 435 are to be considered HPV and persistent and/or chemicals for which environmental exposure is expected. Of the 231 remaining chemicals, 172 chemicals were neither HPV, persistent nor had expected exposure concern. A number of 40 chemicals involved complex polymers or could not be defined properly. The remaining 19 chemicals were excluded because it involved group names, double inputs or phytoestrogens.
Step 2: A number of 94 out of the 204 chemicals were identified as category 1 chemicals (evidence for endocrine disruption in a living organism) whereas 53 others were categorised as potentially endocrine disruptive. For 19 chemicals, ED study results indicated that there was no evidence for endocrine disruptive behaviour. For the remaining 38 substances no or insufficient results involving endocrine disruption were available.
Step 3: After a detailed evaluation 84 category 1 chemicals were considered as having a high exposure concern, 5 having medium exposure concern and 4 having low exposure concern.

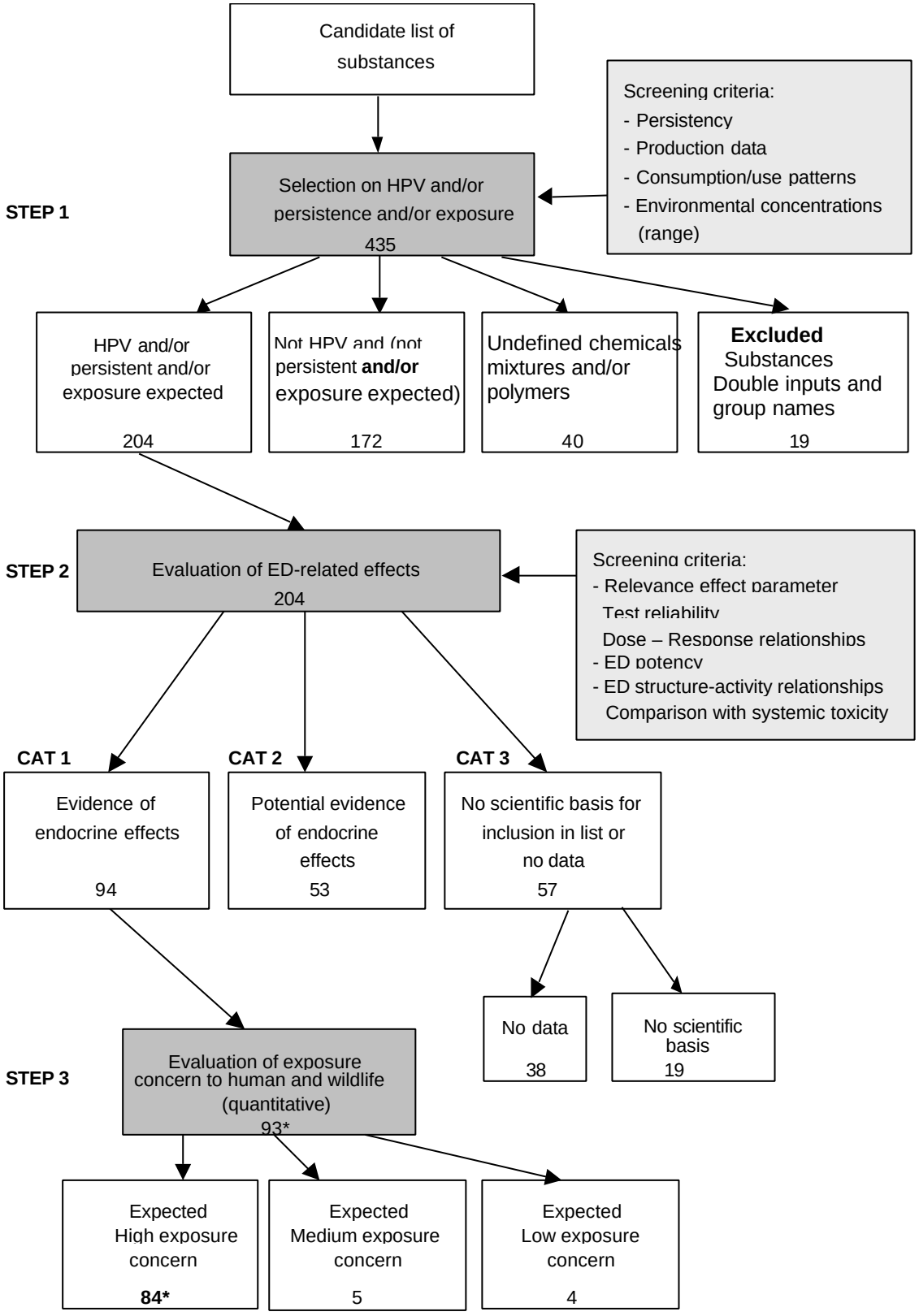
As an indication of the relevance of the ED effects observed in Category 1 substances, two types of comparisons are made:

1. Comparison between ED-effect doses and effect doses, which are related to systemic toxicity for Category 1 substances.
2. A comparison between ED-effect of Category 1 substances and an ED-effect induced by the natural ligand 17-β-estradiol in vivo in rats. This results in a ratio which can be considered as a "ED potency" level of the compound related to 17-β-estradiol.

Most levels reported for ED-effects are below those reported for systemic toxicity. Considering "potency" levels, only for dioxin an ED-effect has been reported around the same concentration as 17-β-estradiol. For all other Category 1 substances ED effects are far below those induced by 17-β-estradiol. It should be emphasised, however, that a direct comparison is not conclusive due to differences in test systems, test species, life stages, effects parameters and exposure periods.

The candidate list including 435 chemicals in the present study should not be considered as final. Based on new data other chemicals may be added to the list. An iterative mechanism has been proposed in the present study for this purpose. Furthermore, the 19 category 1 chemicals for which ED studies presently could not provide evidence on endocrine disruption are not to be excluded from the list as yet. At present there is no consensus on the methodology to assess endocrine disrupting effects. Only when these methodologies and tests become available and are agreed upon, decisive steps can be taken.

Figure 6 Approach and outcome of the evaluation and categorisation (see also annex 4)



* Mestranol as synthetic contraceptive drug is excluded

6.2 Recommendations

Based on earlier results (BKH report 2000) and those in the present study, various needs and gaps in knowledge have been identified. Future efforts should concentrate on the following issues:

1. Testing:

At present there is no consensus yet on the methodology to assess endocrine disrupting effects. Therefore, future attention should be focused on the development of adequate standard testing systems:

Recommendation 1a: It is important that an agreement is reached on the effect parameters indicating endocrine disruption

Recommendation 1b: Standard tests have to be developed to identify endocrine disrupters

Recommendation 1c: These tests should be applied with priority to category 1 substances with evidence of endocrine disrupting activity. Risk assessments will also need to be reconsidered when agreed test methods become available.

Recommendation 1d:Tests should also consider the effect of "total body burden"

Recommendation 1e: Tests should also consider specific working mechanisms on which basis realistic potency levels can be assessed with known reference substances

2. Categorisation:

In the selected group of 204 chemicals, 53 have been categorised as category 2 chemicals due to a lack of sufficient information on endocrine disruption (e.g. in vivo tests). Furthermore, 38 other substances were categorised as category 3b chemicals because no data were available.

Recommendation 2a: For category 2 substances information should be supplemented with additional endocrine disruption data to reach a final categorisation (1 or 3a).

Recommendation 2b: The chemicals categorised as category 3b should be supplemented with additional endocrine disruption data; with the option to exclude these from the list or upgrade these to a category 3a, 2 or 1.

3. Inclusion/exclusion of substances

An iterative mechanism has been proposed to include/exclude substances from the candidate list. If new substances belonging to the "universum of chemicals" are suspected of endocrine disruptive behaviour or when new evidence is found about substances already on the candidate list they should be screened again.

Recommendation 3a: Concerning the need for inclusion of new chemicals, suggestions have been made by participants in the expert meeting of 9-10 September 2002, which includes industrial chemicals and/or cosmetics.

The decision process for inclusion/exclusion of substances has to be defined in consultation with different Scientific Commitees in the Commission and Stakeholders.

In step 1 of the selection process leading to 204 substances, which are HPV and/or persistent and/or for which exposure is expected, also the Low Production Volume (LPV) Plant Protection Products (PPP) have been included. Considering the application and use of PPPs, environmental exposure is expected.

Recommendation 3b: In an iterative process for inclusion/exclusion from the candidate list it is recommended to select also LPV industrial chemicals, for which environmental/human exposure is expected considering their use and application.

4. Improvement of the evaluation process

The evaluation process of substances has been improved. This has been accomplished amongst others by providing the involved experts with the information, as an EDS database with preliminary evaluations, one month before the actual expert meeting took place.

Recommendation 4: The inclusion of additional key studies and information presented by experts after the actual expert evaluation meeting is a recommended procedure. This in order to qualitatively improve the database and to facilitate the evaluation process. Submission of hard copies of additional key studies/information and an adapted categorisation by the experts are required.

5. EDS Database

For the majority of substances in the candidate list information on ED has been included in the developed EDS database.

Recommendation 5a: The EDS database and (evaluation) module is recommended to be used as a tool for evaluation/selection of key studies and categorisation. The EDS database should be regularly updated with new information and/or new substances.

7. REFERENCES

ADEPTS: A Database for Environmental Properties of Toxic Substances, CD-Rom developed by RPS BKH Consulting engineers and WL Delft Hydraulics

BAS2000: The Biocidal Active Substances list 2000, derived from ECB, is an non exhaustive list of possible existing Biocides Active Substances (including High and Low Production Volume Plant Protection Products and carriers) draft version

BKH (2000), Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption. - preparation of a candidate list of substances as a basis for priority setting, Delft, The Netherlands.

Biegel (1998); Biegel and Flaws, 90 day feeding and one generation reproduction study in CRl:cd br rats with 17-B-estradiol.Toxicological science 44, pp 116-142

COM (1999) 706 final, Communication from the Commission to the Council and the European parliament, Community strategy for Endocrine Disrupters, a range of substances suspected of interfering with the hormone systems of humans and wildlife.

Commission Communication to Council and European Parliament on a Community Strategy for Endocrine Disrupters COM(2001)262 of 14 June 2001

COMMPS Procedure, 1999. Revised Proposal for a List of Priority Substances in the Context of the Water Framework Directive. Fraunhofer-Institut, Final Report.

CSTEE, 2000. Opinion on BKH Consulting Engineers Report "Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption" - Opinion adopted at the 17th CSTEE plenary meeting, Brussels, 5 September, 2000

DIMDI-TOXCAS Toxicology and Pharmacology database from the Deutsches Institut fur Medizinische Dokumentation und Information (DIMDI), http://www.dimdi.de

DOSE: Dictionary Of Substances and their Effects database from the Washington University Libraries, http://library.wustl.edu/databases/about/dose.html

ECOTOX: ECOTOXicological Database System, Database on toxicity including aquatic life, terrestrial plants and terrestrial wildlife prepared for the US Environmental Protection Agency (http://www.epa.gov/ecotox)

IPA: International Pharmaceutical Abstracts database, Database containing international coverage of pharmacy and health-related literature information, the practice of pharmacy, pharmaceutical education, and the legal aspects of pharmacy and drugs from the American Society of Health System Pharmacists providede on the Science and Technical information Network (STN), http://stneasy.fiz-karlsruhe.de

IUCLID, International Uniform Chemical Information Database, CD-ROM from the European Chemicals Bureau (ECB) of the Institute of Health and Consumer Products belonging to the Joint Research Centre of the European Commission.

RTECS The Registry of Toxic Effects of Chemical Substances, CD-ROM database from the National Institute of Occupational Safety and Health (NIOSH) of the US Department of Health.

TOXNET Cluster of databases on toxicology, hazardous chemicals and related areas provided by the National Library of Medicine (NLM), http://toxnet.nlm.nih.gov

Verschueren: Handbook of Environmental Data on Organic Chemicals, Van Nostrand Reinhold Company inc., New York, 2nd edition Karel Verschueren.

WRc 2002: Study on the scientific evaluation of 12 substances in the context of Endocrine Disrupter priority list of actions. WRc-NSF. November 2002

ANNEX 1

TASK 1: DESCRIPTION AND EVALUATION OF EARLIER WORK

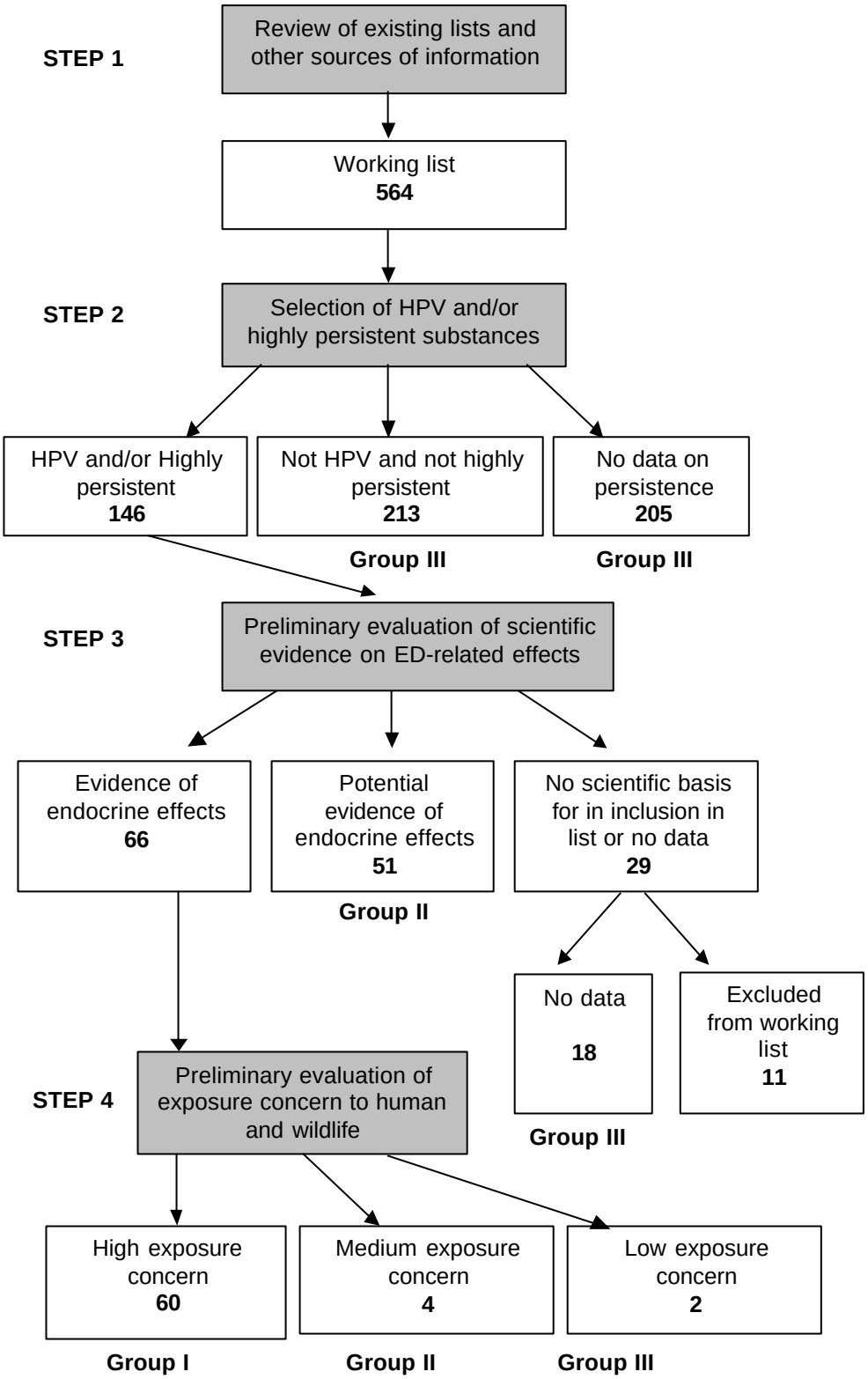
"Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption – preparation of a candidate list of substances as a basis for priority-setting" (BKH 2000).

1. SHORT DESCRIPTION OF METHODOLOGY AND RESULTS (BKH 2000)

In recent years effects were reported in animal species and human beings that are attributed to the influence of certain substances on hormonal systems.
As announced in the Communication from the Commission to the Council and the European Parliament on a Community Strategy for Endocrine Disrupters (COM(1999)706 final), a priority list of substances is to be established to further evaluate their role in endocrine disruption. The objective of the BKH 2000 study was to prepare a candidate list of substances, on the basis of available information for specific selection criteria, which could be used in this priority-setting exercise.

During this previous study (BKH 2000) a multi-step approach was developed to prepare a priority list for endocrine sybstances. In Figure I the project approach and its outcome, represented as the amount of chemicals are presented schematically.

Figure I Schematic overview of multi-step project approach and outcome (represented by the number of selected substances)



The starting point of the study was a working list, compiled from the lists of suspected endocrine disrupting chemicals drawn up by various organisations as well as from an up-to-date literature search. The working list was presented and discussed at a stakeholder meeting with representatives of government, industry and NGOs.

For the working list consisting of 564 substances scientific evidence on endocrine disruption was gathered. A further analysis was made for a number of 146 High Production Volume chemicals and/or highly persistent substances.
A panel of experts in the field of endocrine disrupting effects of substances on human health and wildlife categorised these 146 substances on the basis of the available evidence into three categories:

Category 1.	At least one study providing evidence of endocrine disruption in an intact organism. Not a formal weight of evidence approach.
Category 2.	Potential for endocrine disruption. In vitro data indicating potential for endocrine disruption in intact organisms. Also includes effects in-vivo that may, or may not, be ED-mediated. May include structural analyses and metabolic considerations
Category 3.	No scientific basis for inclusion in list or no data
Category 4.	Substances with insufficient data.

The outcome of the expert meeting was that on the basis on available data on endocrine disruption, 66 substances are to be categorised into category 1, 51 substances into category 2 and 29 in category 3. The category 3 substances included 18 substances with no or insufficient data and 11 substances that had scientific evidence for exclusion from the working list of 564 chemicals.
For a further categorisation of category 1 into substances having high, medium and low exposure-concern summary profiles were prepared with physico chemical properties, production, emissions, use, exposure and monitoring data. Special attention was given to possible exposure of vulnerable groups.

The following guidelines were used:

High exposure concern	Human exposure is expected, due to environmental concentrations and those in food or consumer products, also taking into consideration exposure of vulnerable groups *And/Or* Wildlife exposure is expected, due to use and emission patterns, and the chemical is persistent and bioaccumulative
Medium exposure concern	Human exposure is not expected *And* Wildlife exposure is expected, due to use and emission patterns, but the chemical is readily biodegradable and not bioaccumulative
Low exposure concern	No human exposure *And* No wildlife exposure

After a detailed evaluation 60 (29 chemical groups) of the 66 chemicals (35 chemical groups) in category 1 were considered as substances having high exposure concern and evidence on endocrine disruption. This group of 60 substances included substances such as DDT, PCBs, organo-tins and dioxins as well as chemicals such as styrene, phthalates and some pesticides.

A number of 11 substances were excluded from the initial working list of 564 substances because there was no scientific basis for inclusion in the list. The candidate list consisted therefore of 553 substances sorted into three groups, as shown in Table I.

The list should be open to change. As new information becomes available, chemicals may either be removed from or added to the list.

Table I. List of candidate substances – summary of work to date

GROUP I

Selection criteria			Number of substances	Listing
Highly persistent And/or HPV	At least one study showing endocrine disruption in an intact organism (Category 1)	High concern in terms of human and wildlife exposure	60 (29 chemical groups)	See Annex 1 (BKH 2000 report).

GROUP II

Selection criteria			Number of substances	Listing
Highly persistent And/or HPV	At least one study showing endocrine disruption in an intact organism (Category 1)	Medium concern in terms of human and wildlife exposure	4	See Annex 1. (BKH 2000 report)
	Potential for endocrine disruption (Category 2)		51	

GROUP III

Selection criteria			Number of substances	Listing
Highly persistent And/or HPV	At least one study showing endocrine disruption in an intact organism (Category 1)	Low concern in terms of human and wildlife exposure	2	See Annex 1. (BKH 2000 report)
	No sufficient data (Category 3)		18*	
Not HPV and not highly persistent			213	
Not HPV and no data on persistence			205**	

* Excluding 11 Substances that have been excluded from the candidate list because of data giving no basis for inclusion in the list (Category 3)

** No Smiles notations were readily available for QSAR estimations on persistence.

2. EVALUATION

General

Following the presentation of the BKH report "Towards the establishment of a priority list of substances for further evaluation of their role in endocrine disruption" (BKH report 2000), stakeholders were asked to comment on the report.

Comments from the following National Authorities, Non-Governmental Organisations, Committees and Commissions have been included:
Bundesministerium fur Ernahrung, Landwirtschaft und Forsten (Germany), Umwelt Bundes Amt (Germany), Pesticide Control Service (Ireland), Health and Safety Executive (UK), Department of the Environment, Transport & Regions (UK), Bureau des substances et Preparations Chimique (France), National Chemicals Inspectorate (KEMI, Sweden), Danish EPA, Finnish Environment Institute (Finland), National Product Control Agency for Welfare and Health (Finland). Ministry of Health and Consumer (Spain), directie arbeidsomstandigheden, afdeling arbeidsmilieu (Netherlands), EC DG ENV, Endocrine Disrupters Inter-service group, European Chemicals Bureau (ECB), Scientific Committee for Toxicology, Ecotoxicology and Environment (CSTEE), European Crop Protection Association (ECPA), European Chemical Industry Council (CEFIC), World Wide Fund (WWF).

COMMENTS

The need is recognised to consider endocrine disruption, which is an important effect, and welcome the Commission's activity in this area. Endocrine disruption is an important effect, but it must not be considered in isolation but together with all other effects of a chemical. Any action on endocrine disrupters needs to be consistent with other policies on hazardous chemicals. The BKH study can be used as a first step in developing the priority list. Generally the approach taken in the report is reasonable for a first cut of the data.

The Commission's intention is supported that the priority list of substances for further evaluation of their role in endocrine disruption will be used:

(a) to identify substances for 'priority' testing once agreed test methods become available,
(b) to identify substances which can be, or are already being addressed, under existing Community legislation covering hazard identification, risk assessment and risk management,
(c) to identify gaps in knowledge on aspects such as dose/response relationships, sources/pathways of exposure and epidemiological studies of cause/effect relationships which will help guide further research and/or monitoring efforts, and
(d) to identify specific cases of consumer use, for example, the case of potentially more vulnerable groups of consumers such as children, for special consideration from a consumer policy point of view."

Most stakeholders consider that the overall approach to the definition and application of inclusion and classification criteria should be based on the precautionary principle.

It is noted from the Council Conclusions of March 2000 that the priority list should be dynamic and chemicals added and removed as further evidence becomes available. If this is to be done in a transparent manner then clear criteria are needed for inclusion and exclusion. However, nowhere in the report are these clearly stated or elaborated in a way that 'cut off points' Presence on another priority list, Evidence of ED, HPV, Persistence and Exposure can be easily identified (UK).

The WWF does not support the use of the working definition of ED. Their view is that an EDC may have an effect that may not appear to be 'adverse'. Furthermore they comment that the consultation document does not address the worrying area of multiple, consecutive exposure to EDCs.

Step 1: Review of existing lists and other sources of information

The study started with lists compiled by others and what appears to be a quick search of recent scientific literature rather than a systematic examination of all the information available.

1. The ICCA initiative will provide some information on 20.000 substances and may flag up further priority for consideration for addition to the list.
2. Several substances or substance mixtures (including metabolites and derivatives) have been identified in an ongoing FEI project on evaluation and development of research on endocrine disrupters and can be considered for the list.
3. Non-assessed chemicals should be addressed and screened based on physical-chemical structure (QSAR) so that further substances would be considered and included when updating the priority list.
4. It is recommended to extend the list with synthetic hormones, natural-occurring chemicals, pharmaceuticals and veterinary medicines. WWF however states that industrial chemicals are of highest concern.

Step 2: Selection of highly persistent and HPV substances

1. The tools used for determining persistence and exposure classification methodology should be worked out in greater detail.
2. It is suggested that metals are given a more detailed consideration and not automatically selected solely on grounds of persistence.
3. There is a request for more clarity on the different categories for biodegradation.
4. A number of pesticides mentioned in the appendix of the ECPA paper from August 10, 2000; D/00/JW/5844, that are not registered or marketed in any European country). There is little benefit in further investigating chemicals which are no longer in use.
5. The HPV criteria is questionable, the consumer exposure of some LPV (Low Production Volume) could be higher than HPV chemicals taking into account the use category.
6. Criteria for selection of substances to be evaluated should be on the basis of potency in the first instance, irrespective of volume of production or persistency.

<u>Additional work on primary selection</u>

1. It is strongly recommended to obtain the necessary data such as SMILES codes and these additional substances should be addressed as a matter of urgency.
2. The cut-off values on biodegradation as selected in the DYNAMEC group should be used (biodegradation probability of <0.5 and ultimate biodegradability of < 2.2 instead of <0.1 and <1.0, respectively).
3. Persistency and production volume should not be the only selection criteria at this stage. Considering possible effects in humans and in the environment the exposure (and not only persistency) is important. People and environment may be continuously exposed although a substance is degradable and therefore knowledge about environmental occurrence and/or use patterns should be included at this stage as well.

Step 3: Preliminary evaluation of scientific evidence of ED-related effects:

1. There are concerns on the *inconsistencies in the classification* of the ED potential of substances, quality of the data and the limited assessment of the scientific evidence for endocrine disruption. Most of the data are human health related, and considered evaluation of risk to the environment will need supporting data.
2. Definitions of the three ED groups are not clear such as *what is "reliable in vivo evidence".* Criteria on ED must be developed further.
3. The *explanations given for the exclusion of the 11 chemicals are unclear* and not sufficient, it is preferred at this stage to reintegrate these chemicals in the group III (France).
4. WWF questions why substances with no data but closely related to substances categorised as category 1 were categorised into category 2. WWF feels that a more precautionary approach would have been to place such substances in category 1.
5. WWF wishes to stress the degree of sensitivity of the foetus in utero to naturally occurring hormone levels. This therefore questions the validity of the evaluation of endocrine disrupting effects in comparison with direct toxicity effects. EDS effects occur at much lower concentrations.
6. The grouping of certain substances may be possible but requires careful consideration as not all members of the group may have the same potency (e.g. PBBs, chlorinated paraffins).

<u>Experimental tests</u>

1. The development and validation of test methodologies and a testing strategy should be considered a high priority.

2. For human health tests, it is expected that the uterotrophic and Hershberger tests should be ready for approval by end 2001 – beginning 2002 and that the adoption process should be completed by end 2002- beginning of 2003. For the environment, it is expected that fish tests should be ready for approval by 2003-2004 and then adopted by 2005.
3. Reproductive toxicity is an effect, which is already covered in existing OECD test guidelines.
4. A key issue in the development of ED test methods and testing strategy is the number of animals which is required for the subsequent assessment of EDs. The implications from the point of view of animal welfare will need to be further considered.
5. A test program as recommended in chapter 4.2 is not needed for PPP as there are several possibilities within directive 91/414/EEC to request for additional ED research if a substance is suspected of ED effects (Germany biocides).

Additional work on identification of endocrine disrupting effects

1. It is recommended to use SAR methods, at least in a near future, as additional means to screen for substances to be included in the list in the first place (for consideration by other approaches and criteria), since there are promising results from the use of advanced SAR models in predicting sex hormone reception binding within certain classes of chemicals (e.g., Tong et al. 1997, Environ. Health Perspect. 105(10): 1116-1124).
2. There should be a dedicated programme of research developed to screen a large number of substances for endocrine disrupting effects using data from existing toxicity tests (for example the reduction in the number of pups in mammal reproduction studies or the reduction in eggshell thickness in the bird reproductive study). If data for non-pesticidal substances similar to the above exists then it should be evaluated; if not, then research into these substances to provide data should be undertaken before a substance is excluded from the priority list.

Step 4: Preliminary evaluation of exposure to humans and wildlife

1. The report is focussed on environmental exposure. For occupational exposure persistence is of lower importance and possibly not relevant.
2. Due to their use, all plant protection products (PPP) are considered as having “high exposure concern”, as these substances always are related to foodstuffs. To overcome miss interpretations, it should be made more clear the list I substances should not be considered a priori as problematic substances, but that a more thorough risk assessment is needed.
3. Additional information on estimated or measured exposures or exposure potential (e.g. use information and environmental levels) should be sought and incorporated in the list. For instance, among those prioritised highly, limited data on styrene exposures have been found so far, but additional data are likely to be available. In this case such deficiency in data retrieval is not crucial as the high priority will lead to the collection of more data. However, also for some compounds not prioritised on the basis of effects, important exposures may take place and may have been measured (or approximated) in published or other available sources.
4. WWF supports the evaluation of ‘concern to exposure’ leading to prioritisation for ‘vulnerable’ groups such as the foetus and breastfeeding infants and for groups of chemicals for high exposure concern – for example those in food products (intentionally or unintentionally) and cosmetics. However the Commission document does not go far enough in stating concrete measures for reducing exposure to these substances. The next step in the prioritisation process is significantly lacking here.

Prioritization

1. Recognising that the BKH approach was pragmatic and requires *further clarification of criteria, it could be used as a first cut at the information available.* The single priority list can be subdivided into different categories, for example matching the purposes of the list reported above, e.g.
   I. Priorities for further testing
   II. Priorities which have already been regulated
   Priorities for risk management
   Priorities which are currently under consideration
   Priorities for a fuller evaluation for listing under e.g. ESR, 91/414/EEC,
   III. Priorities for obtaining more information about data poor chemicals
   Priorities for obtaining more detailed exposure information
   IV. Priorities for assessing exposure of vulnerable groups

2. There should be added a category of chemicals where there is adequate information to conclude that they are not potential endocrine disrupters. This approach will go some way to satisfying some of the demands likely to be placed on the list and should help when it comes to allocating resources for different activities within the Commission, Member States and industry.
3. Table 4.1 is misleading. Group II includes substances of 'medium concern in terms of human and wildlife exposure'. The definition of medium concern used is 'human exposure is not expected and wildlife exposure is expected due to use & emission patterns but the chemical is readily biodegradable & not bioaccumulative'.
4. The use of the Categories and Groups can be confusing. For example NP, styrene, BPA and the PBDPEs are in Category 1. But in Annex 1 of the BKH 2000 report only styrene and BPA are included in Group I, with the others in Group II as they are of medium concern for exposure.
5. The indicators of exposure for man and wildlife seem to be too brief in general, and to be made to fit the five life cycle steps in the risk assessment. As commented above, this means that the descriptions for NP and styrene don't really match what actually happens. *(Comment consultant: At the time phase 2 was carried out the draft RARs of styrene, nonylphenol and BPA were not available to the consultant, otherwise this information would have been used for the assessment).*
6. It is recommended to add some of the 52 substances in the Group II and of the 121 substances in the Group III to the first category of priority. The value of the additional data on the Annex 8 of the BKH 2000 report should not be neglected. Some of the chemicals are tested in vitro but the tests applied are relevant to the endocrine disruption effect. These include the substances listed in ANNEX 12 (BKH 2000), specially dieldrin (63), o-phenylphenol (97), many PCB derivates (98 – 103), BDE derivates (105, 106), furans (107 – 114) and perchloroethylene (116). These substances and others with similar in vitro results should be included to the fast and first priority to be evaluated with the standardized test methods (UBA).

Priority of category 1 substances

Group I substances are mainly: i) well known and characterised, ii) in many cases are banned or strictly limited, iii) included in other priority list to evaluate the risk assessment.

For Group I substances not covered by existing legislation, it was proposed that the Commission could request data to be submitted and a risk assessment to be carried out on the basis of available information. Such action should be based on the precautionary principle.

For this category further testing should only be considered in the light of more detailed exposure assessments and a critical appraisal of existing data. Thus instead of further testing of category 1 substances resources should be directed towards further work on the non-assessed and the category 2 substances to clarify if further substances should be placed in category 1.

Chemicals that have already been regulated shouldn't be forgotten, but there is little point in committing further major resources to evaluating these particularly where there is little current exposure. It maybe also necessary to consider whether ED effects are likely to result in further regulation.

Priority of group 2 substances

1. Also as a high priority Category 2 chemicals should be subjected to further investigations to determine whether or not they are endocrine disrupters in vivo.
2. Prioritisation for further work should be given to the category 2 substances (i.e., potential for endocrine disruption) and to the 417 chemicals excluded at the step 2.
3. The use of selection criteria such as high production volume (HPV) and high persistence are appropriate for a preliminary prioritisation. The other, qualitative, selection criteria (evidence of endocrine effect and exposure concern to human and wildlife) are also relevant.

Priority of group 3 substances

1. Category 3 includes chemicals where there is no evidence of endocrine disrupting effects and chemicals for which there is no data. These should be separated and data-poor chemicals identified as a high priority for obtaining further information.

2. In particular for substances with specific uses, the absence/lack of data should not be used to imply that a substance is safe or of low priority.
3. Substances on the candidate list for which insufficient data was available should be given high priority for further evaluation i.e. data collection. In particular 205 substances for which persistence data was not gathered should be prioritised.
4. It is not clear, why substances with "no evidence on ED" were classified as group III substances, instead of deleted from the list. Combining group III with indistinct substances is unfortunate *(comment consultant: this group contains substances with no evidence for ED effects based on mammalian information* ***or*** *wildlife information, for one of the categories no data were available).*

Further action:

1. The priority list chemicals must be treated as candidate substances and go through the usual procedures before being subject to any existing Community legislation. For example, candidates for classification and labelling should undergo the usual assessment before being classified.
2. The list should be subjected to an additional screening to sort out those substances that are sufficiently regulated on the basis of their other toxicological properties (such as the PCB- and DDT-clusters).
3. An additional annex ranking the substances by their mode of actions (oestrogenic, anti-oestrogenic, androgenic, anti-androgenic, thyroid, anti-thyroid) could be very useful for further actions.
4. Further activities should be focused on those chemicals that require future regulation within the EU.
5. Attention should now focus on the next tranche of substances which we know less about.
6. Make a list with substances nowadays reviewed according to EU processes or in different international forum.

No action

1. It should be noted that the endocrine disruptive potential of substances used in plant protection products will be assessed in the context of the Review Programmes under Council Directive 91/414/EEC. Therefore all substances used in plant protection products should be excluded from the scope of this study so as to avoid unnecessary duplication of effort and waste of resources (UK Biocides, Ireland, ECPA).
2. According ECPA the concept of the ED priority list would conflict the existing European regulatory process used in plant protection products Under directive 91/414/EEC. By 2003 full data packages for all existing active ingredients will be available, including relevant endocrine disrupting endpoints, with respect to toxicological studies and acute ecotoxicity studies.
3. Substances as Styrene, BBP, DEHP, DBP, Bisphenol A, 3,4-Dichloroaniline, are being reviewed for risk assessment in different Members States. It appears convenient to wait the definitive results before adopting other measures in order to avoid duplicity and loss of time.

Substance (group) specific information

Out of the 15 PPPs 2 chlordanes, kepone, mirex, toxaphene and 3 DDTs are not registered in any of the European Member State and not on the European market.

Out of the 10 PPPs, 7 PPPs are presently under priority review under directive 91/414/EEC, Reg 3600/92. The review is near completion and all available information including ED is being taken into account.

1 PPP lindane is reviewed and a decision is made not to include (13 July 2000). The remaining 2 PPPs will also be registered according to directive 91/414/EEC (acetochlor and metam natrium, March 2002 and May 2003, respectively).

Synthetic pyrethroids are listed under category III though at least Pyrethrin, Bioallethrin, Fenvalerat, Fenothrin, Fluvalinat, Permethrin and Resmethrin have been shown to bind to human androgen receptors (Eil & Nisula, 1990). It might be more appropriate to list this group of substances under category II.

Diuron is not listed under category I though it is known that it is metabolised to 3,4-dichloroaniline (category I) and 1-(3-4-dichlorophenyl)-3-methoxyurea, which is also anti-androgenic. It should be considered including Diuron in category I.

It seems anomalous that atrazine was placed in Group I, simazine in Group II and triazines in Group III.

There are a number of substances used in plant protection products have been identified as having endocrine effects on insects which may signal their potential as endocrine disruptors for other organisms (De Fur et al., 1999). These substances include fenoxycarb, tebunfenozide, hydroprene, methoprene and pyriproxyfen. None of these substances are listed in the candidate list of 553 substances.

DDT
There appear to be some duplicate substances and wrongly assigned CAS numbers from a quick scan. So substance Nr. 156 has the name for p,p'-DDT which is substance Nr. 7 - but the CAS No for 156 is that of a different substance. The CAS No for substance Nr 6 is that for p,p'-DDT in DOSE, and comes up as p,p'-DDT in the CAS Number database in the SRC programs. Numbers 8 and 164 appear to be the same.

Organo-tin compounds
The value in looking further at organo-tin compounds is questioned. These substances cause imposex in dog whelks and bans are already in force on the use of these substances in antifoulants. Nevertheless these compounds are still used in timber treatment and as non-systemic fungicides (e.g. on potatoes). If further research on ED is to contribute to the decision-making process, this must be targeted and consideration given to the availability of suitable analytical methods. We do not see them as a high priority compared to other chemicals that we know far less about.

PAH
There are positive Allen-Doisy tests for the PAHs: Phenanthren, Chrysene, Benzanthracene, and Dibenzanthracene. Inclusion into category I should be considered.

Styrene
The major industrial release of styrene is from unsaturated polyester resins which are used in glass fibre production - this accounts for 50% of the regional emissions in the RAR. This can lead to significant consumer exposure, but not particularly to wildlife.

The description of styrene uses covers the main areas. It appears to have taken the industry categories from IUCLID. We would remove the references to paints, lacquers, varnishes, paper, pulp and board as we don't think styrene has direct use in these areas - polymeric products may do. We would emphasis the use in UPE resins for glass fibre.

A note on the ecotoxicity - there are no indications of endocrine effects in the data included in the RAR, but all of the aquatic data are short-term.

Nonylphenol
Octyl- and nonylphenols are category 1 substances based on evidence for endocrine disruption and placed in group II. We think, however, that replacement to group I more properly reflects the concern for these substances in the environment as they are widely used and are found in measurable levels in the environment.

Alkyl phenols and alkyl phenol ethoxylates are classed as Category 3 substances on the basis of lack of data on persistence and toxicity. This should not be the case .. we have enough information to set an EQS for nonyl phenol (see UK EQS Steering Group). We are also concerned that some of the highest profile chemicals in the UK do not appear on the present list.

Bisphenol A
This appears in Group I, as Category 1 for effects and high concern. Table 3.6 indicates it is persistent; this is based on the SRC Biodegradation program. The information in the RAR shows that BPA is biodegradable, and the TM agreed on readily biodegradable. There is evidence for degradation in natural waters. Depending on how the human exposure is considered, this might reduce the concern from high to medium - but there is no entry under Wildlife exposure in Table 3.6 so this may not have been considered of concern. The toxicity data appear to include some environmental effects (sex ratios).

The legal status (Annex 14 BKH 2000) of bisphenol A it should be added that it is included in the priority lists of Council Regulation 793/93/EEC.

PBDPEs
From the RAR these have a low general exposure but are persistent and some are clearly accumulative (for the higher brominated compounds it is not so clear as yet). There is no evidence for endocrine effects in the ecotoxicity data available at the moment. The parallel with PBBs is not strong in all areas. For substances of this type it has generally been found that the planar compounds are the most toxic; some PBBs can be planar whereas PBDPEs are not. However, it is not clear if this would be a factor in endocrine effects, where the shape of the receptors does not seem to be as critical. In terms of physico-chemical properties and environmental behaviour the two groups are likely to be similar (although both will cover a wide range of behaviours).

Data in the draft RAR documents on polybrominated diphenyl ethers PBDE should be included in category 1 based on evidence in animals. Furthermore these substances should be placed in group I as they are widely used substances and increasing levels have been determined in biota and in human breast milk.

The legal status (Annex 14 BKH 2000) of brominated flame retardants, it should be added that they are included in the priority lists of Council Regulation 793/93/EEC.

PBB
The name of the substance is indicated as "PBB = Brominated flame retardants = PBB (mixed group of 209 congeners)", whereas it should indicate "PBB = polybrominated biphenyls". The group of PBB has no specific CAS number. The CAS number corresponds to only one specific commercial PBB, FireMaster BP6, no longer in production.

MTBE
According to the latest draft of the RAR document on MTBE this substance should be considered as a candidate for the priority list.

Tetrachloroethylene
No specific data in the papers available. No information available on endocrine effects in the ecotoxicity data for the RAR.

Toluene
Based on the Danish work on the RAR document on toluene we think that toluene should be considered as a candidate for the priority list as toluene exposure has been found to affect FSH hormone level in occupational exposed workers and in experimental animal experiments toluene exposure was found to induce developmental toxic effects.

Parabens
Recent data on parabens in fish (used as preservatives in food and cosmetics) indicate that these substances should be included on the priority list as well.

Additional comments of the CSTEE

- There are objections against the use of the term “list”. It is preferred to use the term “compilation of selected substances”, rather than priority list.
- Endocrine disruptions should not be used as a classification category, instead better described endpoints such as primarily reproduction toxicity and impaired development should be used.
- For assessing the action of endocrine disrupters, dose-response and potency aspects should be considered.
- a comparison between endocrine disruption and other toxic effects should be made. Little importance should be assigned to situation where the ED-NOEC is substantially higher than that for other adverse effects.
- Potency considerations and quantification of exposure (physical-chemical characteristics, use, production and dispersion patterns should have been included at early in the process. The TGD should have been used for this.
- HPV and Persistence criteria are too simplistic and restrictive.
- In step 4 exposure should have been more quantitative
- It is recommended to include unpublished information available on PPPs such as vinclozolin

Comments on the CEFIC "alternative approach"
The proposed CEFIC system is quite complex and still sensitive to misinterpretations as it remains the work of humans with different view points. There is a tendency to rule out positive test results. The system ends with carrying out risk assessments.

The out ruling of positive results by negative test results is only possible when the same experiment is repeated and a negative test result is obtained. Strong positive against strong negative is not worked out further.

Endocrine disruption represents a modification in the physiological function of the endocrine system including complex interactions such as relationships between immune system and nervous system. These effects are more complex than the simplified toxicological data. The search for information should not restricted to simplified toxicological data

Is considered that one scientifically-sound study should always overrule a series of scientifically less rigorous approaches.

It is emphasised that in contrast with the traditional toxicology testing, for endocrine disrupting substances the threshold model does not exist. There is no NOAEL, and no dose-effect relation (He refers to two reports of Butterworth and Slaga, 1987 and Travis and Belefant, 1992).
Furthermore other aspects may of importance, such as
- feedback systems,
- opposite effects at different period of life,
- strong prenatal influence;
- extreme importance of time-windows of exposure, etc.
These aspects have not been dealt with in the alternative procedure.

ANNEX 2

TASK 1: EVALUATION OF ALTERNATIVE APPROACH OF CEFIC/EMSG

Content

1 INTRODUCTION

The CEFIC/EMSG working document “Towards the establishment of a weight of evidence approach to prioritising action in relation to endocrine disruption” describes a method of how to evaluate laboratory in-vivo and in-vitro experiments on endocrine disruption.

CEFIC/EMSG identifies three steps:
1. Identification of substances for evaluation
2. Evaluation of evidence and prioritise action – ‘weight of evidence’
3. Risk assessment and risk management

In the first step all substances relevant to environmental and human health are identified. These substances are prioritised on the basis of production volume, likelihood of exposure, pattern of use suspicion of hazard and extent of regulatory control.

Substances that come out of the first step should be evaluated in the second step on the basis of ‘weight of evidence’: This means:
- Data collection
- Evaluation significance of evidence
- Evaluation evidence for coherence and identify gaps
- Identification of outstanding actions required for risk assessment

Expert judgement is required at each stage and it is important to record the basis of decisions to aid transparency.

In step 3 gaps are filled where necessary, risk assessments are undertaken for the different regulative frameworks and risk management controls are introduced.

In contrast The BKH report started with the collection of list with substances that were considered as causing endocrine disrupting effects. A first group of substances were selected on the basis of production volume and persistence. ED effects data were collected and were evaluated by experts (**Not a weight of evidence approach)**. Substances were identified as with ED evidence with potential ED, no evidence and insufficient data.

In the last step the regulatory status of first group of substances is identified and proposals for priorities are given for further testing, further research and further regulation.

2 WEIGHT OF EVIDENCE

The CEFIC/EMSG document refers to the following aspects that have to be considered in evaluating data as indicative of endocrine disrupting behaviour:
- Data relevance (relevance endpoint to effects of ED)
- repeatability, reliability and quality of a study
- significance of a data set based
- and coherence of data
- Study reliability and reporting transparency

They consider that in each stage expert judgement is needed.

2.1 Data collection

CEFIC/EMSG approach refers to many sources of information such as IUCLID, SIDS, a great number of literature databases and grey literature from interested parties such as academia and industry.

Grosso modo BKH followed the same procedure: A number of literature databases with the same information as presented in Appendix III were screened and Key-experts were

contacted from focal contact points, branch organisations, non-governmental organisations to derive grey, recent and/or unpublished publications and reports. Additionally review documents in which extensive literature searches had been carried out, were used as basis for information. For example WHO EHC documents on substances and in literature with ED information on listed substances were screened. Sometimes these sources also included ED information for substances not yet listed.

It should be commented that several databases mentioned in Appendix I of the CEFIC/EMSG document have extensive overlap of information, are more oriented to physical chemical properties, engineering, medical information or contain only very few substances.

Furthermore the CEFIC/EMSG document omits the use of existing review documents as basis for information. This route of data collection focuses and speeds up the search for information and is valuable source for (grey) literature.

2.2 Data evaluation

2.2.1 Data relevance

The CEFIC/EMSG document urges that a weight of evidence approach should be able to differentiate between various toxicological endpoints in relation to their relevance to mechanistic evidence and observed effects. For the approach described here, endpoint relevance has been weighted to enable a hierarchy which can differentiate between:

- Observed adverse health effects with mechanistic support to establish causal linkage
- Observed adverse health effects with limited understanding of mechanism
- Biomarker of exposure
- Mechanistic potential with no observed effect

Substances should only be considered endocrine disrupters if they cause "adverse health effects in an intact organism, or its progeny, consequent to changes in endocrine function". Hence, it is inappropriate to assess a substance as an endocrine disrupter on the basis of mechanistic in vitro assays alone and the approach has been designed to reflect this.

Like the CEFIC/EMSG proposal in vitro tests are used in the BKH report only as an indicator of potential endocrine disrupting effects. As proposed in the CEFIC/EMSG document BKH has included data on reproduction and development only as an indication that there might be endocrine mechanistic causes. However these studies were not considered as conclusive for endocrine disruption or even potential endocrine disruption by BKH and the experts.

Many current testing criteria exist for the in vivo determination of adverse effects on reproduction and/or development without providing evidence of mechanistic cause. Under these circumstances, a negative, result may be sufficient to demonstrate that a substance is not en endocrine disrupter, but a positive result may need further testing to distinguish the mechanistic cause.

In the weighing of test results the CEFIC/EMSG uses this statement as argument to give more weight to negative test results, resulting in a biased process. It is not in coherence with the precautionary principle. A positive test result in a in vivo screening test has the same strength as a negative test result in the same study. The only difference is that in case of a positive test result additional information in mechanistic causes might be needed.

2.2.2 Relevance of in vivo data

The CEFIC/EMSG document distinguishes high medium and low relevance of in vivo assays.
In general it is correct to give in vivo screening tests a lower relevance than multi-generation tests. However, in the CEFIC/EMSG scheme negative data from short term/screening assays are given a high relevance. It makes no sense to give these tests a higher relevance than positive short term tests. It biases the weighing process.

In the BKH report endocrine disrupting evidence derived from in-vivo experiments and epidemiological studies are considered as sufficient evidence for identifying EDs.

In the CEFIC/EMSG document short term in vivo assays which indicate the mechanistic potential of chemicals should be included in the review. However screening tests **(short term tests)** for both mechanisms and biomarkers are not considered as conclusive evidence and not indicative that the substance is an endocrine disrupter. Mechanistic endpoints from screening tests are weighted such that they are considered less relevant than effects data from chronic exposure studies.

In the BKH study in principle experts used only long term tests as evidence for endocrine disruption. Positive Short term tests (screening) were mainly used as indicator of potential ED.

2.2.3 Relevance of in vitro data

The CEFIC/EMSG document recommends that for the evaluation of in vitro tests the following aspects should be considered:

- Whether the assay is designed to indicate simple receptor binding potential or the more indicative receptor binding coupled with transcriptional activation.
- whether the assay is a cellular or subcellular assay, which would be indicative of
- whether or not the endocrine receptor was likely to be exposed to metabolites of the parent compound.
- Whether the assay examines relevant endocrine parameters such as steroid metabolism.

Direct receptor effects (e.g. agonist/antagonist effects) should have greater significance than one which is indicative of non-receptor effects (e.g. hormone synthesis).

Receptor endpoints which are based upon whole cell assays should have greater priority than those which simply incorporate receptor/ligand binding technology (e.g. in subcellular assays).

In the BKH study in vitro screening tests with endocrine disrupting related endpoints are used only to detect potential endocrine disrupters. It was not considered necessary to this stage to distinguish between more or less potential endocrine disrupters.

2.3 Study repeatability

The CEFIC/EMSG document states: An assessment of study repeatability takes into account:

• The extent to which protocols have been validated and the limits within which conclusions can be drawn
• The extent to which the toxicological endpoints are understood
• The extent of the historical database and the confidence that this provides
• Basic experimental design - adequacy controls; suitability of concentration range
• Exposure data - purity of test material, verification of exposure concentrations
• Test species - suitability, general health, environmental conditions
• Analysis of results - statistical validity of observed effects
• Transparency of the study report

It is essentially, an assessment of the confidence one might have in being able to repeat the study and reproduce the results.

2.3.1 Data significance

In the former CEFIC/EMSG document it was tried to weight positive and negative test results. In the new document a paragraph of “Data significance” is prepared. In this paragraph weight is given to the combination ‘relevance’ and ‘repeatability’. 4 levels are recognised: High, indicative, and low significance and unusable.

According to CEFIC/EMSG the evaluation of 'Significance' for in vivo data should be based on the following basic principles:

- As tests for chronic effects are the most relevant, if the effects are of High Relevance, studies of Medium and High Repeatability should be considered as of High Significance.
- As the overall significance of screening tests is lower than chronic tests, in vivo screening endpoints of High Relevance from studies of Medium and High Repeatability should be considered as only of Indicative Significance.
- If the effects from a chronic study are of Medium Relevance, studies of Medium and High Repeatability should also be considered as only of Indicative Significance.
- Screening studies of only Medium Relevance, but of Medium and High Repeatability should be considered as of Low Significance and used merely as supporting information.
- Data from studies considered as of Low Repeatability should be considered as Unusable.

The evaluation of 'Significance' for in vitro data should be based on the following basic principles:

- No in vitro study can be considered as being of High Significance. At best it can be only 'Indicative' of rnechanistic potential. However, a negative result of **'Indicative Significance' would be sufficient to be definitive.**
- Only studies meeting both a High Repeatability and a High Relevance should be assessed as being of 'Indicative Significance'.
- Studies with a Medium Repeatability and a High Relevance, or vice versa should be assigned a 'Low Significance' - for support purposes only.
- Data from studies with Low Repeatability should be considered as unusable.

Again more weight is given to negative tests results of the same quality compared with positive test results. Furthermore: in vitro tests only high repeatable tests are assigned with high significance, whereas for in vivo tests also medium repeatable tests can be considered as highly significant.

2.3.2 Use of Significance Assessments

Six mechanism are considered: oestrogenic, anti-oestrogenic, androgenic, anti-androgenic, thyroid and anti-thyroid.

Assessments of Significance are used in the process shown. lt shows a 2-step process to be applied to each mechanism and is on the premise that only evidence of 'In Vivo high significance’ can be considered as being definitive in the lst step. Any other in vivo data must be considered alongside in vitro data in the 2nd step as 'Indicative' or as 'supporting,' evidence only.
lt is only necessary to proceed to the 2nd Step if the 1st Step is inconclusive

The report refers to “balance from strongly positive to strongly negative”, but does not indicate when the balance is strong negative/positive (3 to 1?? or 10 to 1??).

The problem with balancing data is that experiments are rarely comparable: mostly there are differences in the species used, the test conditions, test concentrations and/or species life stage. These differences may cause differences in test results and make it therefore difficult to balance out positive test results.

A good point in the balancing is that data should be available for all 6 mechanisms when a substance is evaluated for ED. This should be applied to substances on the negative ED list.

Stakeholders already indicated that the “precautionary principle should be used”. This in fact implies that if there is a positive result then this should be taken seriously and should not be ruled out. However, if the same experiment is replicated under the same conditions and concentrations, and no effects are observed, then overruling of the experiment might be considered. This should be part of the expert judgement. In the case of the substances studied in the BKH report, none of the experiments with positive results have been ruled out by negative results in replicated experiments.

3 COMMENTS OF EEB ON CEFIC/EMSG REPORT

Endocrine disruption represents a modification in the physiological function of the endocrine system including complex interactions such as relationships between immune system and nervous system. These effects are more complex than the simplified toxicological data.

The search for information should not restricted to simplified toxicological data

The EEB considers that one scientifically-sound study should always overrule a series of scientifically less rigorous approaches.

The EEB emphasises that in contrast with the traditional toxicology testing, for endocrine disrupting substances the threshold model does not exist. There is no NOAEL, and no dose-effect relation (He refers to two reports of Butterworth and Slaga, 1987 and Travis and Belefant, 1992).
Furthermore other aspects may of importance, such as

- feedback systems,
- opposite effects at different period of life,
- strong prenatal influence;
- extreme importance of time-windows of exposure, etc.

These aspects have not been dealt with in the evaluation distributed for the expert meeting.

4 GENERAL COMMENTS:

The proposed CEFIC/EMSG system is quite complex and still sensitive to misinterpretations as it remains the work of humans with different view points. There is a tendency to rule out positive test results. The system ends with carrying out risk assessments.

The out ruling of positive results by negative test results is only possible when the same experiment is repeated and a negative test result is obtained. Strong positive against strong negative is not worked out further.

It should be emphasised that the experts in a number of cases also used epidemiological test results as evidence for endocrine disruption.

ANNEX 3

ECB NON-EXHAUSTIVE LIST OF BIOCIDAL SUBSTANCES WITH POSSIBLE EXISTING ACTIVE SUBSTANCES

ECB non-exhaustive list on BIOCIDAL SUBSTANCES, with possible existing active substances

This provisional list is a working document Prepared by the ECB containing a non-exhaustive list with possible existing active substances in the sense of Art. 3 Par. 3 of the Review Regulation. The final list of active substances will be published in the second half of 2002.

Remarks on the non-exhaustive list with examples of possible existing active substances:
Active substances in biocides have a desired effect, an activity, e.g. disinfection of drinking water by killing bacteria and viruses in the water. Such desired effects are very important for the general public health and without it (as many third world countries are) significant public health problems may occur.
For specific applications there may be a range of active substances to choose from and the important step is then to know the undesired effct(s), if any, and then select the one causing the minimum adverse effect. In addition, there must be a range of actives on the market to allow change of substances to avoid resistence to an active.

The list of existing active substances is being drafted with input from CEFIC (Conseil Europeen de l'Industrie Chimique) which has submitted a list containing 915 entries.
The Commission has added EC numbers (EINECS or ELINCS numbers) to the entries, and has checked for double entries.
As CEFIC does not represent every single industry, the list has been circulated in 1998 to the 15 member states of the European Union for comments and additions. In this intermediate stage about 200 substances have been added and tributyltin co-polymers' has been expanded into 98 single entries.
Member States have also been asked to allocate exact product type(s) to the substances where possible.
This list has subsequently been compared with listed information on substances: IUCLID list of High Production Volume Substances, and the list of actives in Plant Protection Products. About 200 active substances are registered in IUCLID and some of these have been risk assessed or are undergoing risk assessment; and about 200 are registered as active substances for plant protection products. Some of these PPPs have undergone risk assessment.

ANNEX 4

WORKING LIST OF 435 CHEMICALS

The grouping of chemicals

Annex 4: Working list of 435 chemicals - the grouping of chemicals

Category 1 chemicals (94 substances):
HPV and/or persistent and/or exposure expected as well as evidence of endocrine disruptive effects.

Grp name	CHEMNO	CASNR	Name	Exposure concern
Alkylbenzenes and styrenes	665	12002-48-1	Trichlorobenzene	High
Alkylphenols and derivatives	457	1806-26-4	Phenol, 4-octyl-	High
	452	11081-15-5	Phenol, isooctyl-	High
Alkylphenol ethoxylates	154	9016-45-9	Nonylphenolethoxylate	High
Bisphenols	441	25036-25-3	2,2'-bis(2-(2,3-epoxypropoxy)phenyl)-propane	High
	656	106-89-8	Epichlorohydrin (1-chloro-2,3-epoxypropane)	High
Carbamates	3	63-25-2	Carbaryl	High
Chlorinated cyclodienes and camphenes	19	5103-73-1	Cis-Nonachlor	Low
	20	39765-80-5	Trans-Nonachlor	Low
Chlorinated paraffins	161	85535-85-9	Intermediate chain chlorinated paraffins	High
	160	85535-84-8	Short chain chlorinated paraffins	High
Chlorophenols and benzenes	675	608-93-5	Pentachlorobenzene	High
	133	87-86-5	Pentachlorophenol (PCP)	High
DDT derivatives and metabolites	49	2971-22-4	1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane	High
	39	65148-80-3	3-MeO-o,p'-DDE	High
	29	43216-70-2	3-OH-o,p'-DDT	High
	40	65148-81-4	4-MeO-o,p'-DDE	High
	30	65148-72-3	4-MeO-o,p'-DDT	High
	35	65148-75-6	5-MeO-o,p'-DDD	High
	41	65148-82-5	5-MeO-o,p'-DDE	High
	32	65148-74-5	5-MeO-o,p'-DDT	High
	31	65148-73-4	5-OH-o,p'-DDT	High
	37	4329-12-8	m,p'-DDD	High
	46	65148-83-6	o,p'-DDA-glycinat = N-[(2-chlorophenyl)(4-chlorophenyl)acettyl]glycin	High
	34	53-19-0	o,p'-DDD	High
	38	3424-82-6	o,p'-DDE	High
	47	14835-94-0	o,p'-DDMU	High
	28	789-02-6	o,p'-DDT	High
	36	72-54-8	p,p'-DDD	High
	42	72-55-9	p,p'-DDE	High
	424	1022-22-6	p,p'-DDMU	High
Dioxins	498	50585-41-6	2,3,7,8-TeBDD	High
Dicarboximides	52	32809-16-8	Procymidon	High
Dithiocarbamates	95	8018-01-7	Mancozeb	High
	97	9006-42-2	Metiram (Metiram-complex)	High
Furans	338	118174-38-2	6-Methyl-1,3,8-trichlorodibenzofuran	High
HCH and isomers	58	319-85-7	Beta-HCH	High
	56	608-73-1	Hexachlorocyclohexane = HCH mixed	High
Hydroxybenzonitrils	580	1689-83-4	Ioxynil	Medium
Methoxychlor and derivatives	435	No CAS 096	1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (HPTE)	High
	70	30668-06-5	1,3-Dichloro-2,2-bis(4-methoxy-3-methylphenyl)propane	High
	67	2971-36-0	Bis-OH-Methoxychlor = 1,1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (HTPE)	High
	65	72-43-5	Methoxychlor	High
	66	72-43-5	p,p'-Methoxychlor	High

Grp name	CHEMNO	CASNR	Name	Exposure concern
Organo phosphorpesticides	438	122-14-5	Fenitrothion	High
PAHs	313	56614-97-2	3,9-Dihydroxybenz(a)anthracene	High
	314	7099-43-6	5,6-Cyclopento-1,2-benzanthracene	High
	318	50-32-8	Benzo[a]pyrene	High
	319	56-49-5	3-Methylcholanthrene	Low
	320	57-97-6	7,12-Dimethyl-1,2-benz(a)anthracene	Low
PCBs and PCB ethers	654	No CAS 127	2,4-6-trichlorobiphenyl	High
	655	No CAS 128	3,4',5-trichlorobiphenyl	High
	283	67651-37-0	3-Hydroxy-2',3',4',5'-tetrachlorobiphenyl	High
	284	100702-98-5	4,4'-Dihydroxy-2,3,5,6-tetrachlorobiphenyl	High
	285	13049-13-3	4,4'-Dihydroxy-3,3',5,5'-tetrachlorobiphenyl	High
	278	53905-33-2	4-Hydroxy-2,2',5'-trichlorobiphenyl	High
	268	67651-34-7	4-Hydroxy-2',3',4',5'-tetrachlorobiphenyl	High
	264	14962-28-8	4-Hydroxy-2',4',6'-trichlorobiphenyl	High
	297	No CAS 040	4-Hydroxy-3,3',4',5'-tetrachlorobiphenyl	High
	279	4400-06-0	4-Hydroxy-3,4',5-trichlorobiphenyl	High
	436	No CAS 097	4-OH-2,2',4',5,5'-pentachlorobiphenyl	High
	292	54991-93-4	Clophen A30	High
	289	8068-44-8	Clophen A50	High
	295	No CAS 038	Mixture of 2,3,4,5-tetrachlorobiphenyl (PCB 61), 2,2',4,5,5'-octachlorobiphenyl (PCB 101) and 2,2',3,3',4,4',5,5'-octachlorobiphenyl (PCB 194)	High
	296	No CAS 039	PCB 104 (2,2',4,6,6'-Pentachlorobiphenyl)	High
	299	No CAS 041	PCB 105 (2,3,3',4,4' -Pentachlorobiphenyl)	High
	431	No CAS 092	PCB 114 (2,3,4,4',5-pentachlorobiphenyl)	High
	543	31508-00-6	PCB 118 (2,3',4,4',5-pentachlorobiphenyl)	High
	301	No CAS 042	PCB 122 (2,3,3',4,5 -Pentachlorobiphenyl)	High
	294	No CAS 037	PCB 126 (3,3',4,4',5-Pentachlorobiphenyl)	High
	300	38380-07-3	PCB 128 (2,2',3,3',4,4'-Hexachlorobiphenyl)	High
	263	37680-65-2	PCB 18 (2,2',5-Trichlorobiphenyl)	High
	277	55702-46-0	PCB 21 (2,3,4-Trichlorobiphenyl)	High
	542	7012-37-5	PCB 28 (2,4,4'-trichlorobiphenyl)	High
	266	35693-99-3	PCB 52 (2,2';5,5'-Tetrachlorobiphenyl)	High
	291	No CAS 036	PCB Aroclor 1016	High
	426	No CAS 087	PCB138 2,2',3,4,4',5'-hexachlorobiphenyl	High
	427	No CAS 088	PCB180 2,2',3,4,4',5,5'-heptachlorobiphenyl	High
PCT	303	12642-23-8	PCT Aroclor 5442	High
Phenylhydroxy phenylmethanes	185	101-53-1	Phenyl-4-hydroxyphenylmethane = 4-Benzylphenol = p-Benzylphenol	High
Phthalates	170	84-61-7	Dicyclohexyl phthalate (DCHP)	High
	171	84-66-2	Diethyl phthalate (DEP)	High
Pyrethroids	549	82657-04-3	Bifenthrin (@Talstar)	High
	548	91465-08-6	Cyhalothrin (@Karate)	High
	86	52918-63-5	Deltamethrin	High
	92	10453-86-8	Resmethrin	High
Pyrimidines and Pyridines	93	60168-88-9	Fenarimol	High
	661	1918-02-1	Picloram	Medium
Triazines and triazoles	574	65277-42-1	Ketoconazol	High
	103	21087-64-9	Metribuzin	High
	663	886-50-0	Terbutryn	Medium
Other substances	362	72-33-3	Mestranol	High
	593	94-82-6	2,4-dichlorophenoxybutyric acid = 2,4-DB	Medium
Other pesticides	588	106-93-4	Dibromoethane (EDB)	Medium

Category 2 chemicals (53 substances):
HPV and/or persistent and/or exposure expected as well as potential evidence of endocrine disruptive effects

Grp name	CHEMNO	CASNR	Name
Alkylphenol ethoxylates	150	14409-72-4	4-Nonylphenolnonaethoxylat (Tergitol NP 9)
Bisphenols	444	25085-99-8	Bisphenol A-diglycidylether polymer (mw<700)
Carbamates	5	116-06-3	Aldicarb
	537	1563-66-2	Carbofuran
	119	72490-01-8	Fenoxycarb
	6	16752-77-5	Methomyl
Chlorinated cyclodienes and camphenes	15	2597-11-7	1-Hydroxychlordene
Chlorophenoxy compounds	23	93-76-5	2,4,5-T = 2,4,5-Trichlorophenoxyaceticacid
Dicarboximides	114	88378-55-6	3,5-Dichlorophenylcarbaminacid-(1-carboxy-1-methyl)-allyl
	115	83792-61-4	N-(3,5-Dichlorophenyl)-2-hydroxy-2-methyl-3-butenacidamid
Dinitroanilides	55	1582-09-8	Trifluralin
Dioxins	558	109333-34-8	1,2,3,7,8-PeBDD
	560	No CAS 112	1,2,4,7,8-PeCDD
	563	No CAS 115	1,3,7,8-TeBCDD
	324	50585-46-1	1,3,7,8-Tetrachlorodibenzodioxin
	326	50585-40-5	2,3-Dibromo-7,8-dichlorodibenzodioxin
	327	109333-32-6	2,8-Dibromo-3,7-dichlorodibenzodioxin
	328	131167-13-0	2-Bromo-1,3,7,8-tetrachlorodibenzodioxin
	432	109333-33-7	2-Bromo-3,7,8-trichlorodibenzodioxin
	323	97741-74-7	7-Bromo-2,3-dichlorodibenzodioxin
	337	112344-57-7	8-Methyl-2,3,7-trichlorodibenzodioxin
	556	103456-39-9	TeBDD
Furans	343	125652-16-6	6-Ethyl-1,3,8-trichlorodibenzofuran
	345	125652-13-3	6-i-Propyl-1,3,8-trichlorodibenzofuran
	347	139883-51-5	6-Methyl-2,3,4,8-tetrachlorodibenzofuran
	339	172485-97-1	6-Methyl-2,3,8-trichlorodibenzofuran
	344	125652-14-4	6-n-Propyl-1,3,8-trichlorodibenzofuran
	346	125652-12-2	6-t-Butyl-1,3,8-trichlorodibenzofuran
	333	103124-72-7	8-Bromo-2,3,4-trichlorodibenzofuran
	348	139883-50-4	8-Methyl-1,2,4,7-tetrachlorodibenzofuran
	341	172485-96-0	8-Methyl-1,3,6-trichlorodibenzofuran
	340	172485-98-2	8-Methyl-1,3,7-trichlorodibenzofuran
	349	172486-00-9	8-Methyl-2,3,4,7-tetrachlorodibenzofuran
	342	172485-99-3	8-Methyl-2,3,7-trichlorodibenzofuran
HCH and isom.	546	319-86-8	Delta-HCH
Hydroxybenzonitrils	571	1689-84-5	Bromoxynil
Organo phosphorpesticides	594	30560-19-1	Acephate
	74	470-90-6	Chlorfenvinphos
	534	7786-34-7	Mevinphos = Phosdrin
	585	13171-21-6	Phosophamidon
	608	52-68-6	Trichlorfon = Dipterex
PAH	429	56-55-3	Benz(a)anthracene
Pyrethroids	84	584-79-2	Bioallethrin = d- trans allethrin
	85	52315-07-8	Cypermethrin
	88	26002-80-2	Fenothrin = sumithrin
	89	51630-58-1	Fenvalerate
	90	69409-94-5	Fluvalinate
	91	52645-53-1	Permethrin

Grp name	CHEMNO	CASNR	Name
Triazines and triazoles	595	21725-46-2	Cyanazine
	666	2593-15-9	Etridiazole
	576	123-88-6	Triadimenol
Other pesticides	676	51-03-6	Piperonyl butoxide
	606	7287-19-6	Prometryn

Category 3 chemicals (57 substances):
HPV and/or persistent and/or exposure expected as well as no scientific basis for/no data on endocrine effects

Grp name	CHEMNO	CASNR	Name	Reason
Alkylbenzenes and styrenes	128	29082-74-4	Octachlorostyrene	No data
Alkylphenols and derivatives	141	53792-11-3	4-(4-Hydroxyphenyl)-2,2,6,6-tetramethylcyclohexanecarbonacid	No data
Alkylphenol ethoxylates	471	2717-05-5	Heptaoctatrikosan-1-ol, 23-(nonylphenoxy)3,6,9,12,15,18,21-nonylphenolmonoethoxylate	No data
	511	9014-90-8	Poly(oxy-1,2-ethanediyl), alpha-sulfo-omega-nonylphenoxy	No data
Biphenyls	247	92-52-4	Diphenyl	No scientific basis
Bisphenols	218	No CAS 027	2,2,6,6-Tetramethyl-4,4-bis(4-hydroxyphenyl)-n-heptan	No data
Benzamidazoles	1	17804-35-2	Benomyl	No scientific basis
Chlorinated cyclodienes and camphenes	12	3734-48-3	Chlordene	No scientific basis
Chlorinated paraffins	162	85535-86-0	Long chain chlorinated paraffins	No data
Chlorophenoxy compounds	599	69806-50-4	Fluazifop-butyl	No data
Dinitroanilides	662	29091-21-2	Prodamine	No data
	54	40487-42-1	Pendimethalin	No scientific basis
Dithiocarbamates	668	142-59-6	Nabam	No data
Diuron derivatives and metabolites	59	35367-38-5	Diflubenzuron	No scientific basis
Naphthalenes and derivatives	238	135-19-3	2-Naphthol	No data
	241	1335-87-1	Halowax 1014	No data
Organo phosphorpesticides	523	2921-88-2	Chlorpyrifos	No scientific basis
	75	919-86-8	Demeton-s-methyl	No scientific basis
	77	62-73-7	Dichlorvos	No scientific basis
	578	51276-47-2	Glufosinate	No scientific basis
	605	301-12-2	Oxydemeton-methyl	No scientific basis
	674	299-84-3	Ronnel = fenchlorfos	No scientific basis
	532	22248-79-9	Tetrachlorvinphos = Gardona	No scientific basis
Phthalates	453	117-84-0	1,2-Benzenedicarboxylic acid, dioctyl ester	No data
	168	103-23-1	Bis(2-ethylhexyl)adipate	No data
	166	117-84-0	Di-n-octylphthalate (DnOP)	No data
Pyrethroids	87	66230-04-4	Esfenvalerate	No data

Grp name	CHEMNO	CASNR	Name	Reason
Triazines and triazoles	572	55179-31-2	Bitertanol	No data
	106	94361-07-6	Cyproconazole	No data
	107	119446-68-3	Difenoconazole	No data
	573	No CAS 121	Epiconazol	No data
	108	No CAS 008	Epoxiconazole	No data
	110	66246-88-6	Penconazole	No data
	111	60207-90-1	Propiconazole	No data
	112	107534-96-3	Tebuconazole	No data
	117	74115-24-5	Clofentezine = chlorfentezine	No data
Other pesticides	598	88-85-7	Dinoseb	No data
	670	80844-07-1	Ethofenprox	No data
	672	120068-37-3	Fipronil	No data
	589	76674-21-0	Flutriafol	No data
	603	2212-67-1	Molinate	No data
	591	88671-89-0	Myclobutanil	No data
	584	4685-14-7	Paraquat = 1,1'-dimethyl-4,4'-bipyridinium	No data
	123	82-68-8	Pentachloronitrobenzene (PCNB)	No data
	371	23950-58-5	Pronamide	No data
	664	117718-60-2	Thiazopyr	No data
	569	71751-41-2	Abamectin	No scientific basis
	570	33089-61-1	Amitraz	No scientific basis
	579	2439-99-8	Glyphosate	No scientific basis
	121	1024-57-3	Heptachlor-epoxide	No scientific basis
	590	3554-44-0	Imazalil	No scientific basis
	373	11141-17-6	Azadirachtin	No scientific basis
	370	19044-88-3	Oryzalin	No scientific basis
Other substances	538	106-47-8	4-chloroaniline	No data
	359	119-61-9	Benzophenone	No data
	611	68-12-2	Dimethylformamide (DMFA)	No data
	689	108-05-4	Vinyl acetate	No data

Not HPV and not persistent or no exposure expected (172 substances):

Grp name	CHEMNO	CASNR	Name
Alkylbenzenes and styrenes	129	104-51-8	n-Butylbenzene
Alkylphenols and derivatives	147	87-26-3	2-sec-Pentylphenol = 2-(1-Methylbutyl)phenol
	144	1131-60-8	4-Cyclohexylphenol
	156	1009-11-6	4-Hydroxy-n-butyrophenone
	146	70-70-2	4-Hydroxypropiophenone
	149	1805-61-4	4-iso-Pentylphenol = 4-(3-Methylbutyl)phenol
	138	104-40-5	4-Nonylphenol (4-NP)
	139	3115-49-9	4-nonylphenoxy acetic acid
	153	No CAS 016	4-Nonylphenoxycarboxylic acid (NP1EC)
	158	99-71-8	4-sec-Butylphenol = 4-(1-Methylpropyl)phenol
	148	94-06-4	4-sec-Pentylphenol = 4-(1-Methylbutyl)phenol = p-sec-amylphenol
	143	No CAS 013	4-tert-Pentylphenol = p-tert-Amylphenol
	145	7786-61-0	4-vinylguaiacol (4-VG)
	136	2628-17-3	4-vinylphenol (4-VP)
	475	27986-36-3	Ethanol, 2-(nonylphenoxy)-

Grp name	CHEMNO	CASNR	Name
	152	No CAS 015	Nonylphenolcarboxylic acid
	497	No CAS 106	nonylphenolethyleneoxyphosphate
	472	27193-28-8	Phenol, (1,1,3,3-tetramethylbutyl)- = Octylphenol
	474	27985-70-2	Phenol, (1-methylheptyl)-
	455	1331-54-0	Phenol, (2-ethylhexyl)-
	486	3884-95-5	Phenol, 2-(1,1,3,3-tetramethylbutyl)-
	456	17404-44-3	Phenol, 2-(1-ethylhexyl)-
	459	18626-98-7	Phenol, 2-(1-methylheptyl)-
	485	37631-10-0	Phenol, 2-(1-propylpentyl)-
	516	949-13-3	Phenol, 2-octyl-
	467	26401-75-2	Phenol, 2-sec-octyl-
	480	3307-00-4	Phenol, 4-(1-ethylhexyl)-
	458	1818-08-2	Phenol, 4-(1-methylheptyl)-
	481	3307-01-5	Phenol, 4-(1-propylpentyl)-
	473	27214-47-7	Phenol, 4-sec-octyl-
	157	25013-16-5	tert.-Butylhydroxyanisole (BHA)
Alkylphenol ethoxylates	140	20427-84-3	4-Nonylphenoldiethoxylate (NP2EO)
	454	1322-97-0	Ethanol, 2-(octylphenoxy)- = Octylphenolethoxylate
	151	No CAS 014	Octylphenol-5-ethoxylate
	155	No CAS 017	Nonylphenolethoxylate carboxylic acid
Biphenyls	244	1806-29-7	2,2'-Dihydroxybiphenyl = 2,2'-Biphenol
	245	92-88-6	4,4'-Dihydroxybiphenyl = 4,4'-Biphenol
	246	92-69-3	4-Hydroxybiphenyl = 4-Phenylphenol
Bisphenols	205	92569-29-4	1,1-Bis(4-hydroxyphenyl)-2-ethyl-n-butane
	213	No CAS 025	1,1-Bis(4-hydroxyphenyl)-2-n-propylpentane
	195	2081-08-5	1,1-Bis(4-hydroxyphenyl)ethane
	199	1844-00-4	1,1-Bis(4-hydroxyphenyl)-iso-butane
	201	2081-32-5	1,1-Bis(4-hydroxyphenyl)-iso-pentane
	198	4731-84-4	1,1-Bis(4-hydroxyphenyl)-n-butane
	210	3373-03-3	1,1-Bis(4-hydroxyphenyl)-n-heptane
	206	24362-98-9	1,1-Bis(4-hydroxyphenyl)-n-hexane
	196	1576-13-2	1,1-Bis(4-hydroxyphenyl)-n-propane
	219	7615-24-9	2,2,5,5-Tetra(4-hydroxyphenyl)-n-hexane
	204	3555-19-9	2,2-Bis(4-hydroxyphenyl)-3-methyl-n-butane
	209	6807-17-6	2,2-Bis(4-hydroxyphenyl)-4-methyl-n-pentane
	200	77-40-7	2,2-Bis(4-hydroxyphenyl)-n-butan = Bisphenol B
	211	41709-94-8	2,2-Bis(4-hydroxyphenyl)-n-heptane
	207	14007-30-8	2,2-Bis(4-hydroxyphenyl)-n-hexane
	214	6052-90-0	2,2-Bis(4-hydroxyphenyl)-n-octane
	202	4204-58-4	2,2-Bis(4-hydroxyphenyl)-n-pentane
	192	131-54-4	2,2'-Dihydroxy-4,4'-dimethoxybenzophenon
	194	52479-85-3	2,3,4,3',4',5'-Hexahydroxybenzophenon
	193	31127-54-5	2,3,4,4'-Tetrahydroxybenzophenon
	190	131-56-6	2,4-Dihydroxybenzophenon = Resbenzophenone
	208	10196-77-7	3,3-Bis(4-hydroxyphenyl)-n-hexane
	203	3600-64-4	3,3-Bis(4-hydroxyphenyl)-n-pentane
	212	7425-79-8	4,4-Bis(4-hydroxyphenyl)-n-heptane
	215	No CAS 026	4,4-Bis(4-hydroxyphenyl)-n-octane
	191	611-99-4	4,4'-Dihydroxybenzophenon
	189	21388-77-2	4-Hydroxyphenyl-4'-methoxyphenylmethane
	216	57547-76-9	5,5-Bis(4-hydroxyphenyl)-n-nonane
	217	59176-75-9	6,6-Bis(4-hydroxyphenyl)-n-undekane
	187	10193-50-7	Bis(3-hydroxyphenyl)methane
	188	620-92-8	Bis(4-hydroxyphenyl)methane

Grp name	CHEMNO	CASNR	Name
Carbamates	4	463-77-4	Carbamate
Chlorophenols and benzenes	131	25167-81-1	Dichlorophenol
Chlorophenoxy compounds	586	76578-14-8	Quizalofop-ethyl
DDT derivatives and metabolites	44	65148-76-7	3-MeO-o,p'-DDA*
	45	65148-77-8	5-MeO-o,p'-DDA*
	43	34113-46-7	o,p'-DDA*
	423	83-05-6	p,p'-DDA*
Diphenylpropane-derivatives	234	4865-83-2	1,3-Bis(4-hydroxyphenyl)pentane
	235	2549-50-0	1,3-Bis(4-hydroxyphenyl)propane
	231	85-95-0	2,4-Bis(4-hydroxyphenyl)-3-ethylhexane
	232	No CAS 030	2,4-Bis(4-hydroxyphenyl)-3-ethylpentane
	233	140131-31-3	3,5-Bis(4-hydroxyphenyl)heptane
Dithiocarbamates	596	79-44-7	Dimethyl carbamyl chloride
Diuron derivatives and metabolites	63	17356-61-5	1-(3,4-Dichlorophenyl)-3-methoxyurea
	64	3567-62-2	1-(3,4-Dichlorophenyl)-3-methylurea
	61	96-45-7	Ethylene Thiourea (ETU)*
Methoxychlor and derivatives	69	14868-03-2	Bis-OH-MDDE*
	68	2132-70-9	MDDE*
	72	75938-34-0	Mono-OH-MDDE*
	71	28463-03-8	Mono-OH-Methoxychlor*
Naphthalenes and derivatives	237	90-15-3	1-Naphthol
	236	553-39-9	2-Hydroxy-6-naphthylpropionacid
	239	1125-78-6	5,6,7,8-Tetrahydro-2-naphthol = 6-Hydroxytetralin
	240	15231-91-1	6-Bromo-2-naphthol
	243	530-91-6	Tetrahydronaphthol-2
Organo phosphorpesticides	533	No CAS 108	1-methyl-2-methylcarbamoylvinyldimethyl phosphate
	544	50-18-0	Cyclophosphamide
	597	682-80-4	Demefion
	437	2597-03-7	Elsan = Dimephenthoate
	600	2540-82-1	Formothion
	660	70393-85-0	Glufosinate-ammonium
	604	1113-02-6	Omethoate
	81	13593-03-8	Quinalphos = Chinalphos
PAH	309	573-22-8	1-Oxo-1,2,3,4-tetrahydrophenanthrene
	311	20291-73-0	1,9-Dimethylphenanthrene
	312	58024-06-9	2,8-Dihydroxy-4b,5,6,10b,11,12-hexahydrochrysene
	428	No CAS 089	2,8-dihydroxy-5,6,11,12,13,14-hexahydrochrysene
	310	5684-12-8	Dehydrodoisynolacid = Bisdehydrodoisynolacid
	690	53-96-3	n-2-fluorenylacetamide
PCBs and PCBEs	651	34883-39-1	2,5-Dichlorobiphenyl*
	273	53905-30-9	2-Hydroxy-2',5'-dichlorobiphenyl*
	652	34883-41-5	3,5-Dichlorobiphenyl*
	274	53905-29-6	3-Hydroxy-2',5'-dichlorobiphenyl*
	272	56858-70-9	4,4'-Dihydroxy-2'-chlorobiphenyl*
	275	53905-28-5	4-Hydroxy-2',5'-dichlorobiphenyl*
	276	79881-33-7	4-Hydroxy-2',6'-dichlorobiphenyl*
	270	23719-22-4	4-Hydroxy-2-chlorobiphenyl*
	653	No CAS 126	4-hydroxy-3,5-dichlorobiphenyl*
	271	28034-99-3	4-Hydroxy-4'-chlorobiphenyl*
	256	2051-60-7	PCB 1 (2-Chlorobiphenyl)*
	261	2050-67-1	PCB 11 (3,3'-Dichlorobiphenyl)*
	262	2050-68-2	PCB 15 (4,4'-Dichlorobiphenyl)*

Grp name	CHEMNO	CASNR	Name
	257	2051-61-8	PCB 2 (3-Chlorobiphenyl)*
	258	2051-62-9	PCB 3 (4-Chlorobiphenyl)*
	259	13029-08-8	PCB 4 (2,2'-Dichlorobiphenyl)*
	260	34883-43-7	PCB 8 (2,4'-Dichlorobiphenyl)*
	252	11104-28-2	PCB Aroclor 1221*
	253	11141-16-5	PCB Aroclor 1232*
Phenylhydroxy phenylmethanes	186	28994-41-4	Phenyl-2-hydroxyphenylmethane = 2-Benzylphenol = o-Benzylphenol
Phenylsiloxanes	178	31751-59-4	2,4-trans-Diphenyltetramethylcyclotrisiloxane - 2,4-trans-[(PhMeSiO)2(Me2SiO)]
	181	33204-76-1	2,6-cis-Diphenylhexamethylcyclotetrasiloxane - 2,6-cis-[(PhMeSiO)2(Me2SiO)2][
	182	33204-77-2	2,6-trans-Diphenylhexamethylcyclotetrasiloxane - 2,6-trans-[(PhMeSiO)2(Me2SiO)2]
	180	30026-85-8	Diphenylhexamethylcyclotetrasiloxane [(PhMeSiO)2(Me2SiO)2]
	177	51134-25-9	Diphenyltetramethylcyclotrisiloxane [(PhMeSiO)2(Me2SiO)]
	175	56-33-7	Diphenyltetramethyldisiloxane PhMe2-SiOSiMe2Ph
	183	35964-76-2	o-Tolylheptamethylcyclotetrasiloxane [(o-TolylMeSiO)(Me2SiO3)]
	184	10448-09-6	Phenylheptamethylcyclotetrasiloxane [(PhMeSiO)(Me2SiO)3]
	179	17156-72-8	Phenylhexamethylcyclotetrasiloxane [(PhHSiO)(Me2SiO)3]
	176	17964-44-2	PhMe[SiCH2CH2SiMePhO]
Phthalates	681	84-69-5	Diisobutylphthalate
	172	84-75-3	Di-n-hexyl phthalate (DnHP) = Dihexylphthalate (DHP)
	169	131-18-0	Di-n-pentylphthalate (DPP) = Dipentylphthalate
	167	131-16-8	Di-n-propylphthalate (DprP) = Dipropylphthalate
	650	4376-20-9	Mono 2 ethyl hexylphthalate (MEHP)
	547	131-70-4	Mono-n-butylphthalate
Pyrethrins	82	121-29-9	Pyrethrin
Pyrimidines and Pyridines	658	314-40-9	Bromacil
Triazines and triazoles	667	114369-43-6	Fenbuconazole
	109	No CAS 009	Indole(3.2-b)carbazole (ICZ)
Triphenylmethane-deriv	224	115489-12-8	1,1-Bis(4-hydroxyphenyl)-1-(4-methoxyphenyl)ethane
	223	1571-75-1	1,1-Bis(4-hydroxyphenyl)-1-phenylethane
	226	81-92-5	2-[Bis(4-hydroxyphenyl)methyl]benzylalkohol = Phenolphthalol
	227	77-09-8	3,3'-Bis(4-hydroxyphenyl)phthalid = Phenolphthaleine
	229	135505-63-4	4-Hydroxyphenyl-di-a-naphthylmethane
	221	791-92-4	4-Hydroxy-triphenylmethane
	225	115481-73-7	Bis(4-hydroxyphenyl)[(2-phenoxysulfonyl)phenyl]methane
	222	4081-02-1	Bis(4-Hydroxyphenyl)phenylmethane
	230	630-95-5	Diphenyl-a-naphthylcarbinol
Other pesticides	519	6164-98-3	Chlordimeform
	118	96-12-8	Dibromochloropropane (DBCP)
	669	25550-58-7	Dinitrophenol
	536	545-55-1	TEPA
	372	64529-56-2	Ethiozin
Other substances	683	303-38-8	2,3-dihydroxybenzoicacid (2,3-DHBA)
	682	490-79-9	2,5-dihydroxybenzoicacid (2,5-DHBA)
	366	No CAS 052	Allenolic acid
	541	57-12-5	Cyanide

Grp name	CHEMNO	CASNR	Name
	363	482-49-5	Doisynolic acid
	364	537-98-4	Ferulic acid (FA)
	680	533-73-3	Hydroxyhydroquinone
	430	1634-04-4	methyl tertiary butyl ether (MTBE)
	365	7400-08-0	p-Coumaric acid (PCA)
	688	463-56-9	Thiocyanate

* This list contains at least 34 chemicals that are highly related to substances classified as Category 1 substances. Although these 34 compounds did not meet step 1 selection criteria, due to their similarity to Category 1 substances these might also exert endocrine disruptive effects. Substances involved are mono- and dichlorated PCBs, methoxchlor derivatives, DDT metabolites and the metabolite ETU of mancozeb and metiram. Other suspicious groups of compounds on this list are e.g. PAHs and phthaltes (several of them are classified as Category 1 compounds). The latter indicates that this list needs further investigation.

Undefined chemicals, mixtures and/or polymers (40 substances):

Grp name	CHEMNO	CASNR	Name	Exposure concern
Alkylphenols and derivatives	514	9040-65-7	Formaldehyde, polymere with nonylphenol	polymer
Alkylphenol ethoxylates	512	9036-19-5	Glycols, polyethylene, mono((1,1,3,3-tet = Poly(oxy-1,2-ethanediyl), .alpha.-[(1,1,3,3-tetramethylbutyl)phenyl]-.omega.-hydroxy-	polymer
	509	9002-93-1	Glycols, polyethylene, mono(p-(1,1,3,3-t = Octoxynol = Poly(oxy-1,2-ethanediyl), alpha-(4-(1.1.3.3.-tetramethyl-butyl)phenyl)-omega-hydroxy-	polymer
	464	26027-38-3	Glycols, polyethylene, mono-(p-nonylphenyl) ether	polymer
	494	No CAS 104	nonylphenolethoxylate with 9<EO<19	polymer
	491	No CAS 103	nonylphenolethoxylate with EO<9	polymer
	496	No CAS 105	nonylphenolethoxylate with EO>19	polymer
	510	9004-87-9	OP-7 = Poly(oxy-1,2-ethanediyl), alpha-(iso-octylphenyl)-omega-hydroxy-	polymer
	495	52623-95-7	Poly(oxy-1,2-ethanediyl), alpha-((1.1.3.3.-tetramethyl-butyl)phenyl)-omega-hydroxy-phosphate	polymer
	507	81642-15-1	Poly(oxy-1,2-ethanediyl), alpha-(3-octylphenyl)-omega-hydroxy	polymer
	492	51651-58-2	Poly(oxy-1,2-ethanediyl), alpha-(4-isooctylphenyl)-omega-hydroxy-	polymer
	504	68891-21-4	Poly(oxy-1,2-ethanediyl), alpha-(dinonylphenyl)-omega-hydroxy-forgrenet	polymer
	484	37205-87-1	Poly(oxy-1,2-ethanediyl), alpha-(iso-nonylphenyl)-omega-hydroxy-phosphate	polymer
	493	51811-79-1	Poly(oxy-1,2-ethanediyl), alpha-(nonylphenyl)-omega-hydroxy-forgrenet	polymer
	502	68412-54-4	Poly(oxy-1,2-ethanediyl), alpha-(nonylphenyl)-omega-hydroxy-forgrenet	polymer
	513	9036-89-2	Poly(oxy-1,2-ethanediyl), alpha-(octylphenyl)-omega-hydroxy-	polymer

Grp name	CHEMNO	CASNR	Name	
	505	68987-90-6	Poly(oxy-1,2-ethanediyl), alpha-(octylphenyl)-omega-hydroxy-forgrenet	polymer
	500	60864-33-7	Poly(oxy-1,2-ethanediyl), alpha-(phenylmethyl)-omega-((1.1.3.3.-tetramethyl-butyl)-phenoxy)	polymer
	499	55348-40-8	Poly(oxy-1,2-ethanediyl), alpha-sulpho-omega-((1.1.3.3.-tetramethyl-butyl)-phenoxy)	polymer
	451	109909-39-9	Poly(oxy-1,2-ethanediyl), alpha-sulpho-omega(2,4,6-tris(1-methylpropyl)phenoxy)-sodium salt	polymer
	506	69011-84-3	Poly(oxy-1,2-ethanediyl), alpha-sulpho-omega-(octylphenyl)-forgrenet, sodium salt	polymer
	490	No CAS 102	malein..anhydride, monoester with ethoxylated nonylphenol, nutrilized with reaction products like dipropylenetriamine	Undefined chemical
Bisphenols	445	36425-15-7	Bisphenol A-(epichlorhydrin) .. metacrylate polymer	polymer
	442	25068-38-6	Bisphenol A-(epichlorhydrin) polymer	polymer
	449	105839-18-7	C16 or C18 polymerized bisphenol-A, butylglydiocylether, epichlorhydrine or 1AN,N'-bis(2aminoethyl)ethane-1,2-diamin	polymer
	450	No CAS 098	cresol-bisphenol-A formaldehyde polymer	polymer
	443	25085-75-0	Formaldehyde, polymer with 4,4'-(1-methylidene)bis(phenol)	polymer
	446	66070-77-7	Dehydrated Castor oil polymere with bisphenol-=A of epichlorhydrine	Undefined chemical
	448	98824-88-5	Epichlorhydrin-bisphenol A/F, reactionproducts, C12-C14 aliphatic ... (DER 353)	Undefined chemical
	447	93572-41-9	Linseed oil, reaction products with 1-[[2-[(2-aminoethyl)amin)-3-phenoxy-2-propanol, bisphenol A-diglycidylether, formaldehyde or pentaethylenehexamnine	Undefined chemical
	220	No CAS 028	Tetrabromobisphenol A (TBBP-A)	Undefined chemical
Naphthalenes and derivatives	242	No CAS 032	Mixture of 1,2,3,5,6,7-hexachloronaphthalene and 1,2,3,6,7-pentachloronaphthalene	Undefined mixture
Organo phosphorpesticides	601	No CAS 122	Metalodemeton	Undefined chemical
PAH	315	No CAS 047	9,10-Dihydroxy-9,10-diethyl-9,10-dihydro-1,2,5,6-dibenzanthracene	Undefined chemical
	316	63041-56-5	9,10-Dihydroxy-9,10-di-n-propyl-9,10-dihydro-1,2,5,6-dibenzanthracene	Undefined chemical
	317	63041-53-2	9,10-Dihydroxy-9,10-di-n-butyl-9,10-dihydro-1,2,5,6-dibenzanthracene	Undefined chemical
PCBs and PCBEs	684	No CAS 134	Polychlorinated diphenyl ether	Undefined mixture
Triphenylmethane-derivatives	228	No CAS 029	2,4-Dihydroxytriphenylmethancarbonacidlacton	Undefined chemical
Other substances	687	No CAS 136	Tetrachloro benzyltoluenes	Undefined mixture
	685	No CAS 135	Iodine, radioactive	Undefined chemical

Excluded compounds from the list (19 substances):

Excluded substances and the reason for exclusion are depicted in Annex 10.

ANNEX 5

SELECTED 204 CHEMICALS WITH THEIR APPLIED SELECTION CRITERIA.

Annex 5: Selected 204 chemicals with their applied selection criteria.

The second cut of substances are selected on basis of the following criteria:

Abbreviation	Explanation	Nr.
LPV PPP:	Low production volume plant protection product (ECB biocides list (BAS2000))	19
PPP used:	Plant Protection Products used (ECB biocides list (BAS2000))	15
Other PPP:	Other substances on ECB list (BAS2000)	4
Pers/Pers+:	QSAR calculation on persistence	136
HPV:	EU risk assessment on short, medium and long chain paraffins	3
+Monitoring Commps:	Substance is reported upon the first or second inquiry for monitoring data February/July 1998. Derived from Annex 1 of the COMMPS report (1999)	47
SANCO	PPP under evaluation under directive 91/414 EC	13
First	Substances with insufficient data in first BKH study	18
Combined number of substances in second cut selection		**204**

Additional notes:
1: trans nonachlor was evaluated in former project
2: nonylphenol, octylphenol, gamma HCH, a number of triazine, DDT, phthtalate, PCB and dioxin compounds were already evaluated in former project

Grp name	CHEMNO	CASNR	Name	Reason
Benzamidazoles	1	17804-35-2	Benomyl	LPV PPP
Carbamates	2	116-06-3	Aldicarb	+Monitoring Commps
	3	63-25-2	Carbaryl	LPV PPP
	4	1563-66-2	Carbofuran	+Monitoring Commps
	5	72490-01-8	Fenoxycarb	LPV PPP
	6	16752-77-5	Methomyl	LPV PPP\+Monitoring Commps
Chlorinated cyclodienes & camphenes	7	2597-11-7	1-Hydroxychlordene	Pers+
	8	3734-48-3	Chlordene	Pers+\first
	9	5103-73-1	Cis-Nonachlor (1)	Pers+
	10	39765-80-5	Trans-Nonachlor	Pers+\first
Chlorophenoxy comp.	11	93-76-5	2,4,5-T = 2,4,5-Trichlorophenoxyaceticacid	+Monitoring Commps
	12	69806-50-4	Fluazifop-butyl	Pers
DDT, deriv. & metab.	13	2971-22-4	1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane	Pers
	14	65148-80-3	3-MeO-o,p'-DDE	Pers
	15	43216-70-2	3-OH-o,p'-DDT	Pers
	16	65148-81-4	4-MeO-o,p'-DDE	Pers
	17	65148-72-3	4-MeO-o,p'-DDT	Pers
	18	65148-75-6	5-MeO-o,p'-DDD	Pers
	19	65148-82-5	5-MeO-o,p'-DDE	Pers
	20	65148-74-5	5-MeO-o,p'-DDT	Pers
	21	65148-73-4	5-OH-o,p'-DDT	Pers
	22	4329-12-8	m,p'-DDD	Pers
	23	65148-83-6	o,p'-DDA-glycinat = N-[(2-chlorophenyl)(4-chlorophenyl)acettyl]glycin	Pers
	24	53-19-0	o,p'-DDD	Pers\+Monitoring Commps
	25	3424-82-6	o,p'-DDE	Pers\+Monitoring Commps
	26	14835-94-0	o,p'-DDMU	Pers
	27	789-02-6	o,p'-DDT	Other PPP\Pers\ +Monitoring Commps
	28	72-54-8	p,p'-DDD	Pers\+Monitoring Commps
	29	72-55-9	p,p'-DDE	Pers\+Monitoring Commps
	30	1022-22-6	p,p'-DDMU	Pers

Grp name	CHEMNO	CASNR	Name	Reason
Dicarboximides	31	88378-55-6	3,5-Dichlorophenylcarbaminacid-(1-carboxy-1-methyl)-allyl	Pers
	32	83792-61-4	N-(3,5-Dichlorophenyl)-2-hydroxy-2-methyl-3-butenacidamid	Pers
	33	32809-16-8	Procymidon	Pers
Dinitroanilides	34	40487-42-1	Pendimethalin	Pers\+Monitoring Commps
	35	29091-21-2	Prodiamine	Pers
	36	1582-09-8	Trifluralin	Pers\+Monitoring Commps
Dithiocarbamates	37	8018-01-7	Mancozeb	+Monitoring Commps
	38	9006-42-2	Metiram (Metiram-complex)	Sanco
	39	142-59-6	Nabam	LPV PPP
Hexachlorocyclohexane & Isomers	40	319-85-7	Beta-HCH	Pers\+Monitoring Commps
	41	319-86-8	Delta-HCH	Pers\+Monitoring Commps
	42	608-73-1	Hexachlorocyclohexane = HCH mixed	Pers\+Monitoring Commps
	43	1689-84-5	Bromoxynil	Sanco
	44	1689-83-4	Ioxynil	Sanco
Linuron, diuron deriv. & metab. Methoxychlor and derivatives	45	35367-38-5	Diflubenzuron	LPV PPP\Pers
	46	No CAS 096	1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (HPTE)	Pers
	47	30668-06-5	1,3-Dichloro-2,2-bis(4-methoxy-3-methylphenyl)propane	Pers
	48	2971-36-0	Bis-OH-Methoxychlor = 1,1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (HTPE)	Pers
	49	72-43-5	Methoxychlor	PPP used\Pers\+Monitoring Commps
	50	72-43-5	p,p'-Methoxychlor	PPP used\+Monitoring Commps
Organo phosphor-pesticides	51	30560-19-1	Acephate	LPV PPP
	52	470-90-6	Chlorfenvinphos	LPV PPP\Pers\ +Monitoring Commps
	53	2921-88-2	Chlorpyrifos	PPP used\Pers\+Monitoring Commps
	54	919-86-8	Demeton-s-methyl	+Monitoring Commps
	55	62-73-7	Dichlorvos	LPV PPP\+Monitoring Commps
	56	122-14-5	Fenitrothion	LPV PPP\+Monitoring Commps
	57	51276-47-2	Glufosinate	Sanco
	58	7786-34-7	Mevinphos = Phosdrin	+Monitoring Commps
	59	301-12-2	Oxydemeton-methyl	Sanco
	60	13171-21-6	Phosophamidon	Sanco
	61	299-84-3	Ronnel = fenchlorfos	Other PPP\Pers\+Monitoring Commps
	62	22248-79-9	Tetrachlorvinphos = Gardona	PPP used\Pers
	63	52-68-6	Trichlorfon = Dipterex	LPV PPP\Pers
Pyrethroids	64	82657-04-3	Bifenthrin (@Talstar)	PPP used\Pers
	65	584-79-2	Bioallethrin = d- trans allethrin	PPP used
	66	91465-08-6	Cyhalothrin (@Karate)	PPP used\Pers
	67	52315-07-8	Cypermethrin	LPV PPP\+Monitoring Commps
	68	52918-63-5	Deltamethrin	PPP used\+Monitoring Commps
	69	66230-04-4	Esfenvalerate	Sanco
	70	26002-80-2	Fenothrin = sumithrin	PPP used
	71	51630-58-1	Fenvalerate	LPV PPP
	72	69409-94-5	Fluvalinate	Pers
	73	52645-53-1	Permethrin	LPV PPP\+Monitoring Commps
	74	10453-86-8	Resmethrin	PPP used

Grp name	CHEMNO	CASNR	Name	Reason
Pyrimidines and Pyridines	75	60168-88-9	Fenarimol	PPP used\Pers
	76	1918-02-1	Picloram	Pers
	77	55179-31-2	Bitertanol	Sanco
Triazines and triazoles	78	21725-46-2	Cyanazine	Pers\+Monitoring Commps
	79	94361-07-6	Cyproconazole	Pers
	80	119446-68-3	Difenoconazole	Pers
	81	No CAS 121	Epiconazol	Sanco
	82	No CAS 008	Epoxiconazole	Pers
	83	2593-15-9	Etridiazole	Pers
	84	65277-42-1	Ketoconazol	Pers
	85	21087-64-9	Metribuzin	+Monitoring Commps
	86	66246-88-6	Penconazole	Pers
	87	60207-90-1	Propiconazole	LPV PPP\Pers
	88	107534-96-3	Tebuconazole	PPP used\Pers
	89	886-50-0	Terbutryn	LPV PPP\Pers\ +Monitoring Commps
	90	123-88-6	Triadimenol	Sanco
	91	94-82-6	2,4-dichlorophenoxybutyric acid = 2,4-DB	Sanco
Other pesticides	92	71751-41-2	Abamectin	PPP used
	93	33089-61-1	Amitraz	LPV PPP
	94	11141-17-6	Azadirachtin	Pers+
	95	74115-24-5	Clofentezine = chlorfentezine	Pers
	96	106-93-4	Dibromoethane (EDB)	HPV\first
	97	88-85-7	Dinoseb	+Monitoring Commps
	98	80844-07-1	Ethofenprox	Pers
	99	120068-37-3	Fipronil	PPP used\Pers+
	100	76674-21-0	Flutriafol	Pers
	101	2439-99-8	Glyphosate	Sanco
	102	1024-57-3	Heptachlor-epoxide	Pers+\first
	103	3554-44-0	Imazalil	Pers
	104	2212-67-1	Molinate	+Monitoring Commps
	105	88671-89-0	Myclobutanil	Sanco
	106	19044-88-3	Oryzalin	Pers
	107	4685-14-7	Paraquat = 1,1'-dimethyl-4,4'-bipyridinium	Sanco\HPV\first
	108	82-68-8	Pentachloronitrobenzene (PCNB)	Pers\+Monitoring Commps
	109	51-03-6	Piperonyl butoxide	LPV PPP
	110	7287-19-6	Prometryn	LPV PPP\Pers\ +Monitoring Commps
	111	23950-58-5	Pronamide	Pers
	112	117718-60-2	Thiazopyr	Pers
Chloro- phenols and benzenes	113	29082-74-4	Octachlorostyrene	Pers+\first
	114	12002-48-1	Trichlorobenzene	Pers\+Monitoring Commps
	115	608-93-5	Pentachlorobenzene	Pers\+Monitoring Commps
	116	87-86-5	Pentachlorophenol (PCP)	PPP used\Pers\ +Monitoring Commps
Alkylphenols and derivatives	117	53792-11-3	4-(4-Hydroxyphenyl)-2,2,6,6-tetramethylcyclohexanecarbonacid	Pers
	118	1806-26-4	Phenol, 4-octyl-	+Monitoring Commps
	119	11081-15-5	Phenol, isooctyl-	HPV\first
	120	14409-72-4	4-Nonylphenolnonaethoxylat (Tergitol NP 9)	Pers
	121	2717-05-5	Heptaoctatrikosan-1-ol, 23-(nonylphenoxy)3,6,9,12,15,18,21-nonylphenolmonoethoxylate	Pers
	122	9016-45-9	Nonylphenolethoxylate	Other PPP\+Monitoring Commps
	123	9014-90-8	Poly(oxy-1,2-ethanediyl), alpha-sulfo-omega-nonylphenoxy	Pers
Chlorinated paraffins (CPs)	124	85535-85-9	Intermediate chain chlorinated paraffins	HPV
	125	85535-86-0	Long chain chlorinated paraffins	HPV
	126	85535-84-8	Short chain chlorinated paraffins	HPV

Grp name	CHEMNO	CASNR	Name	Reason
Phthalates	127	117-84-0	1,2-Benzenedicarboxylic acid, dioctyl ester	+Monitoring Commps
	128	103-23-1	Bis(2-ethylhexyl)adipate	HPV\first
	129	117-84-0	Di-n-octylphthalate (DnOP)	+Monitoring Commps
	130	84-61-7	Dicyclohexyl phthalate (DCHP)	HPV\first
	131	84-66-2	Diethyl phthalate (DEP)	HPV\first
Phenylhydroxyphenylmethanes	132	101-53-1	Phenyl-4-hydroxyphenylmethane = 4-Benzylphenol = p-Benzylphenol	Other PPP
	133	25036-25-3	2,2'-bis(2-(2,3-epoxypropoxy)phenyl)-propane	Pers
Bisphenols	134	No CAS 027	2,2,6,6-Tetramethyl-4,4-bis(4-hydroxyphenyl)-n-heptan	Pers
	135	25085-99-8	Bisphenol A-diglycidylether polymer (mw<700)	Pers
	136	106-89-8	Epichlorohydrin (1-chloro-2,3-epoxypropane)	HPV\first
	137	92-52-4	Diphenyl	HPV\first
PCBs and PCDEs	138	No CAS 127	2,4-6-trichlorobiphenyl	Pers
	139	No CAS 128	3,4',5-trichlorobiphenyl	Pers
	140	67651-37-0	3-Hydroxy-2',3',4',5'-tetrachlorobiphenyl	Pers
	141	100702-98-5	4,4'-Dihydroxy-2,3,5,6-tetrachlorobiphenyl	Pers
	142	13049-13-3	4,4'-Dihydroxy-3,3',5,5'-tetrachlorobiphenyl	Pers
	143	67651-34-7	4-Hydroxy-2',3',4',5'-tetrachlorobiphenyl	Pers
	144	14962-28-8	4-Hydroxy-2',4',6'-trichlorobiphenyl	Pers
	145	53905-33-2	4-Hydroxy-2,2',5'-trichlorobiphenyl	Pers
	146	No CAS 040	4-Hydroxy-3,3',4',5'-tetrachlorobiphenyl	Pers
	147	4400-06-0	4-Hydroxy-3,4',5-trichlorobiphenyl	Pers
	148	No CAS 097	4-OH-2,2',4',5,5'-pentachlorobiphenyl	Pers
	149	54991-93-4	Clophen A30	Pers
	150	8068-44-8	Clophen A50	Pers
	151	No CAS 038	Mixture of 2,3,4,5-tetrachlorobiphenyl (PCB 61), 2,2',4,5,5'-octachlorobiphenyl (PCB 101) and 2,2',3,3',4,4',5,5'-octachlorobiphenyl (PCB 194)	Pers+
	152	No CAS 039	PCB 104 (2,2',4,6,6'-Pentachlorobiphenyl)	Pers
	153	No CAS 041	PCB 105 (2,3,3',4,4' -Pentachlorobiphenyl)	Pers
	154	No CAS 092	PCB 114 (2,3,4,4',5-pentachlorobiphenyl)	Pers
	155	31508-00-6	PCB 118 (2,3',4,4',5-pentachlorobiphenyl)	Pers\+Monitoring Commps
	156	No CAS 042	PCB 122 (2,3,3',4,5 -Pentachlorobiphenyl)	Pers
	157	No CAS 037	PCB 126 (3,3',4,4',5-Pentachlorobiphenyl)	Pers
	158	38380-07-3	PCB 128 (2,2',3,3',4,4'-Hexachlorobiphenyl)	Pers\first
	159	37680-65-2	PCB 18 (2,2',5-Trichlorobiphenyl)	Pers
	160	55702-46-0	PCB 21 (2,3,4-Trichlorobiphenyl)	Pers
	161	7012-37-5	PCB 28 (2,4,4'-trichlorobiphenyl)	Pers\+Monitoring Commps
	162	35693-99-3	PCB 52 (2,2';5,5'-Tetrachlorobiphenyl)	Pers\first
	163	No CAS 036	PCB Aroclor 1016	Pers
	164	No CAS 087	PCB138 2,2',3,4,4',5'-hexachlorobiphenyl	Pers
	165	No CAS 088	PCB180 2,2',3,4,4',5,5'-heptachlorobiphenyl	Pers+
Polychlorinated terphenyls (PCT)	166	12642-23-8	PCT Aroclor 5442	Pers
Naphthalenes and derivatives	167	135-19-3	2-Naphthol	HPV\first
	168	1335-87-1	Halowax 1014	Pers
PAH	169	56614-97-2	3,9-Dihydroxybenz(a)anthracene	Pers
	170	56-49-5	3-Methylcholanthrene	Pers
	171	7099-43-6	5,6-Cyclopento-1,2-benzanthracene	Pers
	172	57-97-6	7,12-Dimethyl-1,2-benz(a)anthracene	Pers
	173	56-55-3	Benz(a)anthracene	Pers\+Monitoring Commps
	174	50-32-8	Benzo[a]pyrene	Pers\+Monitoring Commps

Grp name	CHEMNO	CASNR	Name	Reason
Dioxins	175	109333-34-8	1,2,3,7,8-PeBDD	Pers
	176	No CAS 112	1,2,4,7,8-PeCDD	Pers
	177	No CAS 115	1,3,7,8-TeBCDD	Pers
	178	50585-46-1	1,3,7,8-Tetrachlorodibenzodioxin	Pers
	179	50585-41-6	2,3,7,8-TeBDD	Pers
	180	50585-40-5	2,3-Dibromo-7,8-dichlorodibenzodioxin	Pers
	181	109333-32-6	2,8-Dibromo-3,7-dichlorodibenzodioxin	Pers
	182	131167-13-0	2-Bromo-1,3,7,8-tetrachlorodibenzodioxin	Pers
	183	109333-33-7	2-Bromo-3,7,8-trichlorodibenzodioxin	Pers
	184	97741-74-7	7-Bromo-2,3-dichlorodibenzodioxin	Pers
	185	112344-57-7	8-Methyl-2,3,7-trichlorodibenzodioxin	Pers
	186	103456-39-9	TeBDD	Pers
Furans	187	125652-16-6	6-Ethyl-1,3,8-trichlorodibenzofuran	Pers
	188	125652-13-3	6-i-Propyl-1,3,8-trichlorodibenzofuran	Pers
	189	118174-38-2	6-Methyl-1,3,8-trichlorodibenzofuran	Pers
	190	139883-51-5	6-Methyl-2,3,4,8-tetrachlorodibenzofuran	Pers
	191	172485-97-1	6-Methyl-2,3,8-trichlorodibenzofuran	Pers
	192	125652-14-4	6-n-Propyl-1,3,8-trichlorodibenzofuran	Pers
	193	125652-12-2	6-t-Butyl-1,3,8-trichlorodibenzofuran	Pers
	194	103124-72-7	8-Bromo-2,3,4-trichlorodibenzofuran	Pers
	195	139883-50-4	8-Methyl-1,2,4,7-tetrachlorodibenzofuran	Pers
	196	172485-96-0	8-Methyl-1,3,6-trichlorodibenzofuran	Pers
	197	172485-98-2	8-Methyl-1,3,7-trichlorodibenzofuran	Pers
	198	172486-00-9	8-Methyl-2,3,4,7-tetrachlorodibenzofuran	Pers
	199	172485-99-3	8-Methyl-2,3,7-trichlorodibenzofuran	Pers
Other substances	200	106-47-8	4-chloroaniline	+Monitoring Commps
	201	119-61-9	Benzophenone	HPV\first
	202	68-12-2	Dimethylformamide (DMFA)	HPV\first
	203	108-05-4	Vinyl acetate	HPV\first
	204	72-33-3	Mestranol	Pers\+Monitoring Commps

ANNEX 8

REFERENCES OF STUDIES AND REPORTS ON ENDOCRINE DISRUPTION INCORPORATED IN THE DATABASE

References with ED related effects data

REFID	REFERENCE
Aba96	Abayasekara DR; Ford SL; Persaud SJ; Jones PM., 1996. Role of phosphoprotein phosphatases in the corpus luteum: II control ofprogesterone secretion by isolated rat luteal cells. JEndocrinol; VOL 150, ISS 2, P213-21
abd94	Abd el-Aziz MI; Sahlab AM; Abd el-Khalik M (1994). Influence of diazinon and deltamethrin on reproductive organs and fertility of male rats.DTW Dtsch Tierarztl Wochenschr; VOL 101, ISS 6, P230-2
Akb00	Akbarsha MA; Latha PN; Murugaian P (2000). Retention of cytoplasmic droplet by rat cauda epididymal spermatozoa after treatment with cytotoxic and xenobiotic agents.Journal of reproduction and fertility; 120; 2; 385-90
Akh96	Akhtar N., et al.. J. Appl. Toxicol. 16: 397-400, 1996
alj00	Al-Jamal JH; Dubin NH (2000). The effect of raloxifene on the uterine weight response in immature mice exposed to 17beta-estradiol, 1,1,1-trichloro-2, 2-bis(p-chlorophenyl)ethane, and methoxychlor.Am J Obstet Gynecol; VOL 182, ISS 5, P1099-102
Ami65	Amir D. and Volcani R., 1965. Effect of dietary ethylene dibromide on bull semen. Nature (Lond), 206 (4979): 99-100.
And02	Andersen HR; Vinggaard AM; Rasmussen TH; Gjermandsen IM; Bonefeld-Jorgensen EC., 2002. Effects of currently usedpesticides in assays for estrogenicity, androgenicity, andaromatase activity in vitro. Toxicology and applied pharmacology; 179; 1; 1-12; 20020215 Language:English
ank01	Ankley GT; Jensen KM; Kahl MD; Korte JJ; Makynen EA (2001) Description and evaluation of a short-term reproduction test with the fathead minnow (Pimephales promelas).Environmental toxicology and chemistry / SETAC; 20; 6; 1276-90; 200106
Arn96	Arnold, S., Robinson, M.K., Guillette, L.J., Jr. and McLachlan, J.A. (1996). A yeast estrogen screen for examining the relative exposure of cells to natural and xeno estrogens. Environ. Health Perspect. 104 (5), 544-548.
Arn96a\ Arn97a	Arnold SF, Klotz DM, Collins BM, Vonier PM, Guillette LJ Jr, McLachlan JA. Synergistic activation of estrogen receptor with combinations of environmental chemicals. Science 272:1489-1492, 1996.. Arn97a: Arnold SF., Klotz DM., Collins BM., Vonier PM., Guillette LJ Jr., McLachlan JA. Synergistic effect of environmental estrogens: report withdrawn. Erratum to document cited in CA125: 28011. Science (Washington, DC), VOL 277, ISS 5325, 1997, 462-463.
Arn96b	Arnold DL, Nera EA, Stapley R, Tolnai G, Claman P, Hayward S, Tryphonas H, Bryce F. Prevalence of endometriosis in rhesus (Macaca mulatta) monkeys ingesting PCB (Aroclor 1254): review and evaluation. Fundam Appl Toxicol 31:42-55, 1996.
Aro84	Arora, N. and S.K. Kulshrestha. Comparison of the Toxic Effects of Two Pesticides on the Testes of a Freshwater Teleost Channa Striatus Bloch. Acta hydrochim. et hydrobiol. 12-4, 435-441, 1984.
Ash97	Ashby, J., H. Tinwell, P.A. Lefevre, J. Odum, D. Paton, S.W. Millward, S. Tittensor and A.N. Brooks. Normal Sexual Development of Rats Exposed to Butyl Benzyl Phtalate from Conception to Weaning. Regulatory Toxicology and Pharmacology 26, 102-118, 1997.
Ast88	Astroff B, Safe S. Comparative antiestrogenic activities of 2,3,7,8-tetrachlorodibenzo-p-dioxin and 6-methyl-1,3,8-trichlorodibenzofuran in the female rat. Toxicol. Appl. Pharmacol 1988; 95: 435-443.
Ast91	Astroff B, Eldridge B, Safe S. Inhibition of the 17 b-estradiol-induced and constitutive expression of the cellular protooncogene c-fos by 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDS) in the female rat uterus. Toxicol. Letters 1991; 305-315.
Ats93b	ATSDR (1993b), Toxicological profile for diethylphthalate, Draft for public comment. U.S. Department of Health & Human Services,
aug93	Aughton, 1993
Bal84	Bal, H.S. (1984), Effect of methoxychlor on reproductive systems of the rat (41861). Proc Soc Exp Biol Med, 7: 187-196.
Bar68	Baron, R.L. (1968), Radioactive lactose in skim milk following administration of carbo nyl-14C-carbaryl to a lactating cow, J Assoc Off Anal Chem 51: 1046-1049.
Bar83	Barnes, T. Bradford, Anthony J. Verlangieri and Marvin C. Wilson. Reproductive Toxicity of Methyl-1-(Butylcarbamoyl)-2-Benzimidazole Carbamate (Benomyl) in Male Wistar Rats. Toxicology, 28, 103-115, 1983.
bar97	Barr AC; Abbitt B; Fiske RA; Jaques JT; Maynard HR; Reagor JC (1997). Reproductive effects of fenoxycarb on sheep.J Vet Diagn Invest; VOL 9, ISS 4,

P401-6
Bee92 Bee, W., (1992). S7131 90 day oral (gavage) subchronic study in the Cynomolgus monkey. Hazleton Deutschland Gmbh. Project No 941-333-006. Sumitomo Chemical Co., Ltd. Ref. No. BT-21-0147. March 17, 1992.
Beh89 Behera BC; Bhunya SP (1989). Studies on the genotoxicity of asataf (acephate), an organophosphate insecticide, in a mammalian in vivo system.Mutat Res; VOL 223, ISS 3, P287-93
Ber91 Van den Berg K.J. et al. (1991) Interactions of halogenated industrial chemicals with tranthyretin and effects on thyroid hormone levels in vivo. Arch. Toxicol., 65, 15-19.
Ber94 Bergeron JM, Crews D, McLachlan JA. PCBs as environmental estrogens: turtle sex determi nation as a biomarker of environmental contamination. Environ Health Perspect 102:780-781, 1994.
bes91 den Besten C; Vet JJ; Besselink HT; Kiel GS; van Berkel BJ; Beems R; van Bladeren PJ (1991). The liver, kidney, and thyroid toxicity of chlorinated benzenes. Toxicol Appl Pharmacol; VOL 111, ISS 1, P69-81. Department of Toxicology, Agricultural University, Wageningen, The Netherlands.
bes93 Besten C. den, M.H. Bennik, I. Bruggeman, P. Schielen, F. Kuper, A. Brouwer, J.H. Koeman, J.G. Vos and P.J. van Bladeren (1993), The role of oxidative metabolism in hexacholoro benzene-induced porphyria and thyroid hormone homeostasis: a comparison with pentachlorobenze ne in a 13-week feeding study, Toxicol. Appl. Pharmacol., 119: 181-194.
Bes96 Besedovsky HO, Del Rey A. Immune-neuro-endocrine interactions: facts and hypotheses. Endocr Rev 17:64-102, 1996.
Bha89 Bhattacharya and Pandey. Overgenomen uit Kim95.
Bit70 Bitman J, Cecil HC. Estrogenic activity of DDT analogs and polychlorinated biphenyls. J Agr Food Chem 18:1108- 1112, 1970.
Bit78 Bitman J, Cecil HC, Harris SJ, Feil VJ. Estrogenic activity of qp'-DDT metabolitus and related compounds. J. Agric. Food Chem 1978; 26: 1, 149-151.
Bla00 Blair RM; Fang H; Branham WS; Hass BS; Dial SL; Moland CL; Tong W; Shi L; Perkins R; Sheehan DM (2000). The estrogen receptor relative binding affinities of 188 natural and xenochemicals: structural diversity of ligands. Toxicol Sci; VOL 54, ISS 1, 2000, P138-53 USA. rblair@nctr.fda.gov
bla88 Black WD; Valli VEO; Ruddick JA; Villeneuve DC (1988). Assessment of Teratogenic Potential of 1,2,31,2,4and 1,3,5-Trichlorobenzenes in Rats. Bulletin of Environmental Contamination and Toxicology; Vol. 41, No. 5, pages 719-726, 22 references1988
Bog94 Bogdanffy et al., 1994
Boo80 Booth et al., 1980
Bra83 Bradford Barnes, T., A.J. Verlangieri and M.C. Wilson (1983), Reproductive toxicity of methyl-1-(butylcarbamoyl)-2-benzimidazole carbamate (benomyl) in male wistar rats, Toxicology, 28: 103-115.
Bre90 Bresch, H., H. Beck, D. Ehlermann, H. Schlaszus and M. Urbanek (1990), A long-term toxicity test comprising reproduction and growth of zebrafish with 4 - chloroaniline, Arch. Env. Contam. Toxicol., 19: 419-27.
bug80 BUGGIANI SS (1980). THE EFFECTS OF POLYCHLORINA TED NAPHTALENES (PCN) ON METAMORPHOSIS OF RANA AGILIS TADPOLES. DEV ANIM VET SCI; 6:326-327
Bul77 Bulger, W.H. and D. Kupfer (1977), Inhibition of the 1-(o-chlorophenyl)-1-(p-chlorophenyl)-2,2,2-trichloroethane(o,p'DDT)- and estradiol-mediated induction of rat uterine ornithine decarboxylase by prior treatment with o,p'DDT estradiol, and tamoxifen, Arch. Biochem. Biophys., 182: 138-146.
Bul78a Bulger WH, Kupfer D. Studies on the induction of rat uterine onithine decarboxylase by DDT analogs. I. Comparison with estradiol-17 activity. Pesticide Biochem. Physiol 1978; 8: 253-262.
Bur72 Burdick, G.E., H.J. Dean, E.J. Harris, J. Skea, R. Karcher and C. Frisa (1972), Effect of rate and duration of feeding DDT on the reproduction of salmonid fishes reared and held under controlled conditions, NY Fish Game J., 19: 97-115.
Bus68 Busey W.M., 1968. Repeated dermal application test on rabbits using a wettable powder formulation (50% benomyl). Falls Church, Virginia, Hazelton Laboratories, Inc. (Unpublis hed report No. HLO 298-68, prepared for E.I Du Peron de Nemours and Co., Inc.).
But71 Butler, 1971. No reference given. From EHC39, Environmental health criteria Paraquat and Diquat, 1984, WHO Geneva
Car82 Carter S.D., 1982. Effects of benomyl on the reproductive development in the prepubertal male rat. Raleigh, North Carolina, North Carolina State University

(Thesis).

Car82a Carter S.D. and Laskey J.W., 1982. Effects benomyl on reproduction in the male rat. Toxicol Lett, 11: 87-94.

cas83 Cassidy, S.L. et al (1983) Evaluation of testicular sperm head counting technique using rats exposed to dimethoxyethyl phthala te (DEMP), glycerol -Monochlorohydrin (GMCH), epichlorohy drin (ECH), formaldehyde (FA), or methyl methanesulphonate (MMS). Arch. Toxicol., 53: 71-78.

cec81 Cecil, H.C. et al. (1981) Feeding three insect growth regulators to white Leghorn hens: Residues in eggs and tissues and effects on production en reproduction. Poult. Sci., 60: 2017-2027.

Cef02/Sot From CEFIC 2002: Soto et al and Sonnenshein (no further details)

Cha92 Chaloupka K, Krishman V, Safe S. Polynuclear aromatic hydrocarbon carcinogens as antiestrogens in MCF-7 human breast cancer cells: role of the Ah receptor. Carcinogenesis 13:2233-2239, 1992.

Che92 Chen Y-CJ, Guo Y-L, Hsu CC, Rogan WJ. Cognitive development of Yu-Chen (oil disease) children prenatally exposed to heat-degraded PCBs. JAMA 268:3213-3218, 1992.

Cho93 Choudhury, C., A.K. Ray, S. Bhattacharya and S. Bhattacharya (1993), Non lethal concentrations of pesticide impair ovarian function in the freshwater perch, Anabas testudineus, Env. Biol. Fishes, 36: 319-24.

Chu82 Chu I; Secours VE; Villeneuve DC; Valli VE (1982). Acute and subacute toxicity of octachlorostyrene in the rat.J Toxicol Environ Health; VOL 10, ISS 2, P285-96

chu84 Chu I; Villeneuve DC; Secours VE; Yagminas A; Reed B; Valli VE (1984). Octachlorostyrene: a 90-day toxicity study in the rat. Fundam Appl Toxicol; VOL 4, ISS 4, P547-57

chu86 Chu I; Villeneuve DC; Secours VE; Valli VE; Leeson S; Shen SY (1986). Long-term toxicity of octachlorostyrene in the rat.Fundam Appl Toxicol; VOL 6, ISS 1, P69-77

Chu94-96 Chu, I., D.C. Villeneuve, A. Yagminas, P. LeCavalier, R. Poon, M. Feely, S.W. Kennedy, R.F. Seegal, H. Hakansson, U.G. Ahlborg and V.E. Valli (1994), Subchronic Toxicity of 3,3',4,4',5-Pentachlorobiphenyl in the Rat. 1. Clinical, Biochemical, Hematological, and Histopatho logical Changes, Fund. Appl. Toxicol., 22: 457-468. and Chu, I., D.C. Villeneuve, A. Yagminas, P. LeCavalier, R. Poon, M. Feeley, S.W. Kennedy, R.F. Seegal, H. Hakansson, U.G. Ahlborg, V.E. Valli and A. Bergmann (1996b), Toxicity of 2,2',4,4',5,5'-hexachlorobiphenyl in rats: Effects following 90-day oral exposure, J. Appl. Toxicol., 16: 121-128.

Chu95 Chu, I., D.C. Villeneuve, A. Yagminas, P. LeCavalier, H. Hakansson, U.G. Ahlborg , V.E. Valli, S.W. Kennedy, A. Bergman, R.F. Seegal, and M. Feeley (1995), Toxicity of PCB 77 (3,3',4,4',5-Tetrachlorobiphenyl) and PCB 77 (2,3',4,4',5-Pentachlorobiphenyl) in the rat following subchronic dietary exposure, Fund. Appl. Toxicol., 26: 282-292.

Chu96 Chu I; Villeneuve DC; Yagminas A; Lecavalier P; Poon R; Hakansson H; Ahlborg UG; Valli VE; Kennedy SW; Bergman A; Seegal RF; Feeley M (1996). Toxicity of 2,4,4'-trichlorobiphenyl in rats following 90-day dietary exposure. J Toxicol Environ Health; VOL 49, ISS 3, 1996, P301-18. Institution: Environmental Health Directorate, Health Protection Branch, Ontario, Canada.

Chu96b Chu, I., D.C. Villeneuve, A. Yagminas, P. LeCavalier, R. Poon, M. Feeley, S.W. Kennedy, R.F. Seegal, H. Hakansson, U.G. Ahlborg, V.E. Valli and A. Bergmann (1996b), Toxicity of 2,2',4,4',5,5'-hexachlorobiphenyl in rats: Effects following 90-day oral exposure, J. Appl. Toxicol., 16: 121-128.

Chu96c Chu, I., D.C. Villeneuve, A. Yagminas, P. LeCavalier, R. Poon, H. Hakansson, U.G. Ahlborg, V.E. Valli, S.W. Kennedy, A. Bergmann, R.F. Seegal, and M. Feeley (1996c), Toxicity of 2,4,4'-trichlorobiphenyl in rats following 90-day oral exposure, J. Toxicol. Environm. Health, 49: 301-318.

Coo34 Cook JW, Dodds EC, Hewett CL, Lawson W. The estrogenic activity of some conden sed-ring compounds in relation to their other biological activities. Proc. Roy. Soc., B 1934; 114: 272-286.

coo74 Cooper, E.R.A. et al. (1974) Effects of -chlorohydrin and related compounds on the reproductive organs and fertility of the male rat. J. Repr. Fert., 38: 379-386.

coo85a Coombs, D.W., Hardy, C.J., Clark, G.C., Street, A.E., Gopinath, C., Lewis, D.J., & Rao, R.S. (1985) Resmethrin 90-day inhalation toxicity study in the rat, Huntingdon, United Kingdom, Huntingdon Research Centre, 80 pp (Report NO. SBP 6/84997) (Unpublished propietary data supplied by Roussel Uclaf).

Cot88 Cote M; Chu I; Villeneuve DC; Secours VE; Valli VE (1988). Trichlorobenzenes: results of a thirteen week feeding study in the rat.Drug Chem Toxicol; VOL 11, ISS 1, P11-28 RC:

Cou74 Coulston, F., I. Rosenblum & W.J. Dougherty (1974), Teratogenic evaluation of carbaryl in the Rhesus Monkey (Maccaca mulatta), Holloman Airforce Base, New Mexico, International Center of Environmental Safety, Albany Medical College, 54 pp. (Unpublished proprietary information submitted to WHO by Rh¶ne-Poulenc Agro, Lyon).

Cou84 Couch, J.A. (1984). Histopathology and enlargement of the pituitary of a teleost exposed to the herbicide trifluralin. J. Fish Diseases, 7, 157-163.

cum00 Cummings AM; Laws SC (2000). Assessment of estrogenicity by using the delayed implanting rat model and examples.Reprod Toxicol; VOL 14, ISS 2, P111-7

cup01 Cupp AS; Skinner MK (2001). Actions of the endocrine disruptor methoxychlor and its estrogenic metabolite on in vitro embryonic rat seminiferous cord formation and perinatal testis growth.Reproductive toxicology; 15; 3; 317-26

Dan97 Danzo BJ. Environmental xenobiotics may disrupt normal endocrine function by interfering with the binding of physiological ligands to steroid receptors and binding proteins. Environ Health Perspect., VOL 105, ISS 3, 1997,294-301

Das00 Das PC; McElroy WK; Cooper RL (2000). Differential modulation of catecholamines by chlorotriazine herbicides in pheochromocytoma (PC12) cells in vitro. Toxicol Sci; VOL 56, ISS 2, P324-31

Das98 Das SK., Tan J., Johnson DC., Dey SK. Differential spatiotemporal regulation of lactoferrin and progesterone receptor genes in the mouse uterus by primary estrogen, catechol estrogen, and xenoestrogen. Endocrinology, VOL 139, ISS 6, 1998, 2905-2915.

Dic95 Dickerson R, Howie Keller L, Safe S, Alkyl polychlorinated dibenzofurans and related compounds as antiestrogens in the female rat uterus: Stucture-activity studies. Toxicol. Appl. Pharmacol 1995; 135: 287-298.

Die74 Dieringer, C.S & J.A. Thomas (1974), Effects of carbaryl on the metabolism of andro gens in the prostate and liver of the mouse, Environ Res 7: 381-386.

Dik76 Dikshith, T.S.S., P.K. Gupta, J.S. Gaur, K.K. Datta & A.K. Mathur (1976), Ninety-day toxicvity of carbaryl in male rats, Environ Res 12: 161-170.

Dou62a Doull J, Root M., Vesselinovitch D., Meskauskas J. and Fitch F., 1962a. Chronic oral toxicity of dylox to male and female dogs, (Unpublished report submitted to W.H.O. by farbenfebri ken Bayer A.G., Germany).

Dou62b Doull J., Vesselinovitch D., Root M., Cowan J., Meskauskas J. and Fitch F., 1962b. Chronic oral toxicity of dylox to male and female rats, University of Chicago, Department of Pharmacology (unpublished report).

Dya71 Dyadicheva, T.V. (1971), Experimental data on thyroid and adrenal cortex function during prolongued effect of carbamine pesticides, Vrach Delo 2: 120-123 (in Russian).

ede91 Edes TE, Gysbers DG, Buckley CS, & Thornton WH Jr (1991) Exposure to the carcinogen benzopyrene depletes tissue vitamin A: -Carotene prevents depletion. Nutr Can cer: 15: 159-166

EHC205 EHC 205 (1990), Polybrominated Dibenzo-p-dioxins and Dibenzofurans, Environmental Health Criteria 205, International Program on Chemical Safety (ICPS), World Health Organization, Geneva.

EHC92 EHC 123 (1992), Alpha- and Breta-hexachlorocyclohexanes, Environmental Health Criteria 123 , International Programme on Chemical Safety (IPCS), WHO, Geneva.

EHC93 EHC 149 (1993), Carbendozin, Environmental Health Criteria 149, International Program me on Chemical Safety (IPCS), WHO, Geneva.

EHC94 EHC 153 (1994), Carbaryl, Environmental Health Criteria 153, International Program me on Chemical Safety (IPCS), WHO, Geneva.

eil90 Eil C; Nisula BC (1990). The binding properties of pyrethroids to human skin fibroblast androgen receptors and to sex hormone binding globulin. . J Steroid Biochem; VOL 35, ISS 3-4, P409-14

elc94 Elcombe, C.R. et al. (1994) Chorinated Paraffins (CP): Mecha nisms of carcinogenesis. Toxicologist, 14: 276.

ena97 Enan, E. & Matsumura, F. (1997) Activation of c-Neu Kinase by qp'-DDT and -HCH in Cell-Free and Intact Cell Preparations from MCF-7 Human Breast Cancer Cells. J. Biochem. Mol. Toxicol. 12 (2): 83-92.

ero00 Eroschenko VP; Johnson TJ; Rourke AW (2000). Estradiol and pesticide methoxychlor do not exhibit additivity or synergism in the reproductive tract of adult ovariectomized mice.J Toxicol Environ Health A; VOL 60, ISS 6, P407-21

Ero95 Eroschenko VP, Awad Abuel-Atta A, Grober MS. Neonatal exposure to technical methoxychlor alters ovaries in adult mice. Reprod. Toxicol 1995; 9: 4, 379-387.

Fry81 Fry D.M., Toone C.K. (1981) DDT-induced feminization of gull embryos. Science 213: 922- 924.

fuj77 Fujita, K. et al. (1977) Examination of the effects of dichlor vos on the testis. Nippon Noson Igakkai Zasshi, 26 (3): 328- 329 (in Japanese).

Gar98 Garey J., Wolff MS. Estrogenic and antiprogestagenic activities of pyrethroid insecticides. Biochem Biophys Res Commun., VOL 251, ISS 3, 1998, 855-859

Gel74 Gellert RJ, Heinrichs WL, Swerdloff R. Effects of neonatally-administered DDT homologs on reproductive function in male and female rats. Neuroendocrinology 1974; 16: 84-94.

Ger92 Gerhard I, Runnebaum B. Grenzen der hormonsubstitution bei Schadstoffbelastung und fertilitatsstorungen. Zent bl Gynakol 114:593-602, 1992.

ghi80 Ghinea E; Simionescu L; Oprescu M (1980). Studies on the action of pesticides upon the endocrines using in vitro human thyroid cells culture and in vivo animal models. II. Herbicides-prometrin and terbutrin. Endocrinologie; 18; 3; 167-73 Jul-Sep

Gho89 Ghosh P., Bhatttacharya S. and Bhattacharya S., 1989. Impact of nonlethal levels of metacid - 50 and carbaryl on thyroid function and cholinergic system of Channa punctatus. Biomed. Environ. Sci., 2: 92-97.

Gho90 Ghosh, P., S. Bhattacharya and S. Bhattacharya (1990), Impairment of the regulation of gonadal function in Channa punctatus by metacid 50 and carbaryl under laboratory and field conditions, Biomed. Environ. Sci., 3: 106-12.

Gie97 GIERTHY JF., ARCARO KF., FLOYD M. Assessment of PCB estrogenicity in a human breast cancer cell line. CHEMOSPHERE., 34 (5-7). 1997. 1495-1505.

glo-- Glomot, R. (undated) Etude de la toxicité chronique de 3 semaines chez le rat du RU11484 (NRDC 107) (Unpublis hed data of Roussel Uclaf submitted to WHO by Welcome Foundation Ltd.).

gol80b/ ric83 Goldenthal, E.I., Jefferson, N.D., Blair, M., Thorestenson, J.H.M, Spicer, E.J.F., Arceo, R.J.& Kahn, A., III (1980b) RU 22974. Two year oral toxicity and carcinonenicity study in rats, Mattawan, Michigan, International Research and Deve lopment Corporation (Unpublished report IRDC 406- 002/A.4, submitterd to WHO by Roussel Uclaf). Richter, W.R. & Goldenthal, E.I. (1983) Two-year oral toxicity and carcinogenicity study in rts. Amendment to the final report. Matawanm, Michinga, Internationa; Research and Develop ment Corporation (Unpublished proprietary report IRDC 406.002/AS5, submitted to WHO by Roussel Uclaf).

Gol89 Goldstein, J.A. and S. Safe (1989), Mechanism of action and structure-activity relationship for the chlorinated dibenzo-p-dioxins and related compounds, In: Kimbrough, R.D. and A.A. Jensen, ed. Halogenated biphenyls, terphenyls, naphthalenes, dibenzodioxins and related products, 2nd ed., Amsterdam, Oxford, New York, Elsevier Science Publishers, chapter 9, pp. 239-293.

Goo78/ Fao85a Gooch J.J., 1978. Fertility of workers potentially exposed to benomyl. Wilmington, Delawa re, E.I. Du Pont de Nemours and Co., Inc. (Unpublished report No. B/TOX 7). From: FAO/WHO, 1985a. Benomyl. In: Pesticide residues in food - Evaluations 1983. Rome, Food and Agriculture Organisation of the United Nations, pp 7-46 (FAO Plant Production and Protection Paper 61).

gor01 Gore AC (2001). Environmental toxicant effects on neuroendocrine function.Endocrine; 14; 2; 235-46

Gra89 Gray LE Jr, Ferrell J, Ostby J, Rehnberg G, Linder R, Cooper R, Goldman J, Slott V, Laskey J. A dose response analysis of methoxychlor-induced alterations of reproductive development and function in the rat. Fundam Appl Toxicol 12:92-108, 1989.

gra91 Gray, L.E. et al. (1991) A fungicide (fenarimol) that inhibits fungal sterol synthesis also reduces mating behavior and fertility in male rats. Biol. Reprod. 44 (suppl. 1):132.

Gra96 GRAY L E JR., KELCE WR. Latent effects of pesticides and toxic substances on sexual differentiation of rodents. TOXICOLOGY AND INDUSTRIAL HEALTH., 12 (3-4). 1996. 515-531.

Gra98b Gray LE Jr (1998). Xenoendocrine disrupters: laboratory studies on male reproductive effects. Toxicol Lett 1998 Dec 28; 102-103:331-5 gray.earl@epamail.epa.gov

gra99 Gray LE Jr; Wolf C; Lambright C; Mann P; Price M; Cooper RL; Ostby J (1999). Administration of potentially antiandrogenic pesticides (procymidone, linuron, iprodione, chlozolinate, p,p'-DDE, and ketoconazole) and toxic substances (dibutyl- and diethylhexyl phthalate, PCB 169, and ethane dimethane sulphonate) during sexual differe. Toxicol Ind Health; VOL 15, ISS 1-2, 1999, P94-118 MD-72, Research Triangle Park, NC 27711, USA. gray.earl@epamail.epa.gov

Guh88 Guhathakurta, S., and S. Bhattacharya, 1988. Target and Nontarget Actions of Phenthoate and Carbofuran: Brain Acetylcholinesterase, Kidney Iodide Peroxidase,

and Blood Thyroxine Profiles in. Biomed.Environ.Sci. 1:59-63. Aquire code:C

Gul82 Gulka, G. et al. (1982) Histopathological effects of diflubenzuron on the cirripede crustacean, Balanus eburneus. Bull. Environ. Contam. Toxicol., 11: 11-16.

Haa80 Ter Haar G., 1980. An investigation of possible sterility and health effects from exposure to ethylene dibromide. In: Ames B., Infante O. and Peirtz R. ed. Ethylene dichloride: A potentional health risk? Cold Spring Harbor, New York, Cold Spring Harbor Laboratory, pp. 168-188 (Banbury Report No.5).

Hai85 Haider, S. and N. Upadhyaya (1986), Effect of commerical formulation of four organop hosphorus insecticides on the ovaries of a freshwater teleost, Mystus vittatus (Bloch) - a histological and histochemical study, J. Env. Sci. Health, B20: 231-40.

Hai98 Hainzl D; Cole LM; Casida JE (1998). Mechanisms for selective toxicity of fipronil insecticide and its sulfone metabolite and desulfinyl photoproduct. Chem Res Toxicol; VOL 11, ISS 12, 1998, P1529-35 University of California, Berkeley, California 94720-3112, USA.

Ham91b Hamada, N.N. (1991b), Oncogenicity with carbaryl technical in CD-1« mice, Vienna, Virginia, Hazleton Laboratories America, Inc. (Report No. N656-138) proprietary information submitted to WHO by Rh¶ne-Poulenc Agro, Lyon).

Har74 Harris SJ, Cecil HC, Bitman J. Effect of several dietary levels of technical metoxychlor on reproduction in rats. J. Agr. Food Chem 1974; 22: 969-973.

Har94 Harper N, Wang X, Liu H, Safe S. Inhibition of estrogen-induced progesterone receptor in MCF-7 human breast cancer cells by aryl hydrocarbon (Ah) receptor agonists. Molec. Cell. Endrocin 1994; 104: 47-55.

Har95 Harries JE, Jobling S, Matthiessen P, Sheahan DA, Sumpter JP. Effects of trace organics in fish--phase 2. Report to the Department of the Environment, Foundation for Water Research, The Listons, Liston Road, Marlow Bucks SL7 1 FD, Great Britain. Report No. FR/D 0022, 1995.

har97 Harris CA; Henttu P; Parker MG; Sumpter JP (1997). The estrogenic activity of phthalate esters in vitro.Environ Health Perspect; VOL 105, ISS 8, P802-11

hay01 Hayes FJ; DeCruz S; Seminara SB; Boepple PA; Crowley WF Jr (2001). Differential regulation of gonadotropin secretion by testosterone in the human male: absence of a negative feedback effect of testosterone on follicle- stimulating hormone secretion.The Journal of clinical endocrinology and metabolism; 86; 1; 53-8101

Hay88 Hayes R.H., 1988. Oncogenicity study of technical grade trichlorfon with mice, Stillwell, Kansas, mobay corporation (proprietary study report No. 1039 submitted to W.H.O. by Bayer A.G., Germany).

hem01 Hemmer MJ; Hemmer BL; Bowman CJ; Kroll KJ; Folmar LC; Marcovich D; Hoglund MD; Denslow ND (2001). Effects of p-nonylphenol, methoxychlor, and endosulfan on vitellogenin induction and expression in sheepshead minnow (Cyprinodon variegatus).Environmental toxicology and chemistry / SETAC; 20; 2; 336-43

Hes91 Hess, Rex A., B.J. Moore, Janet Forrer, Ralph E. Linder and Ahmed Awad Abuel-Atta. The Fungicide Benomyl (Methyl 1-(Butylcarbamoyl)- 2-benzimidazolecarbamate) Causes Testicular Dysfunction by including the Sloughing of Germ Cells and Occlusion of Efferent Ductules. Fundamental and Applied Toxicology 17, 733-745, 1991.

hin86 Hinton RH; Mitchell FE; Mann A; Chescoe D; Price SC; Nunn A; Grasso P; Bridges JW (1986). Effects of Phthalic Acid Esters on the Liver and Thyroid. Environmental Health Perspectives; Vol. 70, pages 195-210, 91 references

Hir87 Hirsch KS, Weaver DE, Black LJ, Falcone JF, MacLusky NJ. Inhibition of central nervous system aromatase activity: a mechanism for fenarimol-induced infertility in the male rat. Toxicol Appl Pharmacol 91:235-245, 1987.

hod00 Hodges LC; Bergerson JS; Hunter DS; Walker CL (2000). Estrogenic effects of organochlorine pesticides on uterine leiomyoma cells in vitro.Toxicol Sci; VOL 54, ISS 2, P355-64

hol69 Holsing, G.C., 1969

Hoo69 Hood D.B., 1969. Fifteen exposure dermal tests on rabbits using a wettable powder formula tion (50% benomyl). Newark, Delaware, E.I. Du Pont de Nemours and co., Inc., Haskell Laboratory (Unpublished report No. HLR 211-69).

Hos93 Hosokawa S, Murakami M, Ineyama M, Yamada T, Yoshitake A, Yamada H, Miyamoto J. (1993) The affinity of procymidone to androgen receptor in rats and mice. J Toxicol Sci 18:111-124, 1993.

Hur98 Hurley PM (1998). Mode of carcinogenic action of pesticides inducing thyroid follicular cell tumors in rodents.Environ Health Perspect; VOL 106, ISS 8, P437-45

iox01b Ioxynil, endpotnts mammalian toxicology. Filenaam: IOXYNIL_end_points_mamtox(011025) dated 21-03-02

irdc81a IRDC (1981a) 14-Day oral toxicity study in rats. Chlorinated parrafin: 58% chlorination of short chain length n-paraffins. Mattawan, Michigan, International Research and Development Corporation, 104 pp (report no. 438-006).

irdc82e IRDC (1982e) Teratology study in rabbits. Chlorinated paraffin: 43% chlorination of short chain lenght n-paraffins. Mattawan, Michigan, International Research and Development Corporation, 102 pp (report no. 438-030).

irdc83b IRDC (1983b) Teratology study in rats. Chlorinated paraffin: 70% chlorination of long chain lenght n-paraffins. Mattawan, Michi gan, International Research and Development Corporation, 245 pp (report no. 438-045).

irdc83d IRDC (1983d) Teratology study in rats. Chlorinated paraffin: 43% chlorination of long chain lenght n-paraffins. Mattawan, Michi gan, International Research and Development Corporation, 197 pp (report no. 438-015).

irdc83f IRDC (1983f) Teratology study in rabbits. Chlorinated parffin: 52% chlorination of intermediate chain lenght n-paraffins. Matta wan, Michigan, International Research and Development Corpora tion, 195 pp (report no. 438-032).

irdc84b IRDC (1984b) 13-Week oral (dietary) toxicity study in rats with combined excretion, tissue level and elimination studies: determi nation of excretion, tissue level and elimination after single oral (gavage) administration to rats. Chlorinated paraffin: 52% chlori nation of intermediate chain lenght n-paraffins. 14C labeled CP. Mattawan, Michigan, International Research and Development Corporation, 328 pp (report no. 438-023/026).

irdc84c IRDC (1984c) 13-Week oral (dietary) toxicity study in rats with combined excretion, tissue level and elimination studies: determi nation of excretion, tissue level and elimination after single oral (gavage) administration to rats. Chlorinated paraffin: 58% chlori nation of short chain lenght n-paraffins. 14C labeled CP. Matta wan, Michigan, International Research and Development Corpora tion, 435 pp (report no. 438-035/022).

irdc84d IRDC (1984d) Teratology study in rats. Chlorinated paraffin: 52% chlorination of intermediate chain lenght n-paraffins. Mattawan, Michigan, International Research and Development Corporation, 105 pp (report no. 438-017).

irdc84e IRDC (1984e) Teratology study in rats. Chlorinated paraffin: 70% chlorination of long chain lenght n-paraffins. Mattawan, Michi gan, International Research and Development Corporation, 99 pp (report no. 438/045).

Ire80 Ireland JS, Mukku VR, Robinson AK, Stancel GM. Stimulation of uterine deoxyribonucleic acid synthesis by 1,1,1-trichloro-2-(p-chlorophenyl)-2-(o-chlorophenyl)ethane (o,p'-DDT). Biochem. Pharmcol 1980; 29: 1469-1474.

IRIS94 IRIS (1994) EPA's Integrated Risk Information System, US Environmental Protection Agency, Silverplatter 3.11 CD-Rom sytrem (through October 1994). Silverplatter International, N.V. USA.

Ive92 Ivens, I.A., E. L"ser, M. Rinke, U. Schmidt & M. Neupert, Toxicity of 2,3,7,8-tetrabromi dobenzo-p-dioxin in rats after single oral administration, Toxicology 73: 53-69 (1992).

Ive93 Ivens, I.A., E. L"ser, M. Rinke, U. Schmidt & U. Mohr, Subchronic toxicity of 2,3,7,8-tetrabromidobenzo-p-dioxin in rats, Toxicology 83: 181-201 (1993).

Jan93 Jansen, H.T., Cooke, P.S., Porcelli, J., Liu, T.C. and Hansen, L.G. (1993). Estrogenic antiestrogenic actions of PCBs in the female rat: in vitro and in vivo studies. Reprod. Toxicol. 7 237-248.

Jek94 Jekat F.W., Meisel M.L., Eckard R., Winterhoff H. (1994) Effects of pentachlorophenol (PCP) on the pituitary and thyroidal hormone regulation in the rat. Toxicol. Letters 71: 9-25.

Jew98 Jewell WT; Miller MG (1998). Identification of a carboxylesterase as the major protein bound by molinate. Toxicol Appl Pharmacol; VOL 149, ISS 2, 1998, P226-34

Job93 Jobling S, Sumpter JP. Detergent components in sewage effluent are weakly oestrogenic to fish: an in vitro study using rainbow trout (Oncorhynchus mykiss) hepatocytes. Aquatic Toxicol 27:361-372, 1993.

Job96 Jobling S, Sheahan D, Osborne JA, Mathiessen P, Sumpter JP. Inhibition of testicular growth in rainbow trout (Oncorhynchus mykiss) exposed to estrogenic alkylphenolic chemicals. Environ Toxicol Chem 15:194-202, 1996.

Jon93 Jones HB; Garside DA; Liu R; Roberts JC (1993). The influence of phthalate esters on Leydig cell structure and function in vitro and in vivo. Exp Mol Pathol; VOL 58, ISS 3, P179-93

jor00 Jorgensen M; Vendelbo B; Skakkebaek NE; Leffers H (2000). Assaying estrogenicity by quantitating the expression levels of endogenous estro gen-regulated genes.Environ Health Perspect; VOL 108, ISS 5, P403-12

Kap78 Kapur, K., K. Kamaldeep and H.S. Toor (1978), The effect of fenitrothion on

reproduction of a teleost fish, Cyprinus carpio communis, Linn: a biochemical study, Bull. Env. Contam. Toxicol., 20: 438-42.

KAT2000 Katsuda, S. et al., 2000. Dose0 and treatment duration-related effects of p-tert-octylphenol on femal rats. Reproductive Toxiclogy, 14, 119-126.

Kav82 Kavlock R.J., Chernoff N., Gray L.E., Gray L.E., Gray J.A. and Whitehouse D., 1982, Teratogenic effects of benomyl in the Wistar rat and CD-1 mouse, with emphasis on the route of administration. Toxicol Appl. Pharmacol, 62: 44-54.

Kee76b Keet, 1976b, (cited in FAO1981)

Kel94 Kelce WR, Monosson E, Gamcsik MP, Laws SC, Gray LE Jr. Environmental hormone disruptors: evidence that vinclozolin developmental toxicity is mediated by antiandrogenic metaboli tes. Toxicol Appl Pharmacol 126:276-285, 1994.

Kel95a Kelce WR, Stone CR, Laws SC, Gray LE Jr, Kemppainen JA, Wilson EM. Persistent DDT metabolite p,p'-DDE is a potent androgen receptor antagonist. Nature 375:581-585, 1995a

Kel97 Kelce W. et al., Toxicol. Appl. Pharmacol., Vol. 142, 192-200, 1997

kha96 Khan P.K. and S.P. Sinha. (1996) Ameliorating effect of Vitamin C in murine sperm toxicity induced by three pesticides (endosulfan, phosphamidon and mancozeb). Mutagenesis vol. 11, no. 1, 33-36, 1996.

Kim95 Kime, D.E. (1995). The effects of pollution on reproduction in fish. Revs. Fish Biol. Fisheries 5 52-96.

Klo97 KLOTZ DM., ARNOLD SF., MCLACHLAN JA. Inhibition of 17 beta-estradiol and progesterone activity in human breast and endometrial cancer cells by carbamate insecticides. LIFE SCIENCES., 60 (17). 1997. 1467-1475.

Klu83 Kluwe WM; Gupta BN; Lamb JC (1983). The Comparative Effects Of 1,2-Dibromo-3-chloropropane (DBCP) And Its Metabolites, 3-Chloro-1,2-propaneoxide (Epichlorohydrin), 3-Chloro-1,2-propanediol (Alphachlorohydrin), and Oxalic Acid. Toxicology and Applied Pharmacology; Vol. 70, No. 1, pages 67-86, 31 references, 19831983

Kni79 Kniewald J; Mildner P; Kniewald Z (1979). Effects of s-triazine herbicides on hormone-receptor complex formation, 5 alpha-reductase and 3 alpha-hydroxysteroid dehydrogenase activity at the anterior pituitary level. J Steroid Biochem; VOL 11, ISS 1C, 1979, P833-8

kni95 Kniewald, J., V. Osredecki, T. Gojmerac, V. Zechner and Z. Kniewald (1995). Effect of s-Triazine Compounds on Testosterone Metabolism in the Rat Prostate. Journal of Applied Toxicology, vol.15(3), 215-218, 1995.

Kora88 Korach KS, Sarver P, Chae K, McLachlan JA, McKinney JD. Estrogen receptor-binding activity of polychlorinated hydroxybiphenyls: conformationally restricted structural probes. Molec. Pharmacol 1988; 33: 120-126.

kra72/74 Krause, W. & Homola, S. (1972) Influence on spermatogene sis by DDVP (dichlorvos). Arch Dermatol Forsch., 244: 439- 441 (in German). Krause, W. & Homola, S. (1974) Alterati ons of the seminiferous epithelium and the Leydig cells of the rat* testis after the application of dichlorvos (DDVP). Bull. environ. Contam. Toxicol., 154 (4): 429-433 (*study was performed on mice).

kra74 Krause, W. & Homola, S. (1974) Alterations of the seminiferous epithelium and the Leydig cells of the rat* testis after the application of dichlorvos (DDVP). Bull. environ. Contam. Toxicol., 154 (4): 429-433 (*study was performed on mice).

kra76/ xin83 Krause, W. et al. (1976) Damage to spermatogenesis in juvenile rat treated with DDVP and malathion. Bull. environ. Contam. Toxicol. 15 (4): 458-462. Xing-Shu, H. (1983) Preventing chemical damage to germ cells. Am. Ind. Hyg. Assoc. J., 44: 699-703.

kra77 Krause, W. (1977) Influence of DDT, DDVP, and malathionn on FSH, LH, and testosterone concentrations in testis. Bull. environ. Contam. Toxicol., 18(2): 231-242.

Kri93 Krishnan, V. & Safe, S. (1993). Polychlorinated biphenyls (PCBs), dibenzo-p-dioxins (PCDDs) and dibenzofurans (PCDFs) as antiestrogens in MCF-7 human breast cancer cells: quantative structure-activity relationships. Toxicol. Appl. Pharmacol., 120, 55-61.

Kry70 Krylov, D.G., The effect of Sevin on red vole poulation, Gig Primen Toxicol Pestic Klin Otrav 1970: 218-110 (in Russian).

kub81 Kubena LF (1981). The influence of diflubenzuron and several weight characteristics in growing male broiler and layer chickens. Poult Sci; 60(6): 1175-1182 1981 (9 References)

kub82 Kubena, L.F. (1982) The influence of diflubenzuron on several reproductive characteristics in male and female layer-breed chickens. Poult. Sci., 61: 268-271.

Kui98 Kuiper GG., Lemmen JG., Carlsson B., Corton JC., Safe SH., van der Saag PT.,

van der Burg B., Gustafsson JA. Interaction of estrogenic chemicals and phytoestrogens with estrogen receptor beta. Endocrinology., VOL 139, ISS 10, 1998, P4252-63

Kul84 Kulshestra, S.K. and N. Arora. Impairments Induced by Sunblethal Doses of Two Pesticides in the Ovaries of a Freshwater Teleost Channa Striatus Bloch. Toxicology Letters 20, 93-98, 1984.

Kum88 Kumar, S. and S.C. Pant. Comparative Sublethal Ovarian Pathology of Some Pesticides in the Teleost, Puntius conchonius Hamilton. Bull. Env. Contam. Toxocol. 41, 227-232, 1988.

Kup87a Kupfer D, Bulger WH. Metabolic activation of pesticides with proestrogenic activity. Fed. Proc 1987; 46: 1864-1869.

laf00 Lafuente A; Márquez N; Pousada Y; Pazo D; Esquifino AI (2000). Possible estrogenic and/or antiandrogenic effects of methoxychlor on prolactin release in male rats.Archives of toxicology; 74; 4-5; 270-5

lak82 Lake BG; Foster JR; Collins MA; Stubberfield CR; Gangolli SD; Srivastava SP (1982). Studies on the effects of orally administered dicyclohexyl phthalate in the rat.Acta Pharmacol Toxicol (Copenh); VOL 51, ISS 3, P217- 26

lam87 Lamb JC; Chapin RE; Teague J; Lawton AD; Reel JR (1987). Reproductive Effects of Four Phthalic Acid Esters in the Mouse. Toxicology and Applied Pharmacology; Vol. 88, No. 2, pages 255-269, 22 references1987

law00 Laws SC; Carey SA; Ferrell JM; Bodman GJ; Cooper RL (2000). Estrogenic activity of octylphenol, nonylphenol, bisphenol A and methoxychlor in rats.Toxicol Sci; VOL 54, ISS 1, P154-67

Lec97 Lecavalier P; Chu I; Yagminas A; Villeneuve DC; Poon R; Feeley M; Hakansson H; Ahlborg UG; Valli VE; Bergman A; Seegal RF; Kennedy SW (1997). Subchronic toxicity of 2,2',3,3',4,4'-hexachlorobiphenyl in rats. J Toxicol Environ Health; VOL 51, ISS 3, 1997, P265-77 .Institution: Health Protection Branch, Health Canada, Ottawa, Ontario, Canada.

Li95 Li MH, Hansen LG.Uterotropic and enzyme induction effects of 2,2',5-trichlorobiphenyl. Bull. Environ. Contam. Toxicol 1995; 54: 494-500.

Lij83 Lijinsky, W. & Reuber, M.D. (1983) Chronic toxicity studies of vinyl acetate in Fisher rats. Toxicol. Appl. Pharmacol. 68: 43-53.

Lim97 Lim, Junghee and Marion G. Miller. The Role of the Benomyl Metabolite Carbendazim in Benomyl-Induced Testicular Toxicity. Toxicology and Applied Pharmacology 142, 401-410, 1997

Lin00 Lin N; Garry VF (2000). In vitro studies of cellular and molecular developmental toxicity of adjuvants, herbicides, and fungicides commonly used in Red River Valley, Minnesota. J Toxicol Environ Health A; VOL 60, ISS 6, 2000, P423-39

Lin86a Linder RE; Strader LF; McElroy WK (1986). Measurement of epididymal sperm motility as a test variable in the rat. Bull Environ Contam Toxicol; VOL 36, ISS 3, 1986, P317-24

Lin88 Linder R.E., Rehnberg G.L., Strader L.F. and Diggs J.P., 1988. Evaluation of reproductive parameters in adult male Wistar Rats after subchronic exposure. J. Toxicol Environ Health, 25: 285-298.

Lit69 Littlefield N.A. and Busey W.M., 1969. Four-hour acute inhalation exposure test in dogs using a wettable powder formulation (50% benomyl). Falls Church, Virginia, Hazelton Laboratories, Inc. (Unpublished Report No. HLR 192-69, prepared for E.I. du Pont de Nemours and co., Inc.

Lit86 Litton, 1986, cited in Overview and evaluation of the potential endocrine effects of procymidone (Environmental Health Science Laboratory. Sumitomo Chemical Co., Ltd.) April 2001. Filename: Procymidone 4-2A.doc (21-03-02)

Liu92 Liu H, Biegel L, Narasimhan TR, Rowlands C, Safe S. Inhibition of insulin-like growth factor-I responses in MCF-7 cells by 2,3,7,8-tetrachlorodibenzo-p-dioxin and related compounds. Molec. Cell. Endocrin 1992; 87: 19-28.

Luc87 Luca, D. & M. Balan (1987), Sperm abnormality assay in the evaluation of the genotoxic potential of carbaryl in rats, Morphol Embryol (Bucur) 33(1): 19-22.

Lun90 Lundkvist, U. (1990), Clinical and reproductive effects of Clophen A50 (PCB) administered during gestation on pregnant guinea pigs and their offspring, Toxicology, 6: 249-257.

maa80 Maas, W. Van et al. (1980) [Bezoylphenylurea insecticides.] in: Wegler, R. ed. [Chemistry of plant protection chemicals and pesticides.] Berlin, Heidelberg, Springer Verlag, vol 6, pp 432- 470 (in German).

Mac68 Macek, K.J. (1968), Reproduction in brook trout (Salvelinus fontinalis) fed sublethal concentrations of DDT, J. Fish. Res. Bd. Can., 25: 1878-96.

Mah00 Mahadevaswami MP; Jadaramkunti UC; Hiremath MB; Kaliwal BB (2000). Effect of

mancozeb on ovarian compensatory hypertrophy and biochemical constituents in hemicastrated albino rat. Reprod Toxicol; VOL 14, ISS 2, 2000, P127-34 Dharwad, India.

Mah01 Mahgoub AA; El-Medany AH., 2001. Evaluation of chronic exposureof the male rat reproductive system to the insecticide methomyl. Pharmacological research : the official journal of the Italian Pharmacological Society; 44; 2; 73-80; 200108

Man00 Mancozeb Addendum. Filenaam: mancozeb_addendum01_tox(endpoints)-MH dated 14-04-00.

Man85 Mani, K. and P.K. Saxena (1985), Effect of safe concentrations of some pesticides on ovarian recrudescene in the freshwater murrel, Channa punctatus (B1.): a quantitative study, Ecotoxicol. Env. Safety, 9: 241-9./ Sax87: Saxena, P.K. and K. Mani (1987), Effect of safe concentrations of some pesticides on testicular recrudescence in the freshwater murrel, Channa punctatus (Bl.): a morphological study, Ecotoxicol. Env. Safety, 14: 56-63.

Mat90a Mattison DR, et al. (1990a). Reproductive effects of pesticides. In: The effects of pesticides on human health. Baker, S.R., Wilkinson, C.E. (Eds). Proceddings of a workshop Advances in modern Environmental Toxicology, Vol. XVIII, PrincetonSci. Publ. Co., Inc., New Jersey.

May86 Mayer, F.L.J., and M.R. Ellersieck, 1986. Manual of AcuteToxicity: Interpretation and Data Base for 410 Chemicals and 66Species of Freshwater Animals. Resour.Publ.No.160,U.S.Dep.Interior, Fish Wildl.Serv., Washington, DC :505. 6797

Mcb76 McBlain WA, Lewin V, Wolfe FH. Differing estrogenic activities for the enantiomers of o,p,'-DDT in immature female rats. Can. J. Physiol. Pharmacol 1976; 54: 629-632.

McD97a McDougal A; Wilson C; Safe S (1997). Inhibition of 7,12-dimethylbenzaanthracene-induced rat mammary tumor growth by aryl hydrocarbon receptor agonists. Cancer Lett; VOL 120, ISS 1, 1997, P53-63

Mcdo98 McDougal, A., S. Safe, 1998. Induction of 16a-/2-hydroxyestrone metabolite ratios in MCF-7 cells by pesticides, carcinogens, antiestrogens does not predict mammary carcinogens. Environ. Health Perspect. 106, 4, 203-206.

Meb90 Mebus C.A., 1990. Reproductive and fertility effects with DPX-1991-529 (benomyl). Multigeneration reproduction study in rats. Newark, Delaware, E.I. Du Pont de Nemours and co., Inc., Haskell Laboratory (Unpublished report No. HLR 765-90).

meh00 Mehmood Z; Smith AG; Tucker MJ; Chuzel F; Carmichael NG (2000). The development of methods for assessing the in vivo oestrogen-like effects of xenobiotics in CD-1 mice.Food Chem Toxicol; VOL 38, ISS 6, P493-501

Mik79 Mikhail TH; Aggour N; Awadallah R; Boulos MN; El-Dessoukey EA; Karima AI (1979). Acute toxicity of organophosphorus and organochlorine insecticides in laboratory animals.Z Ernaehrungswiss; 18(4): 258-268 (32 References)

mil76b Miller, R.W. et al. (1976b) Feeding TH 6040 to two breeds of chickens. J. Econ. Entomol., 69 (6): 741-743.

Mil79 Miller et al., 1979

mil81 Milby, T.H. et al (1981) Testicular function among epichlorhydrin workers. Br. J. ind. Med., 38: 372-377.

mil98 Milligan SR., Khan O., Nash M. Competitive binding of xenobiotic estrogens to rat alp ha-fetoprotein and to sex steroid binding proteins in human and rainbow trout (Oncorhynchus mykiss) plasma Gen Comp Endocrinol., VOL 112, ISS 1, 1998, 89-95

Mon87a Monsanto, 1987a. 90 days study of glyphosate administered in feed to Sprague/Dawley rats (Project No. ML-86-351/EHL 86128). St. Louis, Missouri, Monsanto Environmental Health Laboratory (Unpublished Report No. MSL-MSL-7575 submitted by Monsanto Ltd.).

Moo01 Moore A; Waring CP., 2001. The effects of a synthetic pyrethroidpesticide on some aspects of reproduction in Atlantic salmon(Salmo salar L.). Aquatic toxicology; 52; 1; 1-12; 200103

Mue78 Mueller GC, Kim UH. Displacement of estradiol from estrogen receptors by simple alkylphe nols. Endocrinology 102:1429-1435, 1978.

Mur86 Murakami et al., 1986 (cited in FAO88)

Mur88 Murakami et al., 188. As cited in "Overview and evaluation of the potential endocrine effects of procymidone (Environmental Health Science Laboratory. Sumitomo Chemical Co., Ltd.) April 2001. Filename: Procymidone 4-2A.doc (21-03-02)

Mur88a Murakami et al., 1988a (cited in FAO88)

Mur88b Murakami et al., 1988 b (cited in FAO88)

Mur95 Murakami M, Hosokawa S, Yamada T, Harakawa M, and others (1995). Species-

specific mechanism in rat Leydig cell tumorigenesis by procymidone. Toxicol Appl Pharmacol 131:244-252, 1995.

Nag86 Nagler, J.J., Aysola, P. and S.M. Ruby. Effect of Sublethal Pentachlorophenol on Early Oogenesis in Maturing Female Rainbow Trout (Salmo gairdneri). Arch. Environ. Contam. Toxicol. 15, 549-555, 1986.

naki Nakai M; Tabira Y; Asai D; Yakabe Y; Shimyozu T; Noguchi M; Takatsuki M; Shimohigashi Y. Binding characteristics of dialkyl phthalates for the estrogen receptor.Biochemical and biophysical research communications; 254; 2; 311-4; 19990119

NCI78 N.C.I., 1978. Bioassay of 1,2-dibromoethane for possible carcinogenicity. Bethesda, Maryland, National Cancer Institute, Division of Cancer Cause and Prevention, Carcinogene sis Testing Program, 64 pp. (Technical Report Series No. 86; DHEW Publication No. (NIH) 78-1336).

Nes93 Ness, D.K., S.L. Schantz, J. Moshteghian and L.G. Hansen. 1993. Effects of perinatal exposure to specific PCB congeners on thyroid hormone concentrations and thyroid histology in the rat. Toxicol. Letters 68:311-323.

Nes97 Nesaretnam K., Darbre P. 3,5,3',5'-tetrachlorobiphenyl is a weak estrogen agonist in vitro and in vivo J Steroid Biochem Mol Biol., VOL 62, ISS 5/6, 1997, 409-418

new01 Newbold RR; Jefferson WN; Padilla-Banks E; Walker VR; Pena DS (2001). Cell response endpoints enhance sensitivity of the immature mouse uterotropic assay.Reproductive toxicology; 15; 3; 245-52

nim97 Nimrod, Alison C. and William H. Benson. Xenobiotic Interaction with and Alteration of Channel Catfish Estrogen Receptor. Toxicology and Apllied Pharmacology 147, 381-390, 1997.

Nis00 Tsutomu Nishihara, 2000. Estrogenic Activities of 517 Chemicals by Yeast Two-Hybrid Assay. Journal of Health Science, 46(4) 282-298

NTP82 N.T.P., 1982. Carcinogenesis biogenesis of 1,2-dibromoethane in F344 rats and B6C3F1 mice (inhalation study). Research Triangle Park, North Carolina, US Department of Helth and Human Services, National Toxicology Program, 163 pp. (NTP Technical Report Series No.210.

NTP84 NTP (1984) NTP-84-262

ntp86a/ buc87 NTP (1986b) Toxicology and carcinogenesis studies on chlorina ted parffins (C12, 60% chlorine) (CAS no. 63449-39-8) in F344/N rats and B6C3F1 mice (gavage studies). Research Triangle Park, North Carolina, US Department of Health and Human Services, National Toxicology Programm, 67 pp (Technical Report Series no. 308). Bucher, J.R. et al. (1987) Comparative toxicity and carcinogenicity of two chlorinated paraffins in F344/n rats and B6C3F1 mice. Fundam. Appl. Toxicol., 9: 454-468.

NTP92 N.T.P., 1992. N.T.P. Technical report on toxicity studies of glyphosate (CAS No. 1071-83- 6). Research Triangle Park, North carolina, National Toxicology Program (Toxicity Report Series No. 16).

Orl68 Orlova, N.V. & E.P. Zhalbe (1968), Experimental material contributive to the problem of maximal permissible amounts of Sevin in food products, Vopr Pitan 27(6): 49-55 (in Russian).

osi99 Osius N; Karmaus W; Kruse H; Witten J (1999). Exposure to polychlorinated biphenyls and levels of thyroid hormones in children. Environ Health Perspect; VOL 107, ISS 10, 1999, P843-9 . Institution: NORDIG Institute for Health Research and Prevention, Hamburg, Germany. NOsius@t-online.de

Ost83 Osterloh J; Letz G; Pond S; Becker C (1983). An Assessment Of The Potential Testicular Toxicity Of 10 Pesticides Using The Mouse-Sperm Morphology Assay. Mutation Research; Vol. 116, No. 3-4, pages 407-415, 31 references, 19831983

Ost99 Ostby J; Kelce WR; Lambright C; Wolf CJ; Mann P; Gray LE Jr (1999). The fungicide procymidone alters sexual differentiation in the male rat by acting as an androgen-receptor antagonist in vivo and in vitro. Toxicol Ind Health; VOL 15, ISS 1-2, 1999, P80-93 27711, USA. gray.earl@epamail.epa.gov

Ous81 Ousterhout, et al., 1981 Estrogenic activities of methoxychlor metabolites. Biochem. Pharmacol. 30, 2869-2871

Pal75b Palmer and Hill 1975 b (cited in FAO1981)

Pal75c Palmer and Hill, 1975c (cited in FAO1981)

pan02 Panter GH; Hutchinson TH; Länge R; Lye CM; Sumpter JP; Zerulla M; Tyler CR. Utility of a juvenile fathead minnow screening assay for detecting (anti-)estrogenic substances.Environmental toxicology and chemistry / SETAC; 21; 2; 319-26; 200202

par80 Parr, L.J. et al. (1980) Chlorophenols from wood preservatives in broiler house litter. J. Sci. Food Agric., 25: 835-841.

par84a Parker, C.M., Patterson, dr., Van Gelder ,G.A., Gordon, E.B. Valerio, M.G. & Hall, C.W. (1984a) Chronic toxicity and carcinogenicity evaluation of renvalerate in rats. J. Toxicol, environ. Health, 13: 83-97.

Par96 Parks, Louise G. and Gerald A. Leblanc. Reductions in Steroid Hormone Biotransformati on/Elimination as a Biomarker of Pentachlorophenol Chronic Toxicity. Aquatic Toxicology 34, 291-303, 1996.

pat80 Paten and Saltolucito, 1980 (cited in FAO1981)

Paw83 Pawar, K.R. and M. Katdare (1983), Effect of sumithion on the ovaries of freshwater fish Garra mullya (Sykes), Curr. Sci., 16: 784-5./Paw84: Pawar K.R. and Katdare M., 1984. Toxic and teratogenic effects of fenitrothion, BHC and carbofuran on embryonic development of the frog Microhyla ornalas. Toxicol Lett., 22: 7-13.

Pen02 Table on pendimethalin, form EC SANCO evaluation. Filename: pendimethalin_list_of_endpoints_2002

pet91 Peters et al.,1991

Pet91c Peters et al., 1991c

Poo95 Poon, R., P. LeCavelier, P. Chan, C. Viau, H. Hakansson, I. Chu and V.E. Valli (1995), Subchronic toxicity of medium-chain chlorinated paraffin in the rat, J. Appl. Toxicol., 15: 455-463.

poo97 Poon R; Lecavalier P; Mueller R; Valli VE; Procter BG; Chu I (1997). Subchronic oral toxicity of di-n-octyl phthalate and di(2-Ethylhexyl) phthalate in the rat.Food Chem Toxicol; VOL 35, ISS 2, P225-39

Por93 Porter, W.P., S.M. Green, N.L. Debbink and I. Carlson. Groundwater pesticides: interactive effects of low concentrations of carbamates Aldicarb and Methomyl and the triazine Metribuzin on Thyroxine and Somatotropin levels in white rats. Journal of Toxicology and Environmental Health, 40:15-34, 1993.

Por99 Porter WP; Jaeger JW; Carlson IH., 1999. Endocrine, immune, andbehavioral effects of aldicarb (carbamate), atrazine (triazine)and nitrate (fertilizer) mixtures at groundwater concentrations. Toxicol Ind Health; VOL 15, ISS 1-2, P133-50

Pro01 Overview and evaluation of the potential endocrine effects of procymidone (Environmental Health Science Laboratory. Sumitomo Chemical Co., Ltd.) April 2001. Filename: Procymidone 4-2A.doc (21-03-02)

Ras90 Rastogi, A. and S.K. Kulshestra. Effect of Sublethal Doses of Three Pesticides on the Ovary of a Carp Minnow Rasbora daniconius. Bull. Environ. Contam. Toxicol. 45, 742-747, 1990.

rat85 Rattner BA; Michael SD (1985). Organophosphorus insecticide induced decrease in plasma luteinizing hormone concentration in white-footed mice.Toxicol Lett; VOL 24, ISS 1, P65-9

Rat87 Ratcliffe J.M., Schrader S.M., Steenland K., Clapp D.E., Turner T. and Hornung R.W., 1987. Semen quality in papaya workers with long term exposure to ethlene dibromide. Br. J. Ind.Med., 44: 233-240.

Raw98 Rawlings NC; Cook SJ; Waldbillig D (1998). Effects of the pesticides carbofuran, chlorpyrifos, dimethoate, lindane, triallate, trifluralin, 2,4-D, and pentachlorophenol on the metabolic endocrine and reproductive endocrine system in ewes. J Toxicol Environ Health; VOL 54, ISS 1, 1998, P21-36 Saskatoon, Canada. raw lings@sask.usask.ca

Rein76 Reinert and Cannon, 1876 (cited in FAO1981)

ren96 Ren L., Lewis SK., Lech JJ., 1996. Effects of estrogen and nonylphenol on the post-transcriptional regulation of vitellogenin gene expression. Chem. Biol. Interact., 100, 67-76

reu81 Reuber MD (1981). Carcinogenicity of picloram.J Toxicol Environ Health; 7(2): 207-222 (13 References)

RIF99 Research Institute for Fragrance Materials, Inc. (1999) Diethyl phthalate: Assessment of oestrogenic potential. Unpublished report from Jones P. and Baker V., 19 August. Report No. 34981.

rob81 ROBINSON KS; KAVLOCK RJ; CHERNOFF N; GRAY LE (1981). MULTIGENERATION STUDY OF 1,2,4-TRICHLOROBENZENE IN RATS. J TOXICOL ENVIRON HEALTH; 8:489-500

Ros77c Ross et al., 1977c (cited in FAO1981)

Ros79 Ross et al., 1979 (cited in FAO1981)

Rou96 Routledge EJ, Sumpter JP. Estrogenic activity of surfactants and some of their degradation products assessed using a recombinant yeast screen. Environ Toxicol Chem 15:241-258, 1996.

Rte01 RTEC Database 2001

rum81 Rumsey TS; Tao H; Bitman J (1981). Effects of ronnel on growth, endocrine function and blood measurements in steers and rats.Journal of animal science; 53;

1; 217-2507

Rum83 Rumsey TS; Bitman J; Tao H (1983). Changes in plasma concen trations of thyroxine, triiodothyronine, cholesterol and total lipid in beef steers fed ronnel. Journal of animal science; 56; 1; 125-31

Ryb67 Rybakova, M.N. (1967), Comparative toxic effect of Sevin and DDT used in the treatment of food crops, Vopr Pitan 26: 9-15 (in Russian with English summary).

Saa95 Saal, F.S. vom, S.C. Nagel, P. Palanza, M. Boechler, S. Parmigani and W.V. Welshons. Estrogenic Pesticides: Binding Relative to Estradiol in MCF-7 cells and Effects of Exposure During Fetal Life on Subsequent Territorial Behaviour In Male Mice. Toxicology Letters 77, 343-350, 1995.

Sad85 Sadhu, A.R. and P.K. Mukhopadhyay (1985), Comparitive effect of two pesticides malathion and carbofuran on testes of Clarias batrachus (Linn.), J. Env. Biol., 6: 217-22.

Sai00 Saito K; Tomigahara Y; Ohe N; Isobe N; Nakatsuka I; Kaneko H.,2000. Lack of significant estrogenic or antiestrogenic activityof pyrethroid insecticides in three in vitro assays based onclassic estrogen receptor alpha-mediated mechanisms. ToxicolSci; VOL 57, ISS 1, P54-60

Sal88 Salem MH; Abo-Elezz Z; Abd-Allah GA; Hassan GA; Shaker N (1988). Effect of organophosphorus (dimethoate) and pyrethroid (deltamethrin) pesticides on semen characteristics in rabbits.J Environ Sci Health B; VOL 23, ISS 3, P279-90

Sar91 Saracci et al., 1991

Sax78 Saxena, P.K. and M. Garg (1978), Effect of insecticidal pollution on ovarian recrudescence in the freshwater teleost, Channa punctatus Bl., Ind. J. Exp. Biol., 16: 690-91.

Sax85 Saxena, P.K. and K. Mani (1985), Quantitative study of testicular recrudescence in the freshwater teleost, Channa punctatus (Bl.) exposed to pesticides, Bull. Env. Contam. Toxicol., 34: 597-607.

Sax87 Saxena, P.K. and K. Mani (1987), Effect of safe concentrations of some pesticides on testicular recrudescence in the freshwater murrel, Channa punctatus (Bl.): a morphological study, Ecotoxicol. Env. Safety, 14: 56-63.

sch01 Schnorr JA; Bray MJ; Veldhuis JD (2001). Aromatization mediates testosterone's short-term feedback restraint of 24-hour endogenously driven and acute exogenous gonadotropin-releasing hormone-stimulated luteinizing hormone and folli cle-stimulating hormone secretion in young men.The Journal of clinical endocrinology and metabolism; 86; 6; 2600-6

Schn76 Schneider, SL., et al., 1976. Estrogenic properties of 3,9-dihydroxybenz[a]anthracene, a potential metabolite of benz[a]anthracene. J. Natl. Cancer. Inst., 57, 1351-1354

Schr00 Schrader TJ; Cooke GM (2000). Examination of selected food additives and organochlorine food contaminants for androgenic activity in vitro. Toxicol Sci; vol. 53(2), 278-88

schr88 Schrader, S. M. et al. (1988) The effcts of ethylene dibromide on semen quality: A comparison of short-term and chronic exposure. Reprod. Toxicol. , 2: 191-198.

Schu98 Schultz TW., Kraut DH., Sayler GS., Layton AC. Estrogenicity of selected biphenyls evaluated using a recombinant yeast assay Environ Toxicol Chem., VOL 17, ISS 9, 1998, 1727-1729

see76 Seegmiller, R.E. & Booth, G.M. (1976) Teratogenic and bioche mical effects of TH-6040 on chicken embryos. Provo, Utah, Brigham Young University (unpublished report submitted to WHO by Solvay Duphar BV, Weesp, The Netherlands).

Sha77 Shain, S.A. J.C. Schaeffer, & R.W. Boesel (1977),, The eefect of chronic ingestion of selectede pesticides upon rat ventral prostate homeostasis, Toxicol. Appl. Pharmacol. 40(1): 115-130.

Sha88 Shaker N; Hassan GA; el-Nouty FD; Abo-Elezz Z; Abd-Allah GA (1988). In vivo chronic effect of dimethoate and deltamethrin on rabbits.J Environ Sci Health B; VOL 23, ISS 4, P387-99

Sha95 Sharpe RM, Fisher JS, Millar MM, Jobling S, Sumpter JP. Gestational and lactational exposure of rats to xenoestro gens results in reduced testicular size and sperm production. Environ Health Perspect 103:1136-1143, 1995.

Sha99 Shafer TJ; Ward TR; Meacham CA; Cooper RL (1999). Effects of the chlorotriazine herbicide, cyanazine, on GABA(A) receptors in cortical tissue from rat brain.Toxicology; VOL 142, ISS 1, P57-68

She66 Sherman H. and Kraus W.C., 1966. Acute oral test (carbendazim). Newark, Delaware, E.I. Du Pont de Nemours and co., Inc., Haskell Laboratory (Unpublished report No. HLR 99-66).

Shi65 Shimamoto K. and hattori K., 1965. Effects of chronic feeding of the organic

phosphorus compounds on the tissue cholinesterase in rats. Acta med. Univ. Kyoto, 39: 128-137.

Shi87a Shivanandappa T., Krishnakumari M.K. and Majumder S.K., 1987. Reproductive potentional of male rats fed dietary ethylene dibromide. J. Food Saf, 8: 147-155.

Sho79 Short R.D., Winston J.M., Hong C.B., Minor J.L., Lee C.C. and Seifter J., 1979. Effects of ethylene dibromide on reproduction in male and female rats. Toxicol Appl. Pharmacol, 49: 97-105.

Sht70\Ry b66\Sht68 Shtenberg, A.I. and L.A. Hovaeva (1970) The effect of Sevin on the state of thyroid gland of rats having received artificial full-value ration withj different content of iodine.) Gig i Sanit, 8, 119-122 (in russian). Ryb66: Rybakova M.N. (1966) Toxic effect of Sevin on animals. Gig i Sanit, 31 (9), 42-47 (in russian with english summary). Sht68: Shtenberg, A.I. and M.N. Rybakova (1968) Effect of carbaryl on the neuroendocrine system in rats. Food Cosmet Toxicol., 6, 461-467.

Shu84 Shukla, J.P. and K. Pandey (1984), Arsenic induced structural changes during the ovarian cycle of a freshwater perch, Colisa fasciatus (Bloch and Schneider), Bull. Inst. Zool. Acad. Sinica, 23: 69-74.

Shu85 Shukla, J.P. and K. Pandey. Ovarian Recrudescence in a Freshwater Teleost Sarotherodon mossambicus. J. Env. Biol. 6, 195-204, 1985. Overgenomen uit Kim95.

sim85 Simon P; Ottenwaelder H; Bolt HM (1985). Vinyl acetate: DNA-binding assay in vivo. Toxicol Lett; vol. 27(1-3), 115-20

Sin00a Singh K; Singh DK (2000). Effect of different combinations of MGK-264 or piperonyl butoxide with plant-derived molluscicides on snail reproduction. Arch Environ Contam Toxicol; vol. 38(2), 182-90

sin00b Singh A; Connell BJ; Chu I (2000). PCB 128-induced ultrastructural lesions in the rat liver. J Submicrosc Cytol Pathol; vol. 32(1), 145-52

Sin87a Singh, S. and T.P. Singh. Impact of Malathion and Hexachlorocyclohexane on Plasma Profiles of Three Sex Hormones during Different phases of the Reproductive Cycle in Clarias batrachus. Pesticide Biochemistry and Physiology 27, 301-308, 1987.

Sin89 Singh, T.P., A.K. Yadav, B. Lal and S. Singh (1989), Impact of pesticide on fish reproducti on: a review, Sci. Res. J., 1: 9-20.

Sin91b Sinha, N., B. Lal, and T.P. Singh, 1991. Carbaryl-Induced Thyroid Dysfunction in the Freshwater Catfish Clarias batrachus. Ecotoxicol.Environ.Saf.21(3):240-247; In: Responses of Mar.Organisms to Pollutants, Part 2, Banaras Hindu University, Varanas, India

Sma76 Smalley, 1976 (cited in FAO1981)

sme99 Smeets JM; van Holsteijn I; Giesy JP; van den Berg M (1999). The anti-estrogenicity of Ah receptor agonists in carp (Cyprinus carpio) hepatocytes. Toxicol Sci; vol. 52(2), 178-88

soh01 Sohoni P; Lefevre PA; Ashby J; Sumpter JP. 2001. Possibleandrogenic/anti-androgenic activity of the insecticide fenitrothion. Journal of applied toxicology : JAT; 21; 3; 173-8;2001 May-Jun

sot91 Soto AM, Justicia H, Wray JW, Sonnenschein C. p-Nonyl-phenol: an estrogenic xenobiotic released from "modified" polystyrene. Environ Health Perspect 92:167-173, 1991.

Sot92 Soto AM, Lin TM, Justicia H, Silvia RM, Sonnenschein C. An "in culture" bioassay to assess the estrogenicity of xenobiotics (E-Screen). In: Chemically Induced Alterations in Sexual and Functional Development: The Wildli fe/Human Connection. Colborn T, Clements C, eds. Princeton Scientific Publishing Co, Inc, Princeton, NJ, 1992, pp 295-309.

Sot94 Soto AM, Chung KL, Sonnenschein C. The pesticides endosulfan, toxaphene, and dieldrin have estrogenic effects on human estrogen-sensitive cells. Environ Health Perspect 102:380-383, 1994.

Sot95 Soto, A.M., Sonnenschein, C., Chung, K.L., Fernandez, M.F., Olea, N. and Serrano, F.O. (1995). The E-screen assay as a tool to identify estrogens: an update on estrogenic environ mental pollutants. Environ. Health Perspect., 103, Suppl. 7, 113-122.

spe82 Spencer, F. & Berhance, Z. (1982) Uterine and fetal charac teristics in rats following a post-implantational exposure to permethrin. Bull. environ. Contam. Toxicol.,29: 84-88.

Spi94 Spink et al., 1994. Stimulation of 17B-estradiol metabolism in MCF-7 cells by bromochlo ro- and chloromethyl- substitute dibenzo-p-dioxins and dibenzofurans: correlations with antiestroge nic activity. J. Toxicol. Environ, Hlth. 41: 451-466.

Suk92 Sukumar, A. and P.R. Karpagaganapathy (1992), Pesticide-induced ateria in ovary

of a freshwater fish, Colisa ialia (Hamilton-Buchanan), Bull. Env. Contam. Toxicol., 48: 457-62.

Sum01 Sumida K; Saito K; Ooe N; Isobe N; Kaneko H; Nakatsuka I, 2001.Evaluation of in vitro methods for detecting the effects ofvarious chemicals on the human progesterone receptor, with afocus on pyrethroid insecticides. Toxicology letters; 118; 3;147-55; 20010103

swe77 Swentzel, K.L. et al. (1977) Toxicological evaluation of pyrethroid insecticide (5-benzyl-1.3-furyl)methyl-2,2- dimethyl-3-(2-methylpropenyl)cyclopropane-carboxylate (resmethrin). Aberdeen Proving ground, US Army Environ mental Hygiene Agency (report no. 51-0830-77).

tam01 Tamura H; Maness SC; Reischmann K; Dorman DC; Gray LE; Gaido KW., 2001. Androgen receptor antagonism by the fenitrothion. Toxicological sciences : an officialjournal of the Society of Toxicology; 60; 1; 56-62; 200103

TaN87 TaNaka I., Igusisu H., Haratake J. Cho S., Mori K., Fujishiro K., Inoue N., Horie A. and Akiyama T., 1987. Culmulative Toxicity potential of methomyl aerosol by repeated inhalation. Am. Ind. Hyg. Assoc. J., 48(4): 330-334.

Tay93 Taylor, 1993

Tea00 Teal PE; Gomez-Simuta Y; Proveaux AT (2000). Mating experien ce and juvenile hormone enhance sexual signaling and mating in male Caribbean fruit flies.Proceedings of the National Academy of Sciences of the United States of America; 97; 7; 3708-12

Tel97 Telang NT., Katdare M., Bradlow HL., Osborne MP. Estradiol metabolism: an endocrine biomarker for modulation of human mammary carcinogenesis. Environ Health Perspect., VOL 105 Suppl 3, 1997, P559-64 (REF: 45).

tho01 Thorpe KL; Hutchinson TH; Hetheridge MJ; Scholze M; Sumpter JP; Tyler CR (2001). Assessing the biological potency of binary mixtures of environmental estrogens using vitellogenin induction in juvenile rainbow trout (Oncorhyn chus mykiss). . Environmental science & technology; 35; 12; 2476-81

Tho74 Thomas, J.H., C.S. Dieringer & L. Schein, Effects of carbaryl on mouse organs of reproduction, Toxicol Appl Pharmacol 28: 142-145.

tho88 Thomas, P.T. Ratajczak, H.V., Eisenberg, W.C. Furedez Machacek, M. Ketels, K.V., & Barbera, P.W. (1987) Evaluti on of host resistance and immunity in mice exposed to the carbamate pesticide aldicarb. Fundam., appl. Toxicol., 9: 82- 89.

Tho90 Thomas P. Effects of Aroclor 1254 and cadmium on reproductive endocrine function and ovarian growth in atlantic croaker. Mar Environ Res 28:499-503, 1990.

tim75 Timmons, E.M. et al. (1975) Dichlorvos effects on estrous cycle onset in the rat. Lab. anim. Sci., 25(1): 45-47

Top95 Toppari J et al. (1995). Male Reproductive Health and Environmental Chemicals with Estrogenic Effects. Miljoprojekt nr. 290. Report of the Ministry of Environment and Energy, Danish Environmental Protection Agency, Kobenhavn, Denmark, 1995.

tra85 Trankina ML; Beitz DC; Trenkle AH (1985). Effects of in vitro ronnel on metabolic activity in subcutaneous adipose tissue and skeletal muscle from steers. Journal of animal science; 60; 3; 652-803

USN78 US National Cancer Institute (1978), Bioassay of trifluralin for possible carcinogenicity (Technical Rport series No 34; DHEW Publ. No. (NIH) 78-834), Bethesda, MD

Vas75 Vashakidze. V.I. (1975), Effect of small dose of Sevin on gonad function following its repeated effect on white rats SbTr NII., Gig Tr Prof Zabol 14: 235-266.

Vav76 Vavrova, M., A. Mikulik and M. Dobes (1976), Chlorovane uhlovodiky v potravinach zivocisneho puvoda a jejich vliv na vlasnosti masa a tuku drubeze, Vet. Med. Praha, 21: 187-93.

Vel86 Velsen, F.L.Van , F.L.H.C. Danse, F.X.R. Van Leeuwen, J.A.M.A. Dormans, M.J. Van Logten (1986), The subchronic oral toxicity of the B-isomer of hexachlorocyclohexane in rats, Fund. Appl. Toxicol. 6: 697-712.

ven80 Venable, J.R. et al. (1980) A fertility study of male employees engaged in the manufacture of glycerine. J. occup. Med., 22: 87- 91.

vin00 Vinggaard AM; Hnida C; Breinholt V; Larsen JC (2000). Screening of selected pesticides for inhibition of CYP19 aromatase activity in vitro. Toxicol Vitr; vol. 14(3), 227-34

Vin99 Vinggaard AM; Breinholt V; Larsen JC (1999). Screening of selected pesticides for oestrogen receptor activation in vitro.Food Addit Contam; VOL 16, ISS 12, P533-42

Von96 Vonier, Peter M., D. Andrew Crain, John A. McLachlan, Louis J. Guilette, Jr. and Steven F. Arnold. Interaction of Environmental Chemicals with the Estrogen and Progesterone Receptors from the oviduct of the American Alligator. Environmental Health Perspectives vol 104, no 12, december 1996.

voy73 Voytenko, G.A. & Medved, I.L. (1973) Effect of some thia carbamates on reproduction function. Gig. i. Sanit., 38 (7): 111-114 (in Russian).

Wal93 Walter, L.M., Rourke, A.W. & Eroschenko, V.P. (1993). Purified methoxyclor stimulates the reproductive tract in immature female mice. Reprod. Toxicol., 7, 509-606.

Wal96 Waller CL., Juma BW., Gray LE Jr., Kelce WR. Three-dimensional quantitative structure-activity relationships for androgen receptor ligands. Toxicol Appl Pharmacol., VOL 137, ISS 2, 1996, 219-27

Was71 Wasserman, D. et al. (1971) Effects of organochlorine insecticides on serum PBI level in occupationally exposed people. Bull. Environ. Contam. Toxicol. 6: 85-88.

Wei73 Weil, C.S., M.D. Woodside, J.B. Bernard, N.I. Condra, J.M. King & C.P. Carpenter (1973), Comparative effect of carbaryl on rat reproduction and guinea-pig teratology when fed either in the diet or by stomach intubation, Toxicol Appl Pharmacol, 26: 621- 638.

Wei82 Weichman B.E., 1982. Long term feeding study with methyl Ĥ(butylcarbamoyl)-2-bezimida zolecarbamate in mice (INT-1991; >95% benomyl): Parts I, II and III. Newark, dealaware, E.I. Du Pont de Nemours and co., Inc., Haskell Laboratory (Unpublished report No. HLR 20- 82).

Wel69 Welcher RM., Levin W., Conney AH., 1969. Estrogenic action of DDT and its analogs. Toxicol. Appl. Pharmcol. 14, 358-367.

Wen83 Wenda-Rozewicka, L., 1983. Morphometric studies of male gonads from mice receiving isecticides (metox-30, Sadofos-30, and Foschlor-50). Folia Biol. , 32: 23-34.

Wes85 Wester, P.W. et al. (1985) Histopathological study of Poecilia reticulata (guppy) after long-term b-hexachlorocyclohexane exposure. Aquat. Toxicol., 6,271-96

Wes91 Wester. P.W. Histopathological Effects of Environmental Pollutants b-HCH and Methyl Mercury on Reproductive organs in Freshwater Fish. Comp. Biochem. Physiol. Vol 100c, no. 1/2, 237-239, 1991.

Whi94 White R, Jobling S, Hoare SA, Sumpter JP, Parker MG. Environmentally persistent alkylphenolic compounds are estrogenic. Endocrinology 135:175-182, 1994.

Who79 Whorton, M.D. T.H Milby, H.A. Stubbs, B.H. Avasha & E.G. Hull (1979), Testicular function among carbaryl exposed employees, J Toxicol Environ Health 5: 925-941.

Wic88b Wickramaratne et al., 1988 b (cited in FAO 1988)

Wil00 Willingham E; Rhen T; Sakata JT; Crews D (2000). Embryonic treatment with xenobiotics disrupts steroid hormone profiles in hatchling red-eared slider turtles (Trachemys scripta elegans). Environ Health Perspect; vol. 108(4), 329-32

Wil91 Williams J., Gladen B.C., Turner T.W., Schrader S.M. and Chapin R.E., 1991. The effects of ethylene dibromide on semen quality and fertility in the rabbit: Evaluation of a model for human seminal Characteristics. Fundam. Appl. Toxicol, 16: 687-700.

Wil99 Willingham E; Crews D (1999). Sex reversal effects of environmentally relevant xenobiotic concentrations on the red-eared slider turtle, a species with temperature-dependent sex determination. Gen Comp Endocrinol; vol. 113(3), 429-35

Won82 Wong L.C.K., Winston J.M., Hong C.B. and Plotnick H., 1982. Carcinogenicity and toxicity of 1,2-dibromoethane in the rat. Toxicol Appl. Pharmacol, 63: 155-165.

wor00 Wormke M; Castro-Rivera E; Chen I; Safe S (2000). Estrogen and aryl hydrocarbon receptor expression and crosstalk in human Ishikawa endometrial cancer cells. J Steroid Biochem Mol Biol; vol. 72(5), 197-207

Wre70 Wrenn et al., 1970. Tests of estrogenity in rats fed low levels of o,p'-DDT. Bull. Environ. Contam. Toxicol., 5, 61-66.

Wya93 Wyatt, I., C.T. Coutts and C.R. Elcombe (1993), The effect of chlorinated paraffins on hepatic enzymes and thyroid hormones, Toxicology, 77: 81-90.

Zac92 Zacharrewski et al., 1992. 6-methyl-1,3,8-trichlorodibenzofuran (MCDF) as an antiestrogen in human and rodent cancer cell lines: evidence for the role of the ah receptor. Toxicol. Appl. Pharmacol. 113, 311-318.

Zob92 Zober, M.A. et al (1992) Morbidity study of extruder personell with potential exposure to brominated dioxins and furans: I. Results of blood monitoring and immunological tests. Brit. J. Ind. Med., 49: 532-544.

zou97a Zou E., Fingerman M. Effects of estrogenic xenobiotics on molting of the water flea, Daphnia magna. Ecotoxicol Environ Saf., VOL 38, ISS 3, 1997, 281-285

zou99 Zou E; Fingerman M (1999). Effects of exposure to diethyl phthalate, 4-(tert)-octylphenol, and 2,4,5-trichlorobiphenyl on activity of chitobiase in the epidermis and hepatopancreas of the fiddler crab, Uca pugilator. Comparative biochemistry and physiology. Part C, Pharmacology, toxicology & endocrinology; 122; 1; 115-20

ANNEX 9

RESULTS OF CATEGORISATION AND QUALIFYING REMARKS IN THE EXPERT MEETING OF 9-10 SEPTEMBER 2002.

Annex 9. Results of categorisation and qualifying remarks in the Expert meeting of 9-10 September 2002.

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
17804-35-2	Benomyl	CAT3a	Strong evidence for reproductive toxicity (males) , however no indication for interference with the endocrine system	CAT3b	No ED references provided.	CAT3a
116-06-3	Aldicarb	CAT2		CAT3b		CAT2
63-25-2	Carbaryl	CAT1	Effect on thyroid ea supports (cf. Gfh255)	CAT2	Insufficient experimental data _ missing hard copy bar68	CAT1
1563-66-2	Carbofuran	CAT2	Other evidence supports, although without adequate test reliability	CAT2	Only 1 of several studies was appointed as a key study.	CAT2
72490-01-8	Fenoxycarb	CAT3b		CAT2	Known endocrine effects in insects (juvenile hormone agonists).	CAT2
16752-77-5	Methomyl	CAT2		CAT3b	Compound induces eggshell thinning, but lack of mechanistic proof on ED mediated action	CAT2
2597-11-7	1-Hydroxychlordene	CAT2	Stimulation of proliferation only at a high concentration (30 µm)	CAT3b	The only ref. Provided does not mention 1-hydroxychlordene at all.	CAT2
3734-48-3	Chlordene	CAT3a	No stimulation of proliferation even at high concentration	CAT3b	No data	CAT3a
5103-73-1	Cis-Nonachlor	CAT2	Estrogenic activity in vitro (see bruhn et al: 1999)	CAT1	Requires further research in other species.	CAT1
39765-80-5	Trans-Nonachlor	CAT2	Estrogenic activity in vitro (see bruhn et al:,1999)	CAT1	Requires further research in other species	CAT1
93-76-5	2,4,5-T = 2,4,5-Trichlorophenoxyaceticacid	CAT2	Binding to transthyretin in vitro (see bruhn et al., 1999)	CAT3b	Plant hormone mimic but no animal ED effects observed.	CAT2
69806-50-4	Fluazifop-butyl	CAT3b	No sufficient data	CAT3b	No data	CAT3b
2971-22-4	1,1,1-Trichloro-2,2-bis(4-chlorophenyl)ethane	CAT1	Supported by other p,p´-DDT analogues	CAT1	More information on DDT is available than presented in this database.	CAT1
65148-80-3	3-MeO-o,p'-DDE	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
43216-70-2	3-OH-o,p'-DDT	CAT1	Other o,p´-DDT-analogues supporting	CAT3b	No data	CAT1
65148-81-4	4-MeO-o,p'-DDE	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
65148-72-3	4-MeO-o,p'-DDT	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
65148-75-6	5-MeO-o,p'-DDD	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
65148-82-5	5-MeO-o,p'-DDE	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
65148-74-5	5-MeO-o,p'-DDT	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
65148-73-4	5-OH-o,p'-DDT	CAT1	Other o,p´-DDT-analogues supporting	CAT3b	No data	CAT1
4329-12-8	m,p'-DDD	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
65148-83-6	o,p'-DDA-glycinat = N-[(2-chlorophenyl)(4-chlorophenyl)acettyl]glycin	CAT1	Other o,p´-DDT-analogues supporting	CAT3b	No data	CAT1
53-19-0	o,p'-DDD	CAT1	Other o,p´-DDT-analogues supporting	CAT2	Only one in vitro study presented.	CAT1
3424-82-6	o,p'-DDE	CAT1	Other o,p´-DDT-analogues supporting	CAT2	Only one in vitro study and one reproductive toxicity study presented.	CAT1
14835-94-0	o,p'-DDMU	CAT1	Other o,p´-DDT-analogues supporting	CAT3b	No data	CAT1
789-02-6	o,p'-DDT	CAT1	Supports other o,p´-DDT-analogues	CAT1	A lot more information is available than presented in this database.	CAT1
72-54-8	p,p'-DDD	CAT1	Supported by analogy to DDT, including analogues	CAT3b	No data	CAT1
72-55-9	p,p'-DDE	CAT1	Supported by analogy to DDT, including analogues	CAT1	A lot more information is available than presented in this database.	CAT1
1022-22-6	p,p'-DDMU	CAT1	Supported by other p,p´-DDT analogues	CAT3b	No data	CAT1
88378-55-6	3,5-Dichlorophenylcarbaminacid-(1-carboxy-1-methyl)-allyl	CAT2		CAT3b	No data	CAT2
83792-61-4	N-(3,5-Dichlorophenyl)-2-hydroxy-2-methyl-3-butenacidamid	CAT2		CAT3b	No data	CAT2
32809-16-8	Procymidon	CAT1	Quality ensured paper showing effects below maternal toxicity	CAT3b	No data	CAT1
40487-42-1	Pendimethalin	CAT3a	Data available do not support	CAT3b	No data	CAT3a

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
			evidence on ed. Cat.3 is applied if available data supply no evidence,			
29091-21-2	Prodiamine	CAT3b	No data	CAT3b	No data	CAT3b
1582-09-8	Trifluralin	CAT3a		CAT2	Pituitary effects - possibly indirect effect of exposure.	CAT2
8018-01-7	Mancozeb	CAT1	Inhibition of T4 and T3 by the metabolite etu.	CAT3b	Relevance of algae immobility assay data.	CAT1
9006-42-2	Metiram (Metiram-complex)	CAT1	Inhibition of T4 and T3 by the metabolite etu.	CAT3b		CAT1
142-59-6	Nabam	CAT3b	Studies not appropriate to make evaluation.	CAT3b	No access to possible relevant study van 86	CAT3b
319-85-7	Beta-HCH	CAT2	Testicular atrophy in rats	CAT1	Dose-resp for vtg induction indicates estr. Action & intersex induction indicates adverse effects	CAT1
319-86-8	Delta-HCH	CAT2	Testosterone binding to androgen binding protein inhibited in vitro.	CAT3b		CAT2
608-73-1	Hexachlorocyclohexane = HCH mixed	CAT3b	Categorisation conform b-HCH and g-HCH	CAT3b	Categorisation conform b-HCH and g-HCH No access to hard copy sin 87	CAT1
1689-84-5	Bromoxynil	CAT2	Probable impact on thyroid hormones (competition for T4 binding site).	CAT3b	No ED related tests	CAT2
1689-83-4	Ioxynil	CAT1	Competes for T4 binding sites. Evidence of thyroid toxicity including tumours.	CAT3b	No ED related tests	CAT1
35367-38-5	Diflubenzuron	CAT3a	No evidence of endocrine effects from the database.	CAT3b	Contradicting effects.	CAT3a
No CAS 096	1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (HPTE)	CAT1	Categorisation conform methoxychlor Very limited information (single study: QSAR).	CAT1	Categorisation conform methoxychlor No data available. Structurally related to methoxychlor, therefore likely to be potential ED	CAT1
30668-06-5	1,3-Dichloro-2,2-bis(4-methoxy-3-methylphenyl)propane	CAT1	Categorisation conform methoxychlor No further data available	CAT1	Categorisation conform methoxychlor No data available. Structurally related to methoxychlor, therefore likely to be potential ED	CAT1
2971-36-0	Bis-OH-Methoxychlor = 1,1,1-	CAT1	Categorisation conform	CAT1	Categorisation conform methoxychlor No data	CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
	trichloro-2,2-bis(4-hydroxyphenyl)ethane (HTPE)		methoxychlor Limited information. One in vitro study suggests binding affinity to estrogen receptor		available. Structurally elated to methoxychlor, therefore likely to be potential ED	
72-43-5	Methoxychlor	CAT1	Estrogenic activity confirmed in many studies in vitro and in vivo.	CAT1	Clear evidence for ED effects in fish and birds.	CAT1
72-43-5	p,p'-Methoxychlor	CAT1	Categorisation conform methoxychlor No specific studies on endocrine disruption available.	CAT1	Categorisation conform methoxychlor No data available. Structurally related to methoxychlor, therefore likely to be potential ED	CAT1
30560-19-1	Acephate	CAT2	Lower testis weight and inhibition of spermatogenesis in mice.	CAT2	1 study only indicating possible ED related effects	CAT2
470-90-6	Chlorfenvinphos	CAT3a	No evidence of endocrine effects from the database.	CAT2	Incomplete reference; needs confirmation	CAT2
2921-88-2	Chlorpyrifos	CAT3a	No evidence of endocrine effects from the database.	CAT3b	No ED related tests	CAT3a
919-86-8	Demeton-s-methyl	CAT3a	No evidence of endocrine effects from the database.	CAT3b	No ED related tests	CAT3a
62-73-7	Dichlorvos	CAT3a	No evidence of endocrine effects from the database.	CAT3b	No ED related tests	CAT3a
122-14-5	Fenitrothion	CAT1	Hershberger assay: positive.	CAT2	Additional studies required	CAT1
51276-47-2	Glufosinate	CAT3a	No data in the database. From other sources no evidence of endocrine effects.	CAT3b	No data	CAT3a
7786-34-7	Mevinphos = Phosdrin	CAT3a	No evidence of endocrine effects, however, specific studies are lacking.	CAT2	Requires further data	CAT2
301-12-2	Oxydemeton-methyl	CAT3a	No data	CAT3b	No ED related tests	CAT3a
13171-21-6	Phosophamidon	CAT2	Possibly hormone-mediated impact of sperm quality.	CAT3b	No ED related tests	CAT2
299-84-3	Ronnel = fenchlorfos	CAT3a	No evidence of endocrine effects from the database.	CAT3b	No ED related tests	CAT3a
22248-79-9	Tetrachlorvinphos = Gardona	CAT3a	No evidence of endocrine effects from the database.	CAT3b	Additional studies required	CAT3a

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
52-68-6	Trichlorfon = Dipterex	CAT2	Possibly hormone-mediated effects of spermatogenesis.	CAT3b	No ED related tests	CAT2
82657-04-3	Bifenthrin (@Talstar)	CAT1	Significant effects on levels of T3, T4 and TSH in vivo	CAT3b	No ED related tests	CAT1
584-79-2	Bioallethrin = d- trans allethrin	CAT2	Inhibition of androgen binding and antagonism of progesterone in vitro	CAT3b	No ED related tests	CAT2
91465-08-6	Cyhalothrin (@Karate)	CAT1	Significant effects on levels of T3, T4 and TSH	CAT3b	No ED related tests	CAT1
52315-07-8	Cypermethrin	CAT3a	Diverse in vitro assays with negative results.	CAT2	Possible ED related effects are observed, but working mechanism need clarification	CAT2
52918-63-5	Deltamethrin	CAT1	Effects on spermatogenesis, testosterone levels and pituitary weight in vivo	CAT2	Could be a potential ED, but this needs further studies (in vitro tests)	CAT1
66230-04-4	Esfenvalerate	CAT3b	No data	CAT3b	No ED related tests	CAT3b
26002-80-2	Fenothrin = sumithrin	CAT2	Estrogenic activity in vitro	CAT3b	No ED related tests	CAT2
51630-58-1	Fenvalerate	CAT2	Inhibition of androgen binding in vitro	CAT2	Some indication for potential ED effects from ELC test findings	CAT2
69409-94-5	Fluvalinate	CAT2	Inhibition of androgen binding in vitro	CAT3b	No ED related tests	CAT2
52645-53-1	Permethrin	CAT2	Inhibition of androgen binding in vitro	CAT3b	No ED related tests	CAT2
10453-86-8	Resmethrin	CAT1	Effects on prostate weight, thyroid	CAT3b	No ED related tests	CAT1
60168-88-9	Fenarimol	CAT1	Inhibition of aromatase in the cns in vivo	CAT2	Some indication for potential ED effects	CAT1
1918-02-1	Picloram	CAT1	Neoplasms in endocrine organs, atrophy of the testes	CAT3b	No ED related tests	CAT1
55179-31-2	Bitertanol	CAT3b	No data	CAT3b	No data	CAT3b
21725-46-2	Cyanazine	CAT2	Interference with GABA receptors and catecholamin metabolism in vitro	CAT3b	No ED related tests	CAT2
94361-07-6	Cyproconazole	CAT3b	Reproductive toxicity	CAT3b	No data	CAT3b
119446-68-3	Difenoconazole	CAT3b	No data	CAT3b	No ED related tests	CAT3b
No CAS 121	Epiconazol	CAT3b	No data	CAT3b	No data	CAT3b
No CAS 008	Epoxiconazole	CAT3b	No data	CAT3b	No data	CAT3b

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
2593-15-9	Etridiazole	CAT2	Induction of thyroid tumors	CAT3b	No ED related tests	CAT2
65277-42-1	Ketoconazol	CAT1	Effects on testosteron levels in humans	CAT3b	No ED related tests	CAT1
21087-64-9	Metribuzin	CAT1	Interference with thyroxin regulation	CAT3b	No ED related tests	CAT1
66246-88-6	Penconazole	CAT3b	No data	CAT3b	No data	CAT3b
60207-90-1	Propiconazole	CAT3b	No data	CAT3b	No ED related tests	CAT3b
107534-96-3	Tebuconazole	CAT3b	No data	CAT3b	No ED related tests	CAT3b
886-50-0	Terbutryn	CAT1	Effects on levels of T3, T4 and LH in vivo	CAT3b	No ED related tests	CAT1
123-88-6	Triadimenol	CAT2	Inhibition of aromatase in vitro	CAT3b	No ED related tests	CAT2
71751-41-2	Abamectin	CAT3a		CAT3b	No data	CAT3a
33089-61-1	Amitraz	CAT3a	Add new information to data base from additional files	CAT3b	No ED related tests	CAT3a
74115-24-5	Clofentezine = chlorfentezine	CAT3b		CAT3b	No data	CAT3b
106-93-4	Dibromoethane (EDB)	CAT1		CAT3b	No ED related tests	CAT1
88-85-7	Dinoseb	CAT3b		CAT3b	No ED related tests	CAT3b
80844-07-1	Ethofenprox	CAT3b		CAT3b	No ED related tests	CAT3b
120068-37-3	Fipronil	CAT3b		CAT3b	No ED related tests	CAT3b
76674-21-0	Flutriafol	CAT3b	Only LD50 data, no assessment of ED possible	CAT3b	No data	CAT3b
2439-99-8	Glyphosate	CAT3a		CAT3b	No ED related tests	CAT3a
1024-57-3	Heptachlor-epoxide	CAT3a		CAT3b	No ED related tests	CAT3a
3554-44-0	Imazalil	CAT3a	Data in summary in the data base are not consistent with original publication	CAT3b	No data	CAT3a
2212-67-1	Molinate	CAT3b		CAT3b	No ED related tests	CAT3b
88671-89-0	Myclobutanil	CAT3b		CAT3b	No ED related tests	CAT3b
4685-14-7	Paraquat = 1,1'-dimethyl-4,4'-bipyridinium	CAT3b		CAT3b	No ED related tests	CAT3b
82-68-8	Pentachloronitrobenzene (PCNB)	CAT3b		CAT3b	No ED related tests	CAT3b
51-03-6	Piperonyl butoxide	CAT3b		CAT2	Some indication for potential ED effects	CAT2
7287-19-6	Prometryn	CAT2		CAT3b	No ED related tests	CAT2
117718-60-2	Thiazopyr	CAT3b		CAT3b	No ED related tests	CAT3b
29082-74-4	Octachlorostyrene	CAT3b		CAT3b		CAT3b
12002-48-1	Trichlorobenzene	CAT1		CAT3b		CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
608-93-5	Pentachlorobenzene	CAT1		CAT3b		CAT1
87-86-5	Pentachlorophenol (PCP)	CAT1	Jekat 1994 indicates that PCP is endocrine active under in vivo conditions	CAT3b		CAT1
53792-11-3	4-(4-Hydroxyphenyl)-2,2,6,6-tetramethylcyclohexanecarbonacid	CAT3b		CAT3b		CAT3b
1806-26-4	Phenol, 4-octyl-	CAT1	Key study Katsuda et al., 2000. Categorisation based on test with structurally related substance.	CAT1	Several studies on structurally similar compounds showing hormonal activity	CAT1
11081-15-5	Phenol, isooctyl-	CAT1	Key study Katsuda et al., 2000. Categorisation based on test with structurally closely related substance	CAT1	Several studies indicating hormonal activity of structural analogues	CAT1
14409-72-4	4-Nonylphenolnonaethoxylat (Tergitol NP 9)	CAT3b		CAT2	Several studies on structurally similar compounds showing hormonal activity	CAT2
2717-05-5	Heptaoctatrikosan-1-ol, 23-(nonylphenoxy)3,6,9,12,15,18,21-nonylphenolmonoethoxylate	CAT3b		CAT3b		CAT3b
9016-45-9	Nonylphenolethoxylate	CAT2	Available data only on nonylphenol and not ethoxylates. Sharpe, 1995 see octylphenolethoxylate	CAT1	Several studies indicating estrogenic activity of structural analogue. Induction of vitellogenin synthesis in fish (Job96)	CAT1
9014-90-8	Poly(oxy-1,2-ethanediyl), alpha-sulfo-omega-nonylphenoxy	CAT3b		CAT3b		CAT3b
85535-85-9	Intermediate chain chlorinated paraffins	CAT1	Several studies show effects on thyroid and hormone levels.	CAT3b		CAT1
85535-86-0	Long chain chlorinated paraffins	CAT3b	No effect on the reproduction. It remains unclear whether thyroid was studied.	CAT3b		CAT3b
85535-84-8	Short chain chlorinated paraffins	CAT1	Several studies suggest that SCCPS cause thyroid tumours, and thyroid hypertrophy.	CAT3b	Effects on eggshell thickness might indicate possible endocrine effects	CAT1
117-84-0	1,2-Benzenedicarboxylic acid, dioctyl ester	CAT3b	See no. 129, same CAS number.	CAT3b		CAT3b
103-23-1	Bis(2-ethylhexyl)adipate	CAT3b	Data is very limited. The effect	CAT3b		CAT3b

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
			on reproduction is weak and at toxic dose level.			
117-84-0	Di-n-octylphthalate (DnOP)	CAT3b	Mild thyroid effects but no effect on reproduction were seen in two key studies (see chemno. 127).	CAT3b		CAT3b
84-61-7	Dicyclohexyl phthalate (DCHP)	CAT1	Some evidence of effect on testes at high dose. Clearly much less potent than e.g. DEHP.	CAT2	Structurally similar phthalates showing hormonal activity	CAT1
84-66-2	Diethyl phthalate (DEP)	CAT1	Very low potency. Four studies suggest effects on testes/spermatogenesis.	CAT3b		CAT1
101-53-1	Phenyl-4-hydroxyphenylmethane = 4-Benzylphenol = p-Benzylphenol	CAT1	Some preliminary findings at low dose level. Only one relevant in vivo study. Estrogenic activity in vivo (Bit70)	CAT3b		CAT1
25036-25-3	2,2'-bis(2-(2,3-epoxypropoxy)phenyl)-propane	CAT3b	No data	CAT1	Structurally similar compound showing hormonal activity	CAT1
No CAS 027	2,2,6,6-Tetramethyl-4,4-bis(4-hydroxyphenyl)-n-heptan	CAT3b	No data	CAT3b		CAT3b
25085-99-8	Bisphenol A-diglycidylether polymer (mw<700)	CAT3b	No data	CAT2	Doubts about chemical name, need to consider data on structurally similar analogue	CAT2
106-89-8	Epichlorohydrin (1-chloro-2,3-epoxypropane)	CAT1	Several studies suggest adverse effect on spermatogenesis.	CAT3b		CAT1
92-52-4	Diphenyl	CAT3a	No evidence/indication of endocrine activity; one neg. In vitro study was made.	CAT3b		CAT3a
No CAS 127	2,4-6-trichlorobiphenyl	CAT1	All PCBs: plenty of evidence shows that PCBs are toxic to reproduction.	CAT2	Structurally similar compounds showing hormonal activity	CAT1
No CAS 128	3,4',5-trichlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
67651-37-0	3-Hydroxy-2',3',4',5'-tetrachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
100702-98-5	4,4'-Dihydroxy-2,3,5,6-tetrachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
13049-13-3	4,4'-Dihydroxy-3,3',5,5'-tetrachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
67651-34-7	4-Hydroxy-2',3',4',5'-tetrachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
14962-28-8	4-Hydroxy-2',4',6'-trichlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
53905-33-2	4-Hydroxy-2,2',5'-trichlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
No CAS 040	4-Hydroxy-3,3',4',5'-tetrachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
4400-06-0	4-Hydroxy-3,4',5-trichlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
No CAS 097	4-OH-2,2',4',5,5'-pentachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
54991-93-4	Clophen A30	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
8068-44-8	Clophen A50	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT2	Structurally similar compounds showing hormonal activity	CAT1
No CAS 038	Mixture of 2,3,4,5-tetrachlorobiphenyl (PCB 61), 2,2',4,5,5'-octachlorobiphenyl (PCB 101) and	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
	2,2',3,3',4,4',5,5'-octachlorobiphenyl (PCB 194)					
No CAS 039	PCB 104 (2,2',4,6,6'-Pentachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
No CAS 041	PCB 105 (2,3,3',4,4' -Pentachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
No CAS 092	PCB 114 (2,3,4,4',5-pentachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
31508-00-6	PCB 118 (2,3',4,4',5-pentachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
No CAS 042	PCB 122 (2,3,3',4,5 -Pentachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
No CAS 037	PCB 126 (3,3',4,4',5-Pentachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
38380-07-3	PCB 128 (2,2',3,3',4,4'-Hexachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
37680-65-2	PCB 18 (2,2',5-Trichlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
55702-46-0	PCB 21 (2,3,4-Trichlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
7012-37-5	PCB 28 (2,4,4'-trichlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
35693-99-3	PCB 52 (2,2';5,5'-Tetrachlorobiphenyl)	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
No CAS 036	PCB Aroclor 1016	CAT1	Categorisation based on group	CAT1	Structurally similar compounds showing	CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
			categorisation of all PCB and derivatives		hormonal activity	
No CAS 087	PCB138 2,2',3,4,4',5'-hexachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
No CAS 088	PCB180 2,2',3,4,4',5,5'-heptachlorobiphenyl	CAT1	Categorisation based on group categorisation of all PCB and derivatives	CAT1	Structurally similar compounds showing hormonal activity	CAT1
12642-23-8	PCT Aroclor 5442	CAT1	Non-standard uterotrophic assay used to raise classification to cat 1	CAT1	Structurally similar compounds showing hormonal activity	CAT1
135-19-3	2-Naphthol	CAT3b	Insufficient data	CAT3b		CAT3b
1335-87-1	Halowax 1014	CAT3b	No appropriate data	CAT3b		CAT3b
56614-97-2	3,9-Dihydroxybenz(a)anthracene	CAT1	Not seen key in vivo raw data.	CAT2	Structurally similar compounds showing hormonal activity	CAT1
56-49-5	3-Methylcholanthrene	CAT1	Old literature, but convincing	CAT3b	Structurally similar compounds showing hormonal activity	CAT1
7099-43-6	5,6-Cyclopento-1,2-benzanthracene	CAT1	Old data but valid	CAT2	Structurally similar compounds showing hormonal activity	CAT1
57-97-6	7,12-Dimethyl-1,2-benz(a)anthracene	CAT1	Relies on RTECS reports	CAT2	Structurally similar compounds showing hormonal activity	CAT1
56-55-3	Benz(a)anthracene	CAT2	Possible evidence of anti-estrogenicity in vitro	CAT2	Structurally similar compounds showing hormonal activity	CAT2
50-32-8	Benzo[a]pyrene	CAT1	Evidence from both in vivo and in vitro data	CAT2	Structurally similar compounds showing hormonal activity	CAT1
109333-34-8	1,2,3,7,8-PeBDD	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
No CAS 112	1,2,4,7,8-PeCDD	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
No CAS 115	1,3,7,8-TeBCDD	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
50585-46-1	1,3,7,8-Tetrachlorodibenzodioxin	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
50585-41-6	2,3,7,8-TeBDD	CAT1	Limited evidence in vivo for effects that may have endocrine toxicity consequences	CAT2	Structurally similar compounds showing hormonal activity	CAT1

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
50585-40-5	2,3-Dibromo-7,8-dichlorodibenzodioxin	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
109333-32-6	2,8-Dibromo-3,7-dichlorodibenzodioxin	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
131167-13-0	2-Bromo-1,3,7,8-tetrachlorodibenzodioxin	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
109333-33-7	2-Bromo-3,7,8-trichlorodibenzodioxin	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
97741-74-7	7-Bromo-2,3-dichlorodibenzodioxin	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
112344-57-7	8-Methyl-2,3,7-trichlorodibenzodioxin	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
103456-39-9	TeBDD	CAT3b	No useful data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
125652-16-6	6-Ethyl-1,3,8-trichlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
125652-13-3	6-i-Propyl-1,3,8-trichlorodibenzofuran	CAT3b	Insufficient data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
118174-38-2	6-Methyl-1,3,8-trichlorodibenzofuran	CAT1	One good laboratory found multiple evidence of antiestrogenic activity in vivo	CAT2	Structurally similar compounds showing hormonal activity	CAT1
139883-51-5	6-Methyl-2,3,4,8-tetrachlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
172485-97-1	6-Methyl-2,3,8-trichlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
125652-14-4	6-n-Propyl-1,3,8-trichlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
125652-12-2	6-t-Butyl-1,3,8-trichlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
103124-72-7	8-Bromo-2,3,4-trichlorodibenzofuran	CAT3b	Insufficient data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
139883-50-4	8-Methyl-1,2,4,7-tetrachlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
172485-96-0	8-Methyl-1,3,6-trichlorodibenzofuran	CAT3b	No appropriate data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
172485-98-2	8-Methyl-1,3,7-trichlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing	CAT2

CASNR	NAME	CAT HH	Qualifying remarks_HH	CAT WL	Qualifying remarks_WL	CAT Overall
					hormonal activity	
172486-00-9	8-Methyl-2,3,4,7-tetrachlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
172485-99-3	8-Methyl-2,3,7-trichlorodibenzofuran	CAT3b	No data	CAT2	Structurally similar compounds showing hormonal activity	CAT2
94-82-6	2,4-dichlorophenoxybutyric acid = 2,4-DB	CAT1	Evidence for Interference with thyroxin levels in vivo (Ber91)	CAT3b	No ED related tests	CAT1
106-47-8	4-chloroaniline	CAT3b	No raw data available. Only tenuous evidence.	CAT3b		CAT3b
11141-17-6	Azadirachtin	CAT3a		CAT3b	No ED related tests	CAT3a
119-61-9	Benzophenone	CAT3b	No raw data available. Only tenuous evidence.	CAT3b		CAT3b
68-12-2	Dimethylformamide (DMFA)	CAT3b	Not appropriately evaluated for ED	CAT3b	Appears to be incorrect citation but indication that dmfa might be estrogenic active	CAT3b
72-33-3	Mestranol	CAT1	Good quality data	CAT2	Wrong interpretation of data from nim97: relative inhibitory potency is different from estr. Equiv.	CAT1
19044-88-3	Oryzalin	CAT3a	All available data LD50 only.	CAT3b	No ED related tests	CAT3a
23950-58-5	Pronamide	CAT3b		CAT3b	No ED related tests	CAT3b
108-05-4	Vinyl acetate	CAT3b	The evidence of inducing thyroid cancer is a weak alert to possible ED	CAT3b		CAT3b

ANNEX 10

ENTRIES EXCLUDED FROM THE CANDIDATE LIST

Entries excluded from the candidate list

Analysis of the working list of 564 revealed that a number of entries on the list were group names of chemicals already on the list. To make the list more coherent these entries were removed from the list.

An overview of the 30 entries / chemicals removed from the original list including the reasoning and reference decision is given below. Out of 28 entries, 11 substances were already excluded during the 1999 expert meeting whereas another 19 were excluded during the present study.

CASnr	Name	Reason for exclusion	Reference decision
7439-97-6	Mercury	These metals and their compounds exert serious developmental and reproductive effects which have been known since a long time and are well documented in the scientific literature.	EM 1999*
7439-92-1	Lead		EM 1999
7429-90-5	Aluminum		EM 1999
7440-43-9	Cadmium		EM 1999
1332-40-7	Copper oxychlor		EM 1999
7758-98-7	Copper sulfate		EM 1999
22967-92-6	Methylmercury		EM 1999
55-38-9	Fenthion	No evidence	EM 1999
68515-49-1	1,2-Benzenedicarboxylic acid, di-C9-11-branched alkyl esters, C10-rich (DIDP)	No evidence	EM 1999
108-95-2	Phenol	No evidence	EM 1999
107-21-1	Ethylene glycol (ethane-1,2-diol)	No evidence	EM 1999
No CAS 003	DDT metabolites	Group name	**
No CAS 007	Triazines (e.g. atrazine)	Group name	**
No CAS 010	Styrenes (e.g. dimers and trimers)	Group name	**
No CAS 012	Penta to Nonyl-Phenols	Group name	**
No CAS 023	Phthalates	Group name	**
No CAS 035	PCB hydroxy metabolites	Group name	**
No CAS 048	PAHs	Group name	**
No CAS 049	Dioxins/Furans = PCDDs/PCDFs	Group name	**
No CAS 086	Tetrachloro DDT	Group name	**
No CAS 113	TeBCDD	Group name	**
No CAS 123	Synthetic pyrethroids	Group name	**
No CAS 133	4-hydroxy alkylphenols	Group name	**
617883-33-8	Polychlorinated Terphenyls (PCT)	Group name	**
No CAS 024	Dioctylphthalate (DOP)	Double input	**
27013-89-4	Phenol, 4-isooctyl-	Double input	**
67554-50-1	Phenol, octyl-	Double input	**
93891-78-2	Phenol, sec-octyl-	Double input	**
485-72-3	Formononetin	Phytoestrogen	**
491-80-5	Biochanin A	Phytoestrogen	**

* EM 1999 = Expert meeting held in 1999

** Present study

ANNEX 11

OVERVIEW OF THE SYSTEMIC TOXICITY DATA
OF CATEGORY 1 SUBSTANCES.

Content

ANNEX 11A. OVERVIEW OF THE HUMAN HEALTH RELEVANT SYSTEMIC TOXICITY DATA OF CATEGORY 1 SUBSTANCES

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
63-25-2	Carbaryl	Rat	Effects on Newborn - weaning or lactation index; Paternal Effects - spermatogenesis (incl. genetic material, sperm morphology, motility, and count); Effects on Newborn - live birth index (measured after birth) Effects on Newborn - growth statistics (e.g.%, reduced weightgain); Maternal and postnatal toxicity (decreased litter size and viability); Decreased number of live-born offspring and growth rate	LOEL-TDLo	27.5-1370	mg/kg	GFh234 / GFh232 / POhs020 / POhs021 / POhs022	367-18267	220-10960
		Mouse	Litter effects: decreased fetal weight; Fetal weight reductions and fetal growth retardation; Litter effects: increased entirely resorbed litters; Specific developmental abnormalities - musculoskeletal system and urgenital system	LOEL-TDLo	833 - 5660	mg/kg diet	GFh 238 / GFh239 / GFh240 / POhs023	833-5660	500-3396
		Rabbit	Significant increased umbilical hernia	LOEL	200	mg/kg body weight. day	GFh245	6667	1212
		Monkey, Rhesus	Higher abortion rate	LOEL	2.0-20	ug/kg body weight. day	GFh248	0.04-0.4	0.02-0.2
789-02-6	o,p'-DDT	Mouse	maternal effects - ovaries, fallopian tubes	TDLo	67.5	mg/kg	POhs063	562.5	338
		Rat	Maternal effects - uterus, cervix, vagina; Specific developmental abnormalities - endocrine system	TDLo	5-250	mg/kg	Poh061 / POhs062	100-5000	50-2500
53-19-0	o,p'-DDD	Human	Paternal Effects - spermatogenesis (incl. genetic material, sperm morphology, motility, and count)	TDLo	16000	mg/kg	POhs071	430769	560000
		Rat	Specific developmental abnormalities - endocrine system and urogenital system	TDLo	250	mg/kg	POhs070	5000	2500

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
72-55-9	p,p'-DDE	Rat	maternal effects - uterus, cervix, vagina	TDLo	3.5	mg/kg	POhs085	70	35
32809-16-8	Procymidon	Rat	Parternal effects, Endocrine -changes in luteinizing hormone and androgenic	TDLo	360	mg/kg	POhs092	6000	3600
8018-01-7	Mancozeb	Rat	specific developmental abnormalities, body wal, central nervous system, eye/ear,craniofa cail, musculoskeletal system, homeostasis	TDLo	1320	mg/kg	POhs136	26400	13200
9006-42-2	Metiram (Metiram-complex)	Rabbit	Embryo/fetotoxicity (decreased litter size and weight); Effects on reproductive parameters	LOEL	120	mg/kg body weight. day	GFh116	4000	727
		Rat	Embryo/fetotoxicity (decreased litter size and weight); Effects on reproductive parameters	LOEL	16-160	mg/kg body weight. day	GFh114 / GFh115	320-3200	160-1600
319-85-7	Beta-HCH	Rat	reproductive paternal effects testes, epididymis, sperm dect	TDLo	672	mg/kg	POhs113	11200	6720
		Rat	Increased mortality and infertility	LOEL	0.5	mg/kg body weight. day	GFh147	6.7	4
608-73-1	Hexachlorocyclohexane = HCH mixed	Mouse	Reproductive paternal effects spermatogenesis, testes, epididymis, sperm dec	TDLo	5460-9120	mg/kg	POhs107 / Pohs108	45500-76000	27300-45600
72-43-5	Methoxychlor	Rat	Reproductive effects	LOEL	1000	ppm	GFh140	50	25
72-43-5	p,p'-Methoxychlor	Mouse	Maternal effects, uterus, cervix, vagina	TDLo	900	mg/kg	POhs129	7500	4500
		Rat	Reproductive paternal effects testes, epididymis, sperm dect, prostate, seminal vesicle, cowper's gland, accessory gland; Specific developmental abnormalities, musculoskeletal system	TDLo	2000-66000	mg/kg	POh127 / POhs128	26667-880000	16000-528000
122-14-5	Fenitrothion	Rat	"Reproductive effects on newborn behavorial Reproductive effects on newborn other post natal measures; Suppressed lactation	LOEL-TDLo	40-100	mg/kg	CGh771 / CGh772 / gphs0644	800-2000	400-1000

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
			indices"						
91465-08-6	Cyhalothrin (@Karate)	Rat	Parental, slightly reduced bw gain and slightly reduced bw gain of the pups	NOEL	1,5	mg/kg body weight. Day	LBh032	20	12
52918-63-5	Deltamethrin	Mouse	"Reproductive effects on newborn live birth index Reproductive effects on newborn viability index Reproductive specific developmental abnormalities musculoskeletal system; Developmental toxicity at maternal toxic doses"	NOAEL / TDLo	6 / 30-50	mg/kg	gphs0400 / gphs0401 / LBh034	50 / 250-417	30 / 150-250
		Rat	Reproductive effects on newborn growth statistics; Reproductive effects on embryo or fetus fetotoxicity; Reproductive paternal effects other effects on male; Maternal toxicity, decreased maternal body weight, teratogenic effects	NOEL / TDLo	2.5 / 10.0-70	mg/kg	gphs397 / gphs398 / gphs399 / LBh038	3.33 / 133-933	2 / 80-560
60168-88-9	Fenarimol	Rat	Reduced fertility and parturition effects, maternal toxicity	NOAEL*	2	mg/kg bodyweight.day	LBh039	40	20
		Rat	Reproductive fertility male fertility index	TDLo	980	mg/kg	gphs0470	16333	9800
1918-02-1	Picloram	Rat	Reproductive specific developmental abnormalities musculoskeletal system; Reproductive specific developmental abnormalities urogenital system	TDLo	5000-7500	mg/kg	gphs0799 / gphs0800	100000-150000	50000-75000
		Mouse	Effects on fetal weight, increased percentage abnormal fetuses	LOEL	20	mg/kg body weight. day	Gph064	167	100
65277-42-1	Ketoconazol	Rat	Reproductive fertility mating performance; Reproductive fertility female fertility; Reproductive paternal effects spermatogenesis	TDLo	300 - 6480	mg/kg	gphs0718 / gphs0719 / gphs0720 / gphs0721 / gphs0722 / gphs0723 /	4000-86400	2400-51840

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
							gphs0724 / gphs0725		
			Endocrine androgenic	TDLo	1029	mg/kg	gphs0717	27703	36014
106-93-4	Dibromoethane (EDB)	chicken	ceased laying eggs	LOEL	25	mg/kg/ day	CGh811	142	99
		Rat	fertility, mating performance; effects on embryo or fetus, fetal death; effects on new born, growth statistics	TCLo / TDLo	39 - 66.67	mg/kg	POhs246 / POhs247 / POhs249	520-889	312-533
		Human	paternal effects, spermatogenesis, sperm morphology, motility and count	TCLo	0.088	mg/kg/ 8h	POhs250	2.37	3.08
608-93-5	Pentachlorobenzene	Rat	Reproductive paternal effects spermatogenesis; Reproductive specific developmental abnormalities musculoskeletal system	TDLo	1802-2000	mg/kg	gphs0275 / gphs0276	24026-26667	14415-16000
87-86-5	Pentachlorophenol (PCP)	Rat	Reproductive Effects on newborn growth; Reproductive specific developmental abnormalities homeostasis; Reproductive specific devellopmental abnormalities; Reproductive effects on embroy or fetus"	TDLo	50 - 4000	mg/kg	gphs0028 / gphs0029 / gphs0030 / gphs0031	1000-80000	500-40000
		Human	Reproductive Effects on newborn delayed effects	TDLo	124	mg/kg	gphs0033	3338	4339
		Mouse	Reproductive effects on embroy or fetus	TDLo	450	mg/kg	gphs0032	3750	2250
85535-84-8	Short chain chlorinated paraffins	Rat	Decrease in ovary weight; Number of post-implantation losses and decrease in viable foetuses per dam	LOEL	2000-3000	mg/kg body weight. day	gph081 / gph085	26667-40000	16000-24000
84-66-2	Diethyl phthalate (DEP)	Mouse	Reproductive paternal effects spermatogenesis; Reproductive effects on newborne live birth index; Reproductive effects on embroyo or fetus; Reproductive specific developmental abnormalities muscoskeletal system; Reproductive paternal effects prostate seminal vesicle; Reproductive effects on newborn physical	TDLo	101000-171000	mg/kg	gphs0082 / gphs0084 / gphs0544 / gphs0545 / gphs0546 / gphs0827	841666-1425000	505000-855000
		Mouse	Maternal and foetal toxicity/teratogenic	LOEL	500	mg/kg/	SWhe005	4166	2500

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
			effects			day			
		Rat	"Reproductive fertility post implantation mortality Reproductive effects on embryo or fetus fetotoxicity; Reproductive specific developmetal abnormalities; reproductive fertility post-implantation mortality	LOEL-TDLo	506-25000	mg/kg	gphs0080 / gphs0081 / gphs0542 / gphs0543 / gph005 / SWhe006	10120-500000	5060-250000
8068-44-8	Clophen A50	guinea pig female	reproductive effects on embryo or fetus- fetal death, specific developmental abnormalities-endocrine system	TDLo	142	mg/kg	POhs173	2367	835
		Mink	decreased kit survival and growth	LOEL	0.1	mg/animal	CGh456	1.67	0.59
31508-00-6	PCB 118 (2,3',4,4',5-pentachlorobiphenyl)	Rat	effects on new born, growth statistics, behavioral, physical, biochemical and metabolic	TDLo	28-112	mg/kg	POhs214 / POhs215	560-2240	280-1120
No CAS 037	PCB 126 (3,3',4,4',5-Pentachlorobiphenyl)	Rat	specific developmental Abnormalities, craniofacial, urogenital system; effects on new born, growth statistics, behavioral, physical	TDLo	0.01-0.522	mg/kg	POhs181 / POhs182	0.2-10.44	0.1-5.22
38380-07-3	PCB 128 (2,2',3,3',4,4'-Hexachlorobiphenyl)	Mouse	effect on embryo or fetus, fetotoxicity(expect death); specific developmental abnormalities carniofacial, urogenital system	TDLo	320-1280	mg/kg	POhs186 / POhs187	2667-10667	1600-6400
7012-37-5	PCB 28 (2,4,4'-trichlorobiphenyl)	Rat	effects on new born, growth statistics, behavioral	TDLo	224	mg/kg	POhs212	4480	2240
No CAS 036	PCB Aroclor 1016	Rat	specific developmental abnormalities, central nervous system; effect on new born, biochemical and metabolic	TDLo	31.5-120	mg/kg	POhs177 / POhs178	630-2400	315-1200
		Monkey	effect on new born,behavioral;	TDLo	18.41	mg/kg	POhs180	368.2	184.1
		Monkey	subtle neurobehavioural effects; decreased birth weights in offspring	LOEL	0.03-0.04	mg/kg/day	CGh457 / CGh459	0.6	0.3
56614-97-2	3,9-Dihydroxy-benz(a)anthrac	Rat	Reproductive maternal effects menstrual cycle change or disorders	TDLo	25	mg/kg	gphs0558	500	250

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
	ene								
56-49-5	3-Methyl-cholanthrene	Mouse	Reproductive effects on newborn biochemical and metabolic; Reproductive effects on newborn growth statistics; Reproductive fertility female fertility index; Reproductive effects on embryo or fetus fetal death; Reproductive effects on newborn viability index; Reproductive maternal effects ogenesis	TDLo	10-189	mg/kg	gphs0588 / gphs0589 / gphs0590 / gphs0591 / gphs0592 / gphs0593 / gphs0594	83.3-1575	50-945
		Rat	Reproductive effects on newborn biochemical and metabolic; Reproductive effects on embryo or other fetus other effects to embryo	TDLo	50-64	mg/kg	gphs0586 / gphs0587	1000-1280	500-640
57-97-6	7,12-Dimethyl-1,2-benz(a)-anthracene	Mouse	Repoductive specific developmental abnormalities musculoskeletal system; Reproductive fertility abortion; Reproductive effects on newborn delayed effects; Reproductive effects on newborn viability index; Reproductive maternal effects ovaries"	TDLo	10-330	mg/kg	gphs0614 / gphs0615 / gphs0616 / gphs0617 / gphs0618 / gphs0619	83-2750	50-1650
		Rat	Reproductive effects on newborn other postnatal measure"	TDLo	10-100	mg/kg	gphs0602 t/m gphs0613	133-1333	80-800
50-32-8	Benzo[a]pyrene	Mouse	Reproductive fertility litter size; Reproductive effects on newborn growth statistics; Reproductive effects on newborn germ cell effects; Reproductive effects on newborn biochemical and metabolic; Reproductive effects on newborn stillbirth; Increased stillbirths; resorptions; malformations; Increased fetal mortality; decreased fetal body weight; increased number of cervical ribs"	LOEL-TDLo	50-1500	mg/kg	gphs0571 t/m gphs0581; POh054 / POh055	417-12500	250-7500
		Rat	Reproductive effects on embryo or fetus fetal; Reproductive effects on newborn live index"	TDLo	2.1-2000	mg/kg	gphs0564 t/m gphs0570	42-40000	21-20000

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
50585-41-6	2,3,7,8-TeBDD	Mouse	effect on embryo or fetus, fetotoxicity(expect death) specific developmental abnormalities carniofacial, urogenital system; Hydronephrosis (at higher doses: cleft palate)	LOEL-TDLo	0.003-0.432	mg/kg	GFh315 / POhs209 / Pohs210	0.025-3.6	0.015-1.8
		Human	"Reproductive fertility other measures of fertility	TDLo	0.16	mg/kg	gphs0128	4.3	5.6
72-33-3	Mestranol	Human	"Reproductive maternal effects ovaries fallopian tubes	TDLo	0.0256	mg/kg	gphs0127	0.59	0.77
		Rat	Reproductive effects on newborn delayed effects; Reproductive fertility preimplantation mortallity "	TDLo	0.0004-2.5	mg/kg	gphs0129 / gphs0141	0.0053-33	0.0032-20
		Rabbit	Reproductive fertility pre-implantation mortality; Reproductive fertility mating performance; Reproductive fertility other measures of fertility"	TDLo	0.025-05	mg/kg	gphs0147 t/m gphs0152	0.83	0.15
		Mouse	Reproductive fertility litter size; Reproductive maternal effects uterus cervix vagina; Reproductive fertility other measures of fertility	TDLo	0.25-2	mg/kg	gphs0143 / gphs0144 / gphs0145	2.08-16.7	1.25-10

ANNEX 11B. OVERVIEW OF THE WILDLIFE RELEVANT SYSTEMIC TOXICITY DATA OF CATEGORY 1 SUBSTANCES

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE CONC.	UNIT_DOSE_	RECNO	WATER CONC (mg/l)
		FISH						
63-25-2	Carbaryl	Medaka (Oryzias latipes)	Increased cardiovascular anomalies	LOEC	5	mg/l	GFe015	5
		Minnow (Pimephales promelas)	Decreased hatchability and number of eggs.	LOEC	0.008-0.68	mg/l	WWe098	0.008-0.68
		Carp (Cyprinus carpio)	Decreased hatching and deformed larvae (3.3%)	LOEC	1.0	mg/l	GFe023	1
122-14-5	Fenitrothion	Guppy (Poecilia reticulata)	Abortion, Decreased egg production	LOEC	0.1-1.5	mg/l	POe026	0.1-1.5
3424-82-6	o,p'-DDE	Herring (Clupea harengus)	Decreased viable hatch	LOEC	0.018	mg/kg ovary	WWe089	
		FROGS						
63-25-2	Carbaryl	Frog (Xenopus laevis)	Decreased embryo growth and decreased activity in tadpoles	LOEC	0.1	mg/l	GFe031	0.1
		Frog (Rana tigrana)	Dose-dependent decreased growth and feeding rate in tadpoles	LOEC	0.5	mg/l	GFe025	0.5
87-86-5	Pentachlorophenol (PCP)	Frog (Xenopus laevis)	Resorption (e.g., Tail Resorption in Frogs); Decrease	NOEC	0.005	mg/l	POse110	0.005
		CRUSTACEANS						
63-25-2	Carbaryl	Water flea (Daphnia magna)	Reproductive performance	MATC	1.5-3.3	ug/l	GFe019	0.0025-0.0033
		Crab (Cancer magister)	Prevention of moulting of prezoeae to zoeae	LOEC	1.0	mg/l	GFe018	1
122-14-5	Fenitrothion	Water flea (Daphnia magna)	Progeny (Includes Counts, Numbers, Clutch, Litter or Brood Size, Numbers of Progeny per Parent)	NOEC	0.000009	mg/l	POse262	0.000009
72-55-9	p,p'-DDE	Copepod (Nitocra spinipes)	Reproduction, General	EC50	0.0003	mg/l	POse078	0.0003
		MOLLUSCS						
63-25-2	Carbaryl	Oyster/Clam (Crasostrea virginica/Venus	Decreased larval development and growth of oysters and clams	LOEC	1.0	mg/l	GFe017	1

CASNR	NAME	SPECIES	EFFECT	CRITERION	DOSE CONC.	UNIT_DOSE_	RECNO	WATER CONC (mg/l)
		mercenaria)						
		BIRDS						
63-25-2	Carbaryl	Duck (Anas platyrhynchos)	Toxic, decreased number of eggs, thinner egg shells	LOEL	3000	mg/kg diet	GFe034	
85535-84-8	Short chain chlorinated paraffins	Duck (Anas platyrhynchos)	decrease in eggshell thickness	LOEL	1000	mg/kg diet	CGe065	
52918-63-5	Deltamethrin	Quail/Duck (Colinus virginianus/Anas platyrhynchus)	reproductive toxicity	NOEC	>450	ppm	LBw012	
60168-88-9	Fenarimol	Quail (Colinus Virginianus)	reproductive toxicity	NOEC	300	ppm	LBW011	
		Duck (Anas platyrhynchos)	reproductive toxicity	NOEC	250	ppm	LBW010	
		MAMMALS						
8068-44-8	Clophen A50	Mink (Mustela vision)	decreased nr. of placentas that contained viable fetuses, decrease in expression of the IGFII gene (in adult liver),	LOEC	1.3	mg/day	MMse015	

ANNEX 12

OVERVIEW OF THE ED EFFECTS DATA
OF CATEGORY 1 SUBSTANCES.

Content

ANNEX 12A. OVERVIEW OF THE HUMAN HEALTH RELEVANT ED EFFECTS DATA OF CATEGORY 1 SUBSTANCES

CASNR	NAME	SPECIES	EFFECT	CRITERIOM	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
63-25-2	Carbaryl	Rat	Inhibition AChE; Affected spermatocytes; Prolonged/increased estrus cycle; Changes hypophysis & thyroid function	LOEL - EL	0.07 - 7	mg/kg bw/day	GFh224 / GFh254	0.42-60.6	0.252-36.36
2971-22-4	1,1,1-Trichloro-2,2-bis(4-chlorophenyl)-ethane	Rat	Increased uterine glycogen content	LOEL	1	mg/ animal	CGh014	100	50
53-19-0	o,p'-DDD	Human	Paternal Effects spermatogenesis (incl. genetic material, sperm morphology, motility, and count)	TDLo	16000	mg/kg food	POhs071	16000	20.8
14835-94-0	o,p'-DDMU	Rat	Increased uterine glycogen content	LOEL	8	mg/ animal	CGh025	800	400
789-02-6	o,p'-DDT	Mouse	Uterine expression of progesterone and lactoferrin receptors	EL	7.5	mg/kg bw	WWh053	62.5	37.5
72-54-8	p,p'-DDD	Mouse	Uterine expression of progesterone and lactoferrin receptors	EL	7.5	mg/kg bw	WWh052	62.5	37.5
72-55-9	p,p'-DDE	Rat	Altering expression of androgen-dependent genes	EL	200	mg/kg bw.day	GFh031	3333	2000
32809-16-8	Procymidon	Rat	Altered reproductive development; Reduction in ano-genital distance; Increased testes weight	LOEL	12.5-25	mg/kg bw.day	MMh078 / MMh075 / MMsh030	167-333	100-200
8018-01-7	Mancozeb	Rat	Ovarian hyperthrophy	LOEL	700	mg/kg bw/day	LBh007	14000	7000
9006-42-2	Metiram (Metiram-complex)	Monkey	Decreased T3 and T4; Increased thyroid weights; Thyroid follicular cell hyperplasia	LOEL	15-75	mg/kg bw.day	GFh113	300-1500	150-750
319-85-7	Beta-HCH	Rat	Decreased testes weight; Testicular atrophy	LOEL	50-250	mg/kg food	GFh052	50-250	30-150
1689-83-4	Ioxynil	Rat	Reduced bw gain, liver (hypertrophy and enzyme induction). Thyroid hyperactivity.	NOAEL*	0,5	mg/kg/ day	MMh058	6.67	4
72-43-5	Methoxychlor	Rat	Accelerated maturation; Disturbed estrous cycle	LOEL-EL	25-50	mg/kg bw.day	CGh043	500-1000	250-500
122-14-5	Fenitrothion	Rat	Decreaseed weights of accessory glands	LOEL	15	mg/kg bw.day	gph094	200	120
82657-04-3	Bifenthrin	Rat	Suppression T3 and T4; Concomitant	LOEL	0.5	mg/	GFh286	33.3	20

CASNR	NAME	SPECIES	EFFECT	CRITERIOM	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
	(@Talstar)		stimulation of TSH			animal			
91465-08-6	Cyhalothrin (@Karate)	Rat	Suppression T3 and T4; Concomitant stimulation of TSH	LOEL	0.2	mg/ animal	GFh285	13.33	8
52918-63-5	Deltamethrin	Rabbit / Rat	Decrease weight of testis and pituitary; Decreased weight of genital organs; Increased percentage dead and abnormal spermatozoa; decreased plasma testosterone concentration and fertility	LOEL	0.87-8.7	mg/kg bw.day	Gph025 / Gph036	11.6-290	5.27-58
10453-86-8	Resmethrin	Rat	Reduced prostate weight; Thyroid changes	LOEL	2000	mg/kg bw	CGh1003 / CGh1004	33333	20000
60168-88-9	Fenarimol	Rat	Decreased mounting	LOEL	70	mg/kg bw.day	WWh024	1167	700
1918-02-1	Picloram	Rat	Increased number of neoplasms in endocrine organs, thyroid gland, pituitary, mammary glands and reproductive organs; Increased atrophy of the testes	LOEL	7437	ppm	Gph063 / POh130	409	225
65277-42-1	Ketoconazol	Human	Suppression of sex steroids; Lowering of testosterone levels	LOEL	1600	mg. day	Gph061	615	800
21087-64-9	Metribuzin	Rat	Enlarged thyroids	LOEL	25 - 75	mg/kg bw.day	GFh083	333-1000	200-600
886-50-0	Terbutryn	Rat	Stimulation of T3 synthesis, inhibition of T4 synthesis, increased synthesis of LH in the hypophysis and decreased secrestion of LH in the serum	LOEL	50	ppm. day	Gph065	3	1.8
106-93-4	Dibromoethane (EDB)	Rabbit	Decreases in sperm velocity, percentage motility and ALH	LOEL	45	mg/kg bw.day	CGh808	1500	273
12002-48-1	Trichlorobenzene	Rat	Histological changes in thyroid	LOEC	0.082	mg/kg food. day	gph007	0.082	0.0492
608-93-5	Pentachlorobenzene	Rat	Decreased levels of plasma T3 and T4	LOEL	0,3	mg/kg bw	Gph068	6	3
87-86-5	Pentachlorophenol (PCP)	Rat	Decreased plasma T4 and T3 levels. Decreased concentrations free T3 and T4 plus T4/T3 quotient.	ED	30	mg/kg bw.day	POh279	600	300
9016-45-9	Nonylphenolethoxyl	Mouse	Uterine weight	LOEL	1000	mg/kg	gph072	5000	3000

CASNR	NAME	SPECIES	EFFECT	CRITERIOM	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
	ate					bw.day			
85535-85-9	Intermediate chain chlorinated paraffins	Rat	Decreased hepatic vitamin A levels; Histopathological changes in thyroid; Decreased plasma T4; Increased TSH	LOEL	43-1000	mg/kg bw.day	CGh656 / CGh658	430-13333	258-8000
85535-84-8	Short chain chlorinated paraffins	Mouse / Rat	Increased incidence of thyroid follicular cell adenomas and carcinomas; Thyroid hyperthrophy; Increased activity of thyroxine-UDPG-glucoronyltransferase	LOEL	125-313	mg/kg bw.day	CGh654 / CGh667 / CGh668	1042-4173	625-2504
84-61-7	Dicyclohexyl phthalate (DCHP)	Rat	Testicular damage	LOEL	2500	mg/kg bw.day	Gph030	8333	5000
84-66-2	Diethyl phthalate (DEP)	Mouse	Decreased sperm concentration; Decreased number of live pups per litter; Fertility/Reproductive performance	LOEL	3640-4400	mg/kg bw.day	Gph004 / CGh1049 / SWhe004	30333-36667	18200-22000
101-53-1	Phenyl-4-hydroxy-phenylmethane = 4-Benzylphenol = p-Benzylphenol	Rat	Increased uterine glycogen content	LOEL	2	mg/ animal	CGh046	200	100
106-89-8	Epichlorohydrin (1-chloro-2,3-epoxypropane)	Rat	Reduced number of sperm heads; Induced antifertility effects; Reduced % fertilised ova	LOEL	6.25-25	mg/kg bw	CGh878 / CGh875 / Gph012	83-333	50-200
8068-44-8	Clophen A50	Mink / Guinea pig	Decreased kit survival and growth; Delayed vaginal opening; Decreased testis weight	LOEL	0.1-2.2	mg/ animal	CGh456 / CGh462	1.7-73	0.6-25.8
No CAS 087	PCB138 2,2',3,4,4',5'-hexachlorobiphenyl	Human	Association blood concentrations of PCB's with thyroid hormone status; Endometriosis	LOEL	130-225	ng/l	LBh041 / GFh003	0.00025-0.00043	0.00033-0.00056
No CAS 088	PCB180 2,2',3,4,4',5,5'-heptachlorobiphenyl	Human	Association blood concentrations of PCB's with thyroid hormone status; Endometriosis	LOEL	80-120	ng/l	LBh042 / GFh004	0.00015-0.00023	0.00020-0.00030
12642-23-8	PCT Aroclor 5442	Rat	Increased uterus glycogen content	LOEL	20	mg/kg	CGh168	100	50
56614-97-2	3,9-Dihydroxybenz-(a)anthracene	Rat	Increased uterus weight	ED	2.5	mg/kg	CGh181	50	25
56-49-5	3-Methylcholan-threne	Mouse	Inhibition of oogenesis	LDLo	100	mg/kg	gphs0582	833	500
7099-43-6	5,6-Cyclopento-1,2-benzanthracene	Rat	Cornification of vaginal epithelium	ED30	100	mg/ animal	CGh185	10000	5000

CASNR	NAME	SPECIES	EFFECT	CRITERIOM	DOSE_CONC.	UNIT_DOSE_	RECNO	INTAKE (mg/kg food.day)	INTAKE (mg/l water.day)
57-97-6	7,12-Dimethyl-1,2-benz(a)anthracene	Rat	"Reproductive effects on newborn live birth index reproductive effects on newborn germ cell effects"	TDLo	15	mg/kg	gphs0602	300	150
50-32-8	Benzo[a]pyrene	Rat	Cornification of vaginal epithelium	ED30	100	mg/animal	CGh189	10000	5000
50585-41-6	2,3,7,8-TeBDD	Rat	Affected spermatogenesis; Defective/Necrotic spermatocytes in epididymis; Increased relative testis weight; Reduced thyroid hormone concentrations	LOEL	0.001-0.033	mg/kg bw	GFh308 / GFh305	0.017-0.55	0.01-0.33
118174-38-2	6-Methyl-1,3,8-tri-chlorodibenzofuran	Rat	Decreased estrogen & progesterone receptors content in uterus	LOEL	43	mg/kg	CGh267	215	107.5
94-82-6	2,4-dichlorophen-oxybutyric acid = 2,4-DB	Human	Increased cancer of the testicle, thyroid, other endocrine glands, nose and nasal cavity	unknown	unknown	Un-known	MMh056	unknown	unknown
72-33-3	Mestranol	Human	Reproductive fertility other measures of fertility	TDLo	0.02	mg/kg	gphs0126	0.46	0.6

ANNEX 12B. OVERVIEW OF THE WILDLIFE RELEVANT ED EFFECTS DATA OF CATEGORY 1 SUBSTANCES

CASNR	NAME	SPECIES	EFFECT	CRITERIUM	DOSE_ CONC.	UNIT_DO SE_	RECNO	WATER CONC (mg/l)
		FISH						
63-25-2	Carbaryl	Medaka (Oryzias latipes)	Increased cardiovascular anomalies	LOEC	5	mg/l	GFe015	5
		Minnow (Pimephales promelas)	Decreased hatchability and number of eggs.	LOEC	0.008-0.68	mg/l	WWe098	0.008-0.68
		Carp (Cyprinus carpio)	Decreased hatching and deformed larvae (3.3%)	LOEC	1.0	mg/l	GFe023	1
122-14-5	Fenitrothion	Guppy (Poecilia reticulata)	Abortion, Decreased egg production	LOEC	0.1-1.5	mg/l	POe026	0.1-1.5
3424-82-6	o,p'-DDE	Herring (Clupea harengus)	Decreased viable hatch	LOEC	0.018	mg/kg ovary	WWe089	
		FROGS						
63-25-2	Carbaryl	Frog (Xenopus laevis)	Decreased embryo growth and decreased activity in tadpoles	LOEC	0.1	mg/l	GFe031	0.1
		Frog (Rana tigrana)	Dose-dependent decreased growth and feeding rate in tadpoles	LOEC	0.5	mg/l	GFe025	0.5
87-86-5	Pentachlorophenol (PCP)	Frog (Xenopus laevis)	Resorption (e.g., Tail Resorption in Frogs); Decrease	NOEC	0.005	mg/l	POse110	0.005
		CRUSTACEANS						
63-25-2	Carbaryl	Water flea (Daphnia magna)	Reproductive performance	MATC	1.5-3.3	ug/l	GFe019	0.0025-0.0033
		Crab (Cancer magister)	Prevention of moulting of prezoeae to zoeae	LOEC	1.0	mg/l	GFe018	1
122-14-5	Fenitrothion	Water flea (Daphnia magna)	Progeny (Includes Counts, Numbers, Clutch, Litter or Brood Size, Numbers of Progeny per Parent)	NOEC	0.000009	mg/l	POse262	0.000009
72-55-9	p,p'-DDE	Copepod (Nitocra spinipes)	Reproduction, General	EC50	0.0003	mg/l	POse078	0.0003
		MOLLUSCS						
63-25-2	Carbaryl	Oyster/Clam (Crasostrea	Decreased larval development and growth of oysters and clams	LOEC	1.0	mg/l	GFe017	1

		virginica/Venus mercenaria)						
		BIRDS						
63-25-2	Carbaryl	Duck (Anas platyrhynchos)	Toxic, decreased number of eggs, thinner egg shells	LOEL	3000	mg/kg diet	GFe034	
85535-84-8	Short chain chlorinated paraffins	Duck (Anas platyrhynchos)	decrease in eggshell thickness	LOEL	1000	mg/kg diet	CGe065	
52918-63-5	Deltamethrin	Quail/Duck (Colinus virginianus/Anas platyrhynchus)	reproductive toxicity	NOEC	>450	ppm	LBw012	
60168-88-9	Fenarimol	Quail (Colinus Virginianus)	reproductive toxicity	NOEC	300	ppm	LBW011	
		Duck (Anas platyrhynchos)	reproductive toxicity	NOEC	250	ppm	LBW010	
		MAMMALS						
8068-44-8	Clophen A50	Mink (Mustela vision)	decreased nr. of placentas that contained viable fetuses, decrease in expression of the IGFII gene (in adult liver),	LOEC	1.3	mg/day	MMse015	

CASNR	NAME	SPECIES	EFFECT	DOSE_ CONC	UNIT_DO SE_	RECNO	Waterconc. (ug/l)
		FISH					
319-85-7	Beta-HCH	Guppy/Medaka (Poecilia reticulata / Oryzias latipes)	Induced vitellogenesis and hermaphrodites	0.003-1.0	mg/l	WWe050 / WWe049	3-1000
608-73-1	Hexachlorocyclohexane = HCH mixed	Guppy (Poecilia reticulata)	Excessive vitellogenin production	0.003-1.0	mg/l	WWe051	3-1000
72-43-5	Methoxychlor	Minnow/Trout (Pimephales promelas/Oncorhynchus mykiss)	Vitellogenin induction; Fecundity of fish	1.8-4.4	ug/l	gpw011 / gpw009 / gpw012	1.8-4.4
		TURTLES					
5103-73-1	Cis-Nonachlor	Turtle (Trachemys scripta elegans)	Sex reversal	0.16	uM/egg	pb4	70.4*
39765-80-5	Trans-Nonachlor	Turtle (Trachemys scripta elegans)	Sex reversal; Affect circulating steroid hormone concentration	0.25	uM/egg	pb3 / LBw003	110*
72-54-8	p,p'-DDD	Turtle (Trachemys scripta elegans)	sex ratio	2.6	uM/egg	LBw004	832*
		BIRDS					
789-02-6	o,p'-DDT	Gull (Larus Californicus)	Feminized males	2	ppm/egg	GFe001	
72-55-9	p,p'-DDE	Gull (Larus Californicus)	Feminized males	100	ppm/egg	GFe003	
72-43-5	Methoxychlor	Gull (Larus Californicus)	Feminized males	2.5	ppm/egg	GFe004	

ANNEX 13

THE SUMMARY PROFILES OF (41) CATEGORY 1 CHEMICAL GROUPS

Content

SUMMARY

High exposure concern

Bifenthrin, cyhalothrin, deltamethrin and **resmethrin** all are insecticides/pesticides belonging to the group of pyrethroids. They are all used on food crops. Human exposure can be expected through consumption of treated crops. All of them are expected to be readily degradable and solely moderately persistent. Cyhalothrin, deltamethrin and resmethrin is also used in public health e.g. in-house pests like houseflies and cockroaches, against ticks, malaria and in pet sprays and shampoos. Although rarely detected in the environment, in-house use of pyrethroid pesticides results in high exposure concern categorisation.

The use or origin of **2,2-BPPP** remains a bit uncertain. It is supposed that 2,2-BPPP is an impurity in BADGE which is used as a raw material for the preparation of commonly used plastics, coating in food and beverage cans and in paints It is supposed to be inherently biodegradable but not bioaccumulative. Human exposure is expected through food (leaching from food packaging) and through other consumer goods like baby toys etc. 2,2-BPPP is categorised as a high exposure concern compound.

Carbaryl is used as a pesticide on cotton, food crops ornamentals and animals. Human exposure might take place through the ingestion of treated crops. However, carbaryl is readily degradable and not bioaccumulative and human exposure is therefore less likely. Nevertheless, carbaryl has been detected in air, water and sediment due to all year use and therefore categorised as high exposure concern.

Short- and **intermediate chain chloroparaffins** are used as plasticisers in PVC, additives in paint, rubber, sealants, flame retardants, leather processing and in metal working- and extreme pressure fluids. They are both persistent and highly bioaccumulative. Chloroparaffins are detected in all environmental compartments, and human exposure is expected through various consumer goods (e.g. food packages and baby toys), therefore chloroparaffins are prioritised as high exposure concern.

Dicyclohexylphthalate and **diethylphthalate** are used as plasticisers and softeners in a broad range of commonly used plastics e.g. baby toys and food packages. Exposure is expected through toys, food (substance leaching from packaging material), insecticide sprays and cosmetics in which DEP is used (e.g. fixative in perfumes and alcohol denaturing substituent in desinfective soaps). Both phthalates are readily degradable and solely transiently bioaccumulative. However, the use of phtalates in consumer products and their observed environmental concentrations in e.g. fish make that both phthalates are prioritised as high exposure concern.

Lindane (**HCHs**) is an insecticide used on seeds and soil with subsequent incorporation. Lindane is used before food crops are being planted. All other uses, especially foliar spraying are severely restricted in the EU, because lindane rapidly evaporates from surface water, soil and especially vegetation. Atmospheric stability would make redistribution via long range air transport an important fate process. However, HCHs are being used in other parts of the world and hence remote sensitive areas might get infected anyhow. Lindane is inherently biodegradable, bioaccumulative and due its (former) wide spread use still present in fish (food) and mother milk. Lindane is also used as a therapeutic drug in e.g. treatment of scabies.
Another notorious insecticide is **DDT**, which is applied against sickness. Its use is prohibited in the EU, USA and Japan, but still used in some other countries. Similar to lindane it is very persistent, bioaccumulative and able to redistribute via long range air transport. Although its use is severely restricted, DDT and its metabolites are still widely found in the environment e.g. fish, human tissue and mother milk. Therefore, both insecticides are prioritised as high exposure concern.

Epichlorohydrin is used as a stabiliser in plastics, solvent in paint, gums and nail varnish, insect fumigant and as a raw material in elastomer production. Human exposure is expected through goods wrapped, packed or consisting of plastic, nail varnish and paint. Epichlorohydrin is readily biodegradable and not bioaccumulative but due to its application in consumer goods categorised as high exposure concern.

Fenarimol is a pyrimidine fungicide used against powdery mildew on food crops, flowers, lawns and golf courts. Fenarimol is persistent and moderately bioaccumulative. Human and wildlife exposure is expected, so high exposure concern.

The organophosporous pesticide **fenitrothion** is used on food crops, is readily biodegradable and moderately bioaccumulative. Environmental concentrations in water and sediment are reported. Human exposure might be expected through ingestion of treated crops or contaminated water. Because fenitrothion is readily biodegradable human exposure is less likely to occur. More important however is indoor use against flies, cockroaches and mosquitoes and use in public health programmes. All together, human exposure is expected and hence fenitrothion is categorised as a high exposure concern compound.

4-isooctylphenol en **4-octylphenol** are used as raw material in the manufacturing of e.g. surfactants, detergents and wetting agents. It is also used as plasticiser, stabiliser in fuels, adhesive in rubbers and intermediate in several bactericides and pesticides. They will mainly arise in wastewater from degradation of octylphenolethoxylates after being used as a cleaning agent. Both octylphenoles are inherently biodegradable and expected to be bioaccumulative. Because environmental levels have been detected and human exposure is expected through consumer goods containing octylphenoles they prioritised as high exposure concern.

Ketokonazole is used as an antifungal drug and applied as a tablet, shampoo or cream. Human exposure in people taking ketokonazole in their treatment against fungal diseases is inevitable. Ketokonazole is prioritised as high exposure concern. Wildlife might be exposed as well as a result from release through wastewater (shampoo), faeces or accidental spills. However, environmental levels are not reported

Mancozeb and **metiram** fungicides used on food crops. Human exposure may be expected by food but because these substances are metabolised rapidly to its metabolites (ETU and MITC), exposure is less likely. Both mancozeb and metiram are not bioaccumulative. The metabolite ETU, however, is detected in different environmental compartments as well as on food. Both mancozeb and metiram are prioritised high exposure concern compounds based upon their more persistent metabolite ETU, which probably is the real endocrine disruptive compound

Methoxychlor is used as an insecticide used on food crops and flowers but is also applied in animal houses dairies and as a household spray. **Methoxychlor derivatives** have no main use but are formed as a result of methoxychlor degradation. Both are persistent and highly accumulative. Environmental levels of methoxychlor are detected in all compartments and biota. Humans might be exposed to through consumption of methoxychlor treated crops, contaminated drinking water and household use. Methoxychlor, and therefore its metabolites as well although environmental levels are not reported, is prioritised as a high exposure concern compound.

Metribuzin belongs to the group of triazol/triazine herbicides against broad-leaved weeds. Metribuzin is used on food crops. Human exposure is expected through consumption of treated crops. Metribuzin is moderately persistent but not bioaccumulative. Metribuzin is applied in households and detected in sediment, water and drinking water. In conclusion, human exposure through food and drinking water can not be excluded, hence categorisation as a high exposure concern compound.

Nonylphenolethoxylate is used as a non-ionic surfactant, detergent and wide range stabiliser in leather-, textile- and polymer industry as well as in paints and wetting agents for agricultural chemicals. Nonylphenol is hardly bioaccumulative and of low persistence. Human exposure however is expected through their use as surfactants and presence in consumer goods like paints and plastics. Nonylphenolethoxylate is prioritised as high exposure concern.

PAHs are present in fossil fuels and unintentionally formed during combustion process. Human exposure is expected through food (charbroiled, roasted, smoked or contaminated), cigarette smoking, residential heating and vehicle traffic. Also natural PAH sources can be pointed out, like volcanoes and forest fires. PAHs are highly persistent and bioaccumulative. They are observed in all environmental compartments including biota. PAHs are classifies as high exposure concern. However, because the use of DMBA and 3-MC is restricted to biochemical research which is considered to be a closed system, these two PAHs are classified as low exposure concern compounds. Both DMBA and 3-MC can not be formed naturally.

p-Benzylphenol is used as a germicide, antiseptic and preservative. It is persistent and highly bioaccumulative. Human exposure is expected through presence in consumer goods, hence high exposure concern.

PCBs and **PCTs** have been used in the past in electrical equipment but are now severely banned and restricted. PCBs and PCTs are still available through existing products, at the production and the waste stage. PCBs are widely found in the environment in food (fish) and mother milk. They are persistent and highly bioaccumulative. PCBs and PCTs are categorised as high exposure concern.

Pentachlorobenzene and **pentachlorophenol** are bot persistent and bioaccumulative. Pentachlorophenol was once widely used as a pesticide, as a wood preservative and during processing of leather and textile. Nowadays use of pentachlorophenol is severely restricted and no longer available for the general public. Pentachlorobenzene is no longer used nowadays, but exposure is still expected as a result of former uses in dielectric fluids, fungicides and as an intermediate of the fungicide quintozene. Furthermore, pentachlorobenzene might result from biodegradation of the severely restricted insecticide HCB. Despite restricted application, high persistence and bioaccumulative properties of both pentachlorophenol and pentachlorobenzene result in the fact that both substances are still observed in the environment. Concomitantly, pentachlorobenzene might redistribute via long-range air transport. Both humans and wildlife might be exposed, hence categorisation as high exposure concern.

PHDDs/PHDFs are unintentionally formed during combustion, various industrial processes and production of halogenated chemicals including flame retardants, pesticides and solvents. Exposure s expected through emission at production and at waste stage. Substances are found in food (fish, meat and dairy products), human tissue and mother milk. PHDDs and PHDF are highly persistent, bioaccumulative and hence prioritised as high exposure concern.

Procymidone is used as a fungicide on food crops. It is persistent and highly bioaccumulative. Human exposure is expected through consumption of food.

Trichlorobenzene is used as an additive in dyes, dielectric fluids, lubricating oils, heat transfer media and as a degreasing solvent. In the past it was used as an insecticide. Trichlorobenzene is persistent and highly bioaccumulative. Environmental concentrations are reported for all compartments including biota. Humans (and wildlife) are expected to be exposed to trichlorobenzene through contaminated food and water and other environmental prevalence. trichlorobenzene is classified as a high exposure concern compound.

Medium exposure concern

2,4-DB and **ioxynil** are used as herbicides against broad-leaved weeds, both are used on food crops. Both compounds are readily biodegradable and not bioaccumulative. Although human exposure through herbicide treated crops might be expected, extensive basket case studies have proved otherwise. Wildlife on the other hand is exposed through appliance directly in the field. Both 2,4-DB and ioxynil are categorised as medium exposure concern chemicals.

EDB was used in the past as a scavenger in leaded gasoline and as a fumigant. Formerly human exposure was expected through spills of leaded gasoline, exhaust of vehicles using leaded fuels and due to its use as a fumigant. EDB is hardly bioaccumulative and moderately biodegradable. The severe restriction of the use of leaded fuels and the fact that it is not used as a fumigant anymore make human exposure unlikely. However, environmental levels of EDB were detected and hence EDB is categorised as a medium exposure concern compound.

Picloram is a pyrimidine herbicide, mainly used on non-food areas like grasslands, forests and non-crop areas. Human exposure is not expected because picloram is not used on food crops. Wildlife exposure might be expected because of its use as a fungicide. However, picloram is not bioaccumulative and solely moderately persistent and therefore it is categorised as medium exposure concern. However, picloram is observed in ground- and surfacewater, some caution via exposure through contaminated drinking water has to be taken into account.

Terbutryn belongs to the group of triazol/triazine herbicides against broad-leaved weeds. It is used on food crops. Human exposure might be expected through consumption of treated crops, however no data indicate terbutryn is actually present. Due to its biodegradability and because it is not bioaccumulative, human exposure is less likely. Wildlife exposure can not be excluded because of its use as a herbicide. Terbutryn is categorised as medium exposure concern. However terbutryn metabolites may be more persistent and less immobile, leaching to groundwater and contamination of drinking water might occur.

Low exposure concern

Nonachlor was used as a constituent of the insecticide chlordane, which was mainly used on non-crops and animals. The use of chlordane is prohibited in the EU, USA and Japan. Nonachlor is persistent and highly bioaccumulative. Due to limited volatility long-range air transport is not likely. Nonachlor will therefore generally be present as an immobile sink. Since chlordane is no longer used as an insecticide, the phase out of the sole use of the chemical results in a low exposure concern.

BIFENTHRIN (CAS NO 82657-04-3)

Bifenthrin, chemical name 3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-cyclopropanecarboxylic acid, or (2-methyl(1,1'-biphenyl)-3-yl)methyl-3-(2-chloro-3,3,3-trifluoro-1-propenyl)-2,2-dimethylcyclopropane-carboxylate belongs to the group of pyretroid insecticides
Trade names include Biflex, Brigade, Capture 2, FMC 54800, Talstar

Chemical characteristics

Molecular formula bifenthrin: C23-H21-Cl1-F3-O2

MW = 422.88

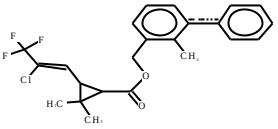


Table 1: Physical/chemical properties of bifenthrin

Parameter	Bifenthrin
Water solubility (mg/L, 25°C)	0.1 (SRC)
Vapour pressure (mm Hg, 25°C)	1.8 x 10-7 (SRC)
log Kow	6.0 (SRC)
Henrys law constant (atm m3/mole)	1.0 x 10-6(SRC)
Koh (cm3/molecule sec)	2.96 x 10-11 (SRC)
Biodegradation	Fast
BCF (L/kg)	38 (SRC) 190 (HSDB)
Koc (L/kg)	323000 (SRC) 131000-302000 (ARS 2002)

Abiotic degradation

A rate for the reaction with hydroxyl radicals in the atmosphere of 2.96 x 10-11 cm3 molecule-1 s-1 at 25°C has been estimated (Meylan 1993 in SRC 2002). This corresponds to an atmospheric half-life of about 13 hours (HSDB). A rate of 1.62 x 10-18 cm3 molecule-1 s-1 for reaction with ozone at 25°C has been estimated (Meylan 1993 in HSDB). This corresponds to a half-life of about 7 days in air with 7°1011 ozone molecules/cm3 (HSDB). Base catalysed hydrolysis rates in water at pH 7 and 8 have been estimated to be 5.5 years and 200 days respectively (Mill 1987 in HSDB). Bifenthrin is also expected to undergo photodegradation (HSDB). Photolysis rate in water has been reported as 0.0033 d-1 at 25°C (ARS 2002). This corresponds to half-lives around 210 days.

Biotic degradation

No actual data on the biotic degradation of bifenthrin are available, but from the pyrethroid structure of bifenthrin it is estimated to be readily biodegradable (Demoute 1989 and Casida 1976 both in HSDB).

Bioconcentration

When estimated from log Kow, bifenthrin has a BCF of 190, which indicates that bifenthrin will bioconcentrate (HSDB). However, some similar substances are readily metabolised in the organism and the actual BCF may thus be smaller (Crosby 1995 in HSDB).

Use, exposure and emissions

Bifenthrin is an insecticide and acaricide effective against a broad range of foliar pests. Crops include cereals, citrus, cotton, fruit, grapes, ornamentals and vegetables (Tomlin 1994).

Release to the environment

Release to the environment is an intended result of the use of bifenthrin as a pesticide. Bifenthrin may also be released from the production site.

Summary of environmental fate

After release to water, bifenthrin is expected to sorb to sediment and suspended particles. Bifenthrin is also expected to volatilise from the water surface and volatilisation half-lives of 50 and 555 days have been calculated for a model stream and a model lake, respectively, when sorption is disregarded (SRC in HSDB). A volatilisation half-life of 3,100 years has been estimated when sorption was taken into account (USEPA 1987 in HSDB). Hydrolysis is not expected to be important at ambient pHs, with low rates. Biotic degradation is expected to take place as bifenthrin is believed to be readily biodegradable (HSDB). Photolysis is expected to take place but only with slow rates (ARS 2002).

After release to soil, bifenthrin is expected to sorb strongly to soil particles. Bifenthrin will thus be rather immobile in the surface soil. Bifenthrin is expected to volatilise from moist soil surfaces, although attenuated by sorption, but not from dry surfaces, as vapour pressure is rather low (HSDB). The major process of removal is expected to be biological degradation, and half-lives between 65 and 125 days have been recorded (HSDB, ARS 2002).

After release to air, bifenthrin is expected to exist both in the vapour phase and in the particulate phase. Vapour phase bifenthrin will degrade by reaction with ozone and hydroxyl radicals. Half-lives of 7 days and 13 hours have been estimated respectively for these reactions (HSDB). Particulate bifenthrin will be removed from the atmosphere by dry and wet deposition (SRC in HSDB).

Environmental concentrations
No data on environmental concentrations have been found.

Vulnerable use and vulnerable groups
People with respiratorial and dermal diseases may be at risk as symptoms may be exacerbated by the contact with bifenthrin (HSDB).

Conclusion
Bifenthrin is used as an insecticide / acaricide used on food crops. Based on its pyrethroid structure it is expected to be readily degradable but moderately bioaccumulative. Because of its use on food crops human exposure might be expected. Bifenthrin is categorised as a compound with high exposure concern.

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

ARS (2002) ARS pesticides properties database http://wizard.arsusda.gov/acsl/

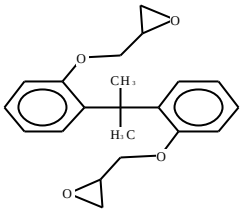
Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

2,2-BIS(2-(2,3-EPOXYPROPOXY)PHENYL)PROPANE (2,2-BPPP) (CAS NO 25036-25-3)

2,2-BPPP is an isomer of 2,2-bis(4-(2,3-epoxypropoxy)phenyl)propane (2,2-BPPP) better known as BADGE. The latter substance belongs to the group of bisphenols and has been evaluated in the WRC study (WRC).

For 2,2-BPPP no specific data have been found. It is assumed it is an impurity in BADGE. Data taken up in this profile (except for table 1) are based on BADGE.

Chemical characteristics



Molecular formula 2,2-BPPP: C21-H24-O4

MW = 340.42

Table 1: Physical/chemical properties of 2,2-BPPP

Parameter	**2,2-BPPP**
Water solubility (mg/L, 25°C)	3.685 (SRC)
Vapour pressure (mm Hg, 25°C)	1.08 x 10-7 (SRC)
log Kow	3.84 (SRC)
Henrys law constant (atm m3/mole)	1.31 x 10-8 (SRC)
Koh (cm3/molecule sec)	6.69 x 10-11 (SRC)
Biodegradation	Slow
BCF (L/kg)	182.1 (SRC)
Koc (L/kg)	1842 (SRC)

Abiotic degradation
When released to the atmosphere BADGE might be degraded by photochemically activated hydroxyl radicals. Atmospheric half life is expected to be 1.92 hours (WRC). Furthermore, BADGE is very stable against thermal and hydrolytic breakdown.

Biotic degradation
BADGE is assumed to be inherently biodegradable (WRC).

Bioconcentration
Based on a BCF value of 182.1, 2,2-BPPP has the ability to accumulate in organisms. However, due to the fact that BADGE (and hence 2,2-BPPP probably as well) is inherently biodegradable concern about bioaccumulation is low.

Use, exposure and emissions
BADGE is solely used in closed systems, however, workers involved in manufacturing and industrial application might be exposed through skin or through inhalation of dust e.g. during bag filling and charging of epoxy resins from bags in the manufacturing process of paint. Assumed is that workers take the precautions needed to prevent exposure.

During in-house measurements for epoxy powder applications carried out by the United Kingdom powder manufacturing industry, the range of personal exposure across four companies for all activities was 0.3 – 10 mg/m3, as 8h time weighted average, for all activities. Based on the assumption that epoxy powder paints typically contain 25-30% of epoxy resins and that powder coating grade epoxy resins contain between 5-10% BADGE, this would correspond to a typical BADGE exposure of 0.0009-0.3 mg/m3. 2,2-BPPP is supposed to be an impurity in BADGE, hence exposure to 2,2-BPPP solely is a small fraction of that (WRC).

Exposure of the general public might occur as a consequence of BADGE containing consumer goods. The major consumer exposure to BADGE is from food and drink cans lined with epoxy based coatings while minor volumes of liquid epoxy resins are used in two-component epoxy glues sold to public in retailer shops.
A number of studies have investigated the migration of BADGE from coated food and drink cans. In 2001 the United Kingdom Food Standards Agency (FSA) conducted a marker survey of BADGE in canned food. Migration levels of BADGE detected in the canned foodstuff were,0.1 mg/kg food. Using information on European consumption pattern for canned food, the total surface areas of cans and the UK FSA survey data, Dionisi and Oldring (2002) calculated per capita exposure to BADGE is 3.0-8.0

ug per person per day., hence 0.05-0.13 ug/kg body weight (assumed a standard person weighs 60 kg). The major sources of exposure appear to arise from canned vegetables (48%), canned fish (18%) and ready meals (5%) (WRC)

Other studies performed by Landenberger (2001) using a Monte Carlo Simulation estimated an average exposure of 0.004 ug/kg bodyweught per person per day. With a maximum of 0.19 ug/kg bodyweight per person per day (WRC).

Summary of environmental fate
If released to air, BADGE is expect to solely exist in the vapour phase. It has low volatility and is removed from atmosphere through wet or dry deposition. When released to water, 2,2-BPPP is assumed to absorb particulate matter and sediment. When released to soil, absorption to the humic fraction is suspected. Leaching to the groundwater compartment is not expected.

Vulnerable groups and vulnerable use.
Workers involved in the manufacturing and industrial application might be exposed to 2,2-BPPP through skin contact or through inhalation of dust (e.g. bag filling).

General public might be exposed as a consequence of the use of BADGE in and on consumer goods, especially through food packages.

Environmental concentrations
No measured environmental (aquatic, terrestrial or aerial) exposure data have been obtained on searches of the COMMPS database and literature sources.

Release of BADGE to the environment through manufacturing sites is expected to be low because they are used in a closed system. Furthermore an environmental release of BADGE (and hence 2,2-BPPP as well) from end-use application is unlikely to occur as epoxy resins are reacted with hardeners/curing agents into cross linked systems which are stable against thermal and hydrolytic breakdown. This taken with the fact that BADGE is inherently biodegradable reduces concern about any possible environmental accumulation.

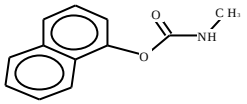
Conclusions
The use or origin of 2,2-BPPP remains a bit uncertain. It is supposed that 2,2-BPPP is an impurity in BADGE which is used as a raw material for the preparation of commonly used plastics and coatings in paints and food cans. It is supposed to be inherently biodegradable but not bioaccumulative. Human exposure is expected through food (leaching from food packaging) and through other consumer goods like baby toys etc. 2,2-BPPP is categorised as a high exposure concern compound.

CARBARYL (CAS NO 63-25-2)

Carbaryl, chemical name 1-naphthol methylcarbamate, belongs to the group of carbamate pesticides. Trade names include Panam, Sevimol, Cekubaryl, Carpolin, Carbatox, OMS 29, UC 7744, Arylam, Carylderm, Clinicide, Derbac, Seffein, Dicarbam, Ravyon, Padrin, Bug Master; Carbamec, Carbamine, Crunch, Denapon,; Devicarb, Hexavin, Karbaspray, Murvin, NAC, Tornado, Tricarnam, Savit, Septene, Tercyl, Thinsec and Sevin

Chemical characteristics

Molecular formula carbaryl: C12-H11-N1-O2



MW = 201.23

Table 1: Physical/chemical properties of carbaryl

Parameter	Carbaryl
Water solubility (mg/L, 25°C)	40 (EHC 153 1994), 110 (SRC)
Vapour pressure (mm Hg, 25°C)	1.17 x 10-6 – 3.1 x 10-7 (EHC153 1994) 1.36 x 10-6 (SRC)
log Kow	1.59-2.3 (EHC153 1994) 2.36 (SRC)
Henrys law constant (atm m3/mole)	4.36 x 10-9 (SRC)
Koh (cm3/molecule sec)	2.6 x 10-11 (SRC)
Biodegradation	
BCF (L/kg)	Does not bioaccumulate (is metabolised) (EHC 153 1994) 13 (SRC)
Koc (L/kg)	100-600 (EHC 153 1994) 241.7 (SRC)

Abiotic degradation
Carbaryl hydrolyses rapidly in alkaline water but slowly in acidic water. The hydrolysis half-lives are a few hours at pH>8, 10-16 days at pH=7 and several weeks at pH<7 (EHC 153 1994). Carbaryl may also photolyse when exposed to sun light. Photodegradation Half-lives of 45 hours, have been measured in water at low pH in mid-day sunlight (EHC 153 1994). Chemical oxidation of carbaryl has also been observed in soil (EHC 153 1994).

Biotic Degradation
In general it is thought that biological degradation plays only a minor role in the degradation of carbaryl in natural waters as hydrolysis is faster in most cases. Several micro-organisms have been shown to be able to degrade carbaryl although some argue that micro-organisms merely continue the degradation commenced by hydrolysis. Biotic degradation has however been found by some to be an important process in the disappearance of carbaryl from water (EHC 153 1994).

Bioconcentration
Because of its very low persistence in water, and its fast degradation in organisms, carbaryl presents no risk of bioaccumulation or biomagnification under practical conditions (EHC 153 1994).

Use, exposure and emissions
Carbaryl has been used for about 30 years as a contact and ingestion pesticide and it controls a wide range of pests. It has been used in cotton, fruits, vegetables, ornamental trees, shrubs and animals and livestock (IARC1976 in HSDB).

Release to the environment
Release to the environment is an intended result of the use of carbaryl as a pesticide. Carbaryl may also be released from the production site. Releases of 0.5 kg of carbaryl for each metric tonne produced have been reported (Sittig 1980 in HSDB).

Summary of environmental fate
After emission to water, carbaryl is expected to sorb moderately to suspended particles and sediments. Volatilisation from the water surface is expected to be very small as Henrys law constant is

small. In the water, carbaryl will be removed by hydrolysis, photodegradation and biological transformation. Half lives between <0.5 days and 20 days have been measured in surface waters (EHC 153 1994). Carbaryl is expected to be more stable in salt water (EHC 153 1994).

After application to soil, carbaryl is expected to sorb at the surface from where it is removed by hydrolysis, photodegradation and biological degradation. In soils with low organic content, some infiltration may take place. In the field, under warm conditions, the half-life of carbaryl in soil is shorter than one month (EHC 153 1994).

If carbaryl is released to air, it is expected to exist in both the particulate phase and the vapour phase. It will be degraded by reaction with hydroxyl radicals with a half-life of 15 hours (SRC in HSDB). Particulate carbaryl will be removed from the atmosphere by wet and dry deposition. Direct photolysis is expected to be an important process in the removal of carbaryl from the atmosphere (Bidleman 1988 in HSDB).

Environmental concentrations
After spraying of a large forest in the US, concentrations in air ranged from 0.0035 to 0.107 $\mu g/m^3$ several miles away (Shehata 1984 in EHC 153 1994).

In a Greek river and lake, respectively 23.7 ng/L and 21.7 ng/L were measured in summer. For the remainder of the year, concentrations were below detection level (Albanis 1986 in EHC 153 1994). After spraying, concentrations of up to 0.314 mg/L have been measured in stream water (Sundaram 1987 in EHC 153 1994). Concentrations of up to 1.47 mg/L have been measured in rice fields after application(Springborn 1988 in EHC 153 1994).

In a tributary to the South Platte river in Colorado, with an agricultural catchment, concentrations of <0.046 – 1.5 µg/L was found in the months where carbaryl was sprayed in the fields whereas a similar tributary with an urban catchment had concentrations of 0.15-2.5 µg/L year round. Probably due to all year use in residential and commercial pest control (Kimbrough 1996 in EHC 153 1994).

In forest soil, 0.06-0.08 ppm was measured five days after application of carbaryl (280 g/Ha). In the sediment of a stream adjacent to the sprayed area, concentrations of 0.03 ppm could be measured two hours after application. After 24 hours concentrations were below detection the limit (Sundaram 1987 in EHC 153 1994).

Vulnerable groups
The humans expected to see the highest exposure is probably workers handling carbaryl. No other vulnerable groups have been identified

Conclusion
Carbaryl is used as a pesticide on cotton, food crops ornamentals and animals. Human exposure might take place through the ingestion of treated crops. However, carbaryl is readily degradable and not bioaccumulative and human exposure is therefore less likely. Nevertheless, carbaryl has been detected in air, water and sediment due to all year use and therefore categorised as high exposure concern.

References
EHC 153 (1994). Environmental health criteria 153 Carbaryl, WHO, Geneva.

SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

CHLOROPARAFFINS, INTERMEDIATE CHAIN C_{14-17} (CAS NO 85535-85-9)

Intermediate chain chloroparaffins were chosen for evaluation because it is a high production volume chemical.

Intermediate chain chloroparaffins comprise chlorinated paraffins with chain lengths of 14 to17 and different levels of chlorination. Chlorination is usually around 40-60 % for commercial mixtures.

As a thorough risk assessment has been drafted by the EU, this chapter on intermediate-chain chlorinated paraffins is entirely an extract of this risk assessment draft.

Chemical characteristics

The formula for this group can be written as $C_xH_{(2x-y+2)}Cl_y$, where x = 14-17 and y = 1-17.

Below, average chemical properties of intermediate-chain chlorinated paraffins are given.

Table 1: Physical/chemical properties of intermediate chain chloroparaffins

Parameter	Intermediate chain chloroparaffins
Water solubility	0.027 mg/L, n-pentadecane, 51% Cl
Vapour pressure	$2.27 \cdot 10^{-3}$ Pa at 40°C, 45 % wt. Cl. $1.3 \cdot 10^{-4}$-$2.7 \cdot 10^{-4}$ Pa at 20°C, C_{14-17},52 % wt. Cl.
log Kow	Values between 5.5 and 8.5 have been given but 7 can be used as average
k_{OH}	$8.0 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1} (med. chain, 40-56% wt. Cl)
Biodegradation	No standard test results available, but other tests suggest no biodegradation and EU use a rate of 0 d^{-1}.
BCF	1087
Koc	589 L/kg Estimated using log K_{ow} = 7

Abiotic degradation

Second order rate constants for the reaction between intermediate-chain chlorinated paraffins and atmospheric hydroxyl radicals have been measured to be $8.0 \cdot 10^{-12}$ -$14.4 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1}. With an atmospheric concentration of hydroxyl radicals of $5.0 \cdot 10^5$ molecules cm^{-3} this corresponds to atmospheric half lives of 24-48 hours . In the EU risk assessment, the slower rate is used. According to data reported in the EU risk assessment, direct photolysis is not a significant degradation mechanism for intermediate-chain chlorinated paraffins .

Biotic Degradation

A number of tests indicate that biotic degradation of intermediate-chain chlorinated paraffins is limited. BOD_5 values of <10 and 20 mg O_2/g have been reported for C_{14-17}, 41% Cl and C_{14-17}, 49% Cl respectively. Other experiments reported also indicate a decrease in biodegradability with increase in chlorination. According to the EU risk assessment, no standard degradation test results are available but on the grounds of BOD and other studies, a degradation rate of 0 d^1 is used for the EU risk assessment .

Bioconcentration

A large number of studies concerning bioconcentration from water is reported in the EU risk assessment. However, in a number of these studies, calculated test concentrations exceeded the solubility, giving rise to suspicions that not all of the intermediate-chain chlorinated paraffin was truly dissolved. A fish BCF of 1087, measured for rainbow trout, was selected in the EU risk assessment as being the most trustworthy. This BCF value is in accordance with a log K_{ow} of approximately 7 .

Use, exposure and emissions

In 1997, 65,256 tonnes of intermediate chain chlorinated paraffins were used in the EU .
The main use of intermediate chain chlorinated paraffins are as secondary plasticisers in polyvinyl chloride (PVC), as extreme pressure additives in metal working fluids, as plasticisers in paint, as additives to adhesives and sealants, in fat liquors used in leather processing and as flame retardant plasticisers in rubbers and other polymeric materials.

Table 2: Distribution of intermediate chain chloroparaffin -use in the EU.

Application	Distribution
PVC	79.4 %
Metal working	9.1 %
Paints, adhesives and sealants	5.4 %
Rubber/polymers (other than PVC)	3.3 %
Leather fat liquors	1.6 %
Carbonless copy paper	1.1 %

Release to the environment

The local release from production of intermediate-chain chlorinated paraffins is rather small, while the local release from e.g. recycling of carbonless paper is large (14.8 kg/day). Other local releases are mostly less than 1 kg/day. At the regional scale, the major releases are from PVC production and from the use of metal cutting fluids containing intermediate-chain chlorinated paraffins.

Table 3: Local releases of intermediate-chain chlorinated paraffins according to EU risk assessment

Use	Comment	Estimated local release
Production (4 sites)	Site A	0.22 kg/day to waste water over 300 days
	Site B	0.06 kg/day to surface water over 300 days
	Site C	0.06 kg/day to surface water over 300 days
	Site D	$1 \cdot 10^{-5}$ kg/day to surface water over 300 days
Use in PVC[e] – plastisol coating[h]	Compounding site (formulation)	0.025[a] kg/day to waste water over 300 days
	Conversion site (processing)	0.185[a] kg/day to waste water; 0.185[a] kg/day to air, over 300 days
	Combined compounding and conversion site	0.21[a] kg/day to waste water; 0.185[a] kg/day to air, over 300 days
Use in PVC[e] – extrusion/other	Compounding site (formulation)	0.092[a], 0.50[b] and 0.0425[c] kg/day to waste water; 0.055[a], 0.3[b] and 0.0255[c] kg/day to air, over 300 days
	Conversion site (processing)	0.28[a], 0.3[b] and 0.255[c] kg/day to waste water; 0.28[a], 0.3[b] and 0.255[c] kg/day to air, over 300 days
	Combined compounding and conversion site	0.372[a], 0.80[b] and 0.298[c] kg/day to waste water; 0.335[a], 0.6[b] and 0.281[c] kg/day to air, over 300 days
Use in rubber/plastics[e]	Compounding site (formulation)	0.0465 kg/day to waste water; 0.0155 kg/day to air, over 300 days
	Conversion site (processing)	0.155 kg/day to waste water; 0.155 kg/day to air, over 300 days
	Combined compounding and conversion site	0.202 kg/day to waste water; 0.171 kg/day to air, over 300 days
Sealants/ adhesives	Formulation/use	negligible

Use	Comment	Estimated local release
Paints and varnishes	Formulation	0.15 kg/day to waste water; 0.05 kg/day to air, over 300 days
	Industrial application of paints (Processing)	{0.059 kg/day to waste water, over 300 days}
	Application by general public (private use)	3 8 * 10^{-7} kg/day to waste water, over 365 days
Metal cutting/working fluids	Formulation	0.83 kg/day to waste water, over 300 days
	Use in oil based fluids (processing)	0.33 kg/day to waste water (large site); 0.3 kg/day to waste water (small site), over 300 days
	Use in emulsifiable fluids (processing)	0.025 kg/day to waste water, over 300 days plus an intermittent discharge of 25 kg/event to waste water
Leather fat liquors	Formulation	{1.1 kg/day to waste water; 0.35 kg/day to air, over 300 days}[i]
	Use – complete processing of raw hides	0.9 kg/day to waste water
	Use – processing of “wet blue”	3.6 kg/day
Carbonless copy paper	Recycling	14.8 kg/day to waste water
Polymers (PVC, other plastics, paints, sealants etc.)	Service life	not applicable

Table 4: Regional and continental releases of intermediate -chain chlorinated paraffins according to EU risk assessment.

Use	Comment	Estimated regional release (kg/year)	Estimated continental release[d] (kg/year)
Production (4 sites)	Site A	65 kg/year to waste water	37 kg/year to surface water
	Site B		
	Site C		
	Site D		
Use in PVC[e] – plastisol coating[h]	Compounding site (formulation)	869 kg/year to waste water and 351 kg/year to air from compounding 10,215 kg/year to waste water and 10,215 kg/year to air from conversion[f]	7,817 kg/year to waste water and 3,155 kg/year to air from compounding 91,935 kg/year to waste water and 91,935 kg/year to air from conversion[f]
	Conversion site (processing)		
	Combined compounding and conversion site		
Use in PVC[e] – extrusion/other	Compounding site (formulation)		
	Conversion site (processing)		
	Combined compounding and conversion site		
Use in rubber/plastics[e]	Compounding site (formulation)	32.25 kg/year to waste water and 10.75 kg/year to air from compounding 107.5 kg/year to waste water and 107.5 kg/year to air from conversion[f]	290.3 kg/year to waste water and 96.75 kg/year to air from compounding 966 kg/year to waste water and 966 kg/year to air from conversion[f]
	Conversion site (processing)		
	Combined compounding and conversion site		
Sealants/ adhesives	Formulation/use	negligible	negligible
Paints and varnishes	Formulation	{354 kg/year to waste water 118 kg/year to air}	{3,186 kg/year to waste water and 1,062 kg/year to air}
	Industrial application of paints (Processing)	{118 kg/year to waste water}	{1,062 kg/year to waste water}
	Application by general public (private use)		
Metal cutting/working fluids	Formulation	1,488 kg/year to waste water	13,875 kg/year to waste water
	Use in oil based fluids (processing)	38,100 kg/year to waste water	342,900 kg/year to waste water
	Use in emulsifiable fluids (processing)	99,200 kg/year to waste water	892,800 kg/year to waste water
Leather fat liquors	Formulation	{315 kg/year to waste water and 105 kg/year to air}	{2,829 kg/year to waste water and 943 kg/year to air}
	Use – complete processing of raw hides	1,050 kg/year to waste water	9,430 kg/year to waste water

Use	Comment	Estimated regional release (kg/year)	Estimated continental release[d] (kg/year)
	Use – processing of "wet blue"		
Carbonless copy paper	Recycling	3,705 kg/year to waste water	33,345 kg/year to waste water
Polymers (PVC, other plastics, paints, sealants etc.)	Service life	14,790 kg/year to waste water and 6,120 kg/year to air	133,110 kg/year to waste water and 55,035 kg/year to air
"Waste remaining in the environment"	Service life and disposal	111-113 kg/year to air 10,000-16,600 to waste water (split 7,000-11,620 kg/year to wwtp and 3,000-4,980 to surface water)[g] 27,500-32,400 kg/year direct to surface water 82,600-97,300 kg/year to urban/industrial soil	990-1,170 kg/year to air 90,000-149,400 to waste water (split 63,000-104,580 to wwtp and 27,000-44,820 to surface water)[g] 247,500-291,600 kg/year direct to surface water 743,400-875,700 kg/year to urban/industrial soil
Total (not including "waste remaining in the environment")		17,027 kg/year to air 170,408 kg/year to water (split 119,286 kg/year to wwtp and 51,122 kg/year to surface water)[g]	153,193 kg/year to air 1,533,582 kg/year to water (split 1,073,482 kg/year to wwtp and 460,101 kg/year to surface water)[g]
Total (including "waste remaining in the environment)		17,138-17,140 kg/year to air 207,908-219,408 kg/year to water (split 126,286-130,906 kg/year to wwtp and 81,622-88,502 kg/year to surface water) 82,600-97,300 kg/year to urban/industrial soil.	154,183-154,363 kg/year to air 1,871,082-1,974,582 kg/year to water (split 1,136,482-1,178,062 kg/year to wwtp and 734,601-796,521 to surface water) 743,400-875,700 to urban/industrial soil

Notes: a) Open systems (as defined in UCD, 1998).
b) Partially open systems (as defined in UCD, 1998).
c) Closed systems (as defined in UCD, 1998).
d) Continental release = total EU release-regional release .
e) Releases estimated from UCD, 1998 assuming that 50% of the initial release to air will condense and eventually reach waste water.
f) Regional and continental releases from conversion assume no air emission control is applied. The estimated emissions would be 10 times lower if his was taken into account, but the actual overall proportion of the industry with such controls is unknown.
g) Releases to waste water assume a 70% connection rate to wwtp.
h) Releases from car underbody coating and sealing, and rotational moulding are thought to be negligible during the processing step.
i) Industry-specific release information is also available and has been used to estimated the PEC_{local} in preference to these default values.
{ } – Denotes estimates are based on the Technical Guidance default values only.

Distribution

After emission, the chlorinated paraffins will redistribute between the environmental compartments. This redistribution has been calculated in the EU risk assessment by using a fugacity model (FUGMOD ver. 1, Jan. 1992).

Table 5: Distribution of intermediate chain chlorinated paraffines using FUGMOD

	Percentage distribution			
Release	**Air**	**Water**	**Soil**	**Sediment**
100 % to air	0.001%	0.004%	99.6%	0.38%
100 % to water	$7 \cdot 10^{-4}$%	0.44%	55.5%	44.1%
100 % to soil	$1 \cdot 10^{-5}$%	0.003%	99.7%	0.34%
50 % to air and 50 % to soil	0.001%	0.012%	98.3%	1.7%

Environmental concentrations

A large number of recent water samples taken upstream and downstream of WWTPs in the vicinity of industries, in the United Kingdom, that use intermediate-chain chlorinated paraffins, showed no concentrations of intermediate-chain chlorinated paraffins above detection level (0.1 µg/L). Previous samples taken in 1986 from different water bodies in the UK showed concentrations between 0.62 and 3.75 µg/L. Freshwater samples from German rivers in 1994 showed concentrations between <0.05 and 0.185 µg/L. In 1987, measured concentrations were considerably higher. In remote freshwater bodies the content of intermediate-chain chlorinated paraffins, when detected, was estimated to be around 0.3-0.7 µg/L based on measurements of $C_{10\text{-}20}$ chlorinated paraffins. $C_{10\text{-}20}$ chlorinated paraffins were found in approx. half of the samples from a number of remote freshwater bodies in the UK .

In summary, a worst case $PEC_{regional}$ of 0.1 µg/L for surface water is used in the EU risk assessment together with an estimated value of 0.389 µg/L.

In marine waters around the UK, concentrations of intermediate-chain chlorinated paraffins is estimated to be in the range 0.3-3 µg/L based on measurements of $C_{10\text{-}20}$ chlorinated paraffins.

In contrast to the absence of intermediate-chain chlorinated paraffins in the surface waters near UK industries (described above), intermediate-chain chlorinated paraffins were found in the corresponding sediments in concentrations ranging from <0.2 to 65.1 mg/kg dry weight in 1999. This corresponds to approx. <0.08 - 25 mg/kg wet weight. In the sediments of German rivers, concentrations of <0.010 to 0.370 mg/kg dry weight were measured in 1994. In 1987, concentrations were apparently higher, at least in river Lech (1.7-2.2 g/kg dry weight) . In the EU risk assessment, $PEC_{regional}$ for sediment of 0.7 mg/kg wet wt. sediment is used together with the predicted value of 8.8 mg/kg wet wt. sediment.

Contents of 4-10 mg $C_{10\text{-}20}$ chlorinated paraffins /kg have been found in sewage sludge from the Liverpool area in 1980. In a more recent study, concentrations of intermediate-chain chlorinated paraffins between 1.8 and 93.1 mg/kg dry weight have been measured in digested sewage sludge from WWTPs treating sewage from industries using chlorinated paraffins in the UK. The digested sludge was in many cases used as fertiliser on farm land soil. The content in soil receiving intermediate-chain chlorinated paraffin contaminated sludge was <0.1 mg/kg dry weight.

In Rotterdam and Hamburg harbours, concentrations of intermediate-chain chlorinated paraffins at 7-10 µg/kg can be estimated on the basis of measurements of total chlorinated paraffins. Likewise, concentrations of 3-98 µg/kg can be estimated at the mud flats Den Helder and Kaiser Wilhelm Koog. It is not specified whether the sediment weight is dry or wet.

Concentrations in air have not been measured, but have been estimated by EUSES in the EU risk assessment. The regional concentration in air is estimated as $3.35 \cdot 10^{-6}$ mg/m^3 or 5.65-$6.12 \cdot 10^{6}$ mg/m^3 when the contribution from “waste remaining in the environment” is included.

Vulnerable uses and vulnerable groups

Use in production of PVC, formulation and use of metal cutting fluids and use of leather fat liquors pose risks to the aquatic phase in the environment and almost all uses pose a risk to sediment living organisms. Thus all uses can be considered vulnerable. Among wildlife, especially crustaceans can be considered vulnerable as they are very sensitive to intermediate chain chloroparaffins. Sediment dwelling organisms can also be considered a vulnerable group as the short chain chloroparaffins accumulate here.

Toxicity
The intermediate-chain chlorinated paraffins seem to be of low acute toxicity to fish, as measured 96 h LC_{50} is larger than 5,000 mg/L. Long term tests also showed little effect on fish.

Whereas no indication of toxicity towards algae and fish have been observed, studies show that intermediate-chain chlorinated paraffins are toxic to daphnids. A long term NOEC of 10 µg/L was considered reliable and was used in the EU risk assessment.

No effects on wwtp micro-organisms have been observed for concentrations up to at least 2,000 mg/L.

For the sediment, NOECs of 1460 mg/kg and 50 mg/kg wet weight has been observed.

The observed toxicities have lead to these Predicted No Effect Concentrations (PNECs) in the EU risk assessment.

Table 6: Predicted PNECs

Compartment	**PNEC**
Aquatic	0.2 µg/L
Sediment	1.0 mg/kg wet weight
Soil	2.12 mg/kg wet weight
Microorganisms	80 mg/L

Conclusion
The PEC/PNEC ratios for water are above one for most life cycle stages of intermediate-chain chlorinated paraffins, but further testing may allow the use of a lower safety factor whereby some PEC/PNEC ratios would fall below one. However, a number of uses have ratios above one irrespective of the results of new testing, and here risk reduction measures should be applied. These uses are: Use in production of PVC, formulation and use of metal cutting fluids and use of leather fat liquors.

For sediments, the PEC/PNEC ratios indicate risk from all local uses except the use and formulation of sealants. As for the water compartment, new toxicity testing may reduce the PEC/PNEC ratio, but in some cases PEC/PNEC will remain above one irrespective of new test results. These local uses are the same as mentioned for water as well as the use in carbonless copy paper (recycling sites).

For sewage treatment plants, the risk is low.

For the terrestrial compartment, there is again the possibility of further testing, but some uses can already be pointed out to pose risks, irrespectively of any new test results. These uses are: use in PVC conversion, use and formulation of metal cutting fluids and use of leather fat liquors.

There is a risk of secondary poisoning from the fish food chain from the use in production of PVC, formulation and use of metal cutting fluids and use of fat liquors.

From the above, medium chain chloroparaffins is considered to be of high concern.

References
European Union risk assessment report on alkanes, C_{14-17}, chloro, DRAFT (March 2002)
Prepared by: Environmental agency, chemical assessment section, Ecotoxicology and hazardous substances national centre, Wallingford, United Kingdom.

CHLOROPARAFFINS, SHORT CHAIN (CAS NO 85535-84-8)

Short chain chloroparaffins were chosen for evaluation because it is a high production volume chemical.

Short-chain chloroparaffins comprise chlorinated paraffins with chain lengths of 10 to13 and different levels of chlorination. For commercial mixtures, the level of chlorination is usually around 40-60% on a weight basis.

As a thorough risk assessment has been done and reported by the EU, this chapter on intermediate-chain chlorinated paraffins is entirely an extract of this risk assessment.

Chemical characteristics

The formula for this group can be written as $C_xH_{(2x-y+2)}Cl_y$, where x = 10-13 and y = 1-13.

Below, average chemical properties of short-chain chlorinated paraffins are given.

Table 1: Physical/chemical properties of short chain chlorinated paraffins

Parameter	Short chain chlorinated paraffins
Water solubility	0.15-0.47 mg/L with partial hydrolysis
Vapour pressure	0.021 Pa at 40°C, 50 % wt.Cl.
log Kow	Values between 4.39 and 8.7 have been measured. A value of 6 is used in the EU risk assessment
k_{OH}	$2.2\text{-}8.2 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1}
BCF	574-7,816
Koc	21,900 L/kg Estimated using log K_{ow} = 6

Abiotic degradation

Second order rate constants for the reaction between short-chain chlorinated paraffins and atmospheric hydroxyl radicals have been measured to be $2.2 \cdot 10^{-12}$ -$8.2 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1}. With an atmospheric concentration of hydroxyl radicals of $5.0 \cdot 10^5$ molecules cm^{-3} this corresponds to atmospheric half lives of 1.9-7.2 days .

Biotic degradation

An OECD test (301 C, modified MITI test) with $C_{10\text{-}12}$, 58 % Cl showed no uptake of oxygen in a 28 day period and short-chain chlorinated paraffins are thus not easily biodegradable according to OECD definitions. An inherent biodegradability test (OECD 302 B) showed that $C_{10\text{-}12}$, 58 % Cl are not inherent biodegradable. A number of experiments confirm this.

Bioconcentration

Several studies concerning bioconcentration from water is reported in the EU risk assessment. Fish BCFs between 574 and 7,816 have been measured for the bioconcentration of 58% Cl short-chain chlorinated paraffins by rainbow trout . For a bleak (Alburnus alburnus) BCFs around 800-1000 were reported for a similar compound.

Use, exposure and emissions

In 1994, 13,208 tonnes of short chain chlorinated paraffins were used in the EU.
The main uses of short chain chlorinated paraffins are in metal working fluids, sealants, in rubbers and textiles (as flame retardants), in leather processing and in paints and coatings. . The use in metal working fluids is with 71 % of total use, by far the largest. However, the use in Europe is in general declining and some uses have been discontinued.

The release from production is rather low. There are currently two production sites in the EU. At one German site the release to waste water was 1 kg total chlorinated paraffins/year, but this was mainly long chained chloroparaffins. However, release to air was estimated to be 250 kg total chlorinated paraffins/year. A total release factor of 0.01% have been reported and this is used in the EU risk assessment. The release factor given in the technical guidance documents is much larger (0.31%). If 10.000 tonnes/year is produced at one site, the ensuing release will be 3.33 kg/day (assuming production is spread over 300 days).

Table 2: The use in 1994 were distributed as

Application	Distribution
Metal working	71.0 %
Rubber	9.9 %
Paints	8.7 %
Sealants	5.3 %
Leather fat liquors	3.0 %
Textiles	1.4 %
Other	0.7 %

Using the same release factor, the total release from production within the EU would be 1.5 tonnes short-chain chlorinated paraffins/year. However, the two producers estimate the release to waste water to be less than 9.9-26.7 kg/year.

Table 3: Release of short chain chlorinated paraffins

Source	Data origin	Amount released/site (local model)	Amount released in region	Amount released in the EU	Main compartment to which release occurs
Production	Evaluation	3.33 kg/day	1,000 kg/year	1,500 kg/year	Water
	TGD	100 kg/day	30,000 kg/year	45,000 kg/year	
	Specific	<0.089 kg/day	<26.7 kg/year	<36.6 kg/year	
Metal working –formulation	Evaluation	1.3 kg/day	2,345 kg/year	23,450 kg/year	Water
Metal working –use	Evaluation	0.33-1.5 kg/day	169 t/year	1,688 t/year	Water
Rubber formulation	Evaluation	<0.004 kg/day	<1.2 kg/year	<12 kg/year	Air/soil/water
Paints and sealing compounds		Negligible	Negligible	Negligible	
Leather formulation	Evaluation	0.01 kg/day	0.39 kg/year	3.9 kg/year	Air Water
	TGD	20 kg/day	780 kg/year	7,800 kg/year	
Leather use	Evaluation	0.5 kg/day	0.39 kg/year	390 kg/year	Air Water
	TGD	25 kg/day	1,950 kg/year	19,500 kg/year	
Textile application		Negligible	Negligible	Negligible	
Total	Evaluation		39.39 kg/year	393.9 kg/year	Air Water
	TGD		204.1 tonnes/year	1,784 tonnes/year	

Evaluation refers to evaluated general data, TGD indicates that figures are based on TGD default release factors, Specific refers to data from specific sites, obtained from industry.

Distribution

After emission, the chlorinated paraffins will redistribute between the environmental compartments. This redistribution has been calculated in the EU risk assessment by using a fugacity model (FUGMOD ver. 1, Jan. 1992).

Table 4:Distribution of short chain chlorinated paraffins using FUGMOD

	Percentage distribution			
	Air	Water	Soil	Sediment
100 % to air	0.11 %	0.02 %	99.0 %	0.8 %
100 % to water	0.05 %	1.16 %	45.3 %	53.5 %
100 % to soil	<0.001 %	0.005 %	99.8 %	0.23 %
20 % to air and 80 % to soil	0.07 %	0.80%	62.5 %	36.6 %

Environmental concentrations

In the UK, levels of short-chain chlorinated paraffins between 0.12 and 1.45 µg/L were found in the surface waters of urban/industrial areas. In Germany, studies in 1994 revealed concentrations of short-chain chlorinated paraffins between 0.05 and 0.12 µg/L. The 1994 German concentrations were lower than 1987 concentrations at the same sites. This may be due to both a reduction in use and differences (improvements) in analytical method. In areas remote from industry, concentrations were either below detection limit (0.g µg/L) or slightly above: 0.5-1.0 µg/L. In marine waters, concentrations in the range <0.5-4.0 µg/L have been measured in 1980 . It is concluded in the EU risk assessment that general concentrations in waters remote from industry are around 0.05-0.3 µg/L while they are 0.1-2 µg/L in waters close to industry .

In German sediments concentrations of short-chain chlorinated paraffins of up to 300 µg/kg dry wt. have been observed in 1992 but typical values in sediments of German surface waters ranged around 10-80 µg/kg in 1994. In the UK concentrations of <50-1000 µg/kg have been measured in rivers remote from industry. In marine sediments, concentrations up to 500 µg/kg have been measured, but in most of the samples, contents were below detection limit (50 µg/kg) .

In sewage sludge from Manchester, concentrations of 4,000-10,000 µg short and intermediate -chain chlorinated paraffins/kg have been measured. In European harbours and mud flats, sediment concentrations between 3 and 47.5 µg/kg have been found. Recently a concentration of 4.5 µg/kg was measured in Lake Hazon, situated in the Arctic part of Canada.

The measured concentrations in German sediments corresponds well with predicted regional concentrations, indicating that the measured concentrations is background concentrations.

From measured concentrations in sludge and assumptions (according to the TGD) on spreading on soil, soil concentrations of 0.10 mg short-chain chlorinated paraffins/kg wet weight soil can be estimated.

Table 5: Predicted regional and continental environmental concentrations that were used in the EU risk assessment.

	PEC	
Media	**Regional**	**Continental**
Surface water	0.33 µg/L	0.033 µg/L
Air	12 ng/m^3	4.6 ng/m^3
Sediment	1.16 g/kg	0.12 mg/kg
Fish	2,600 µg/kg	
Industrial soil	11.5 µg/kg	4.6 µg/kg
Agricultural soil	10.8 mg/kg	0.95 mg/kg

Table 6: Local PECs used in the EU risk assessment

Media	**Release source**	**PEC$_{local}$**
Surface water	Production (default) Production (site spec)	10.5 or 308 µg/L <0.36 and < 0.43 µg/L
	Metal working (formulation)	4.3 µg/L
	Metal working (use)	1.4 or 5.0 µg/L
	Rubber formulations	<0.34 µg/L
	Paints and sealing compounds	negligible
	Leather formulation (A)	62 µg/L
	Leather use (B)	77 µg/L
	Textile applications	negligible
Sediment	Production (default) Production (site spec)	20.8 or 611 mg/kg <0.71 and <0.84 mg/kg
	Metal working (formulation)	8.5 mg/kg
	Metal working (use)	2.8 or 9.8 mg/kg
	Rubber formulations	<0.67 mg/kg
	Paints and sealing compounds	negligible
	Leather formulation (A)	123 mg/kg
	Leather use (B)	153 mg/kg
	Textile applications	negligible

Media	Release source	PEC_{local}
Agricultural soil	Production (default) Production (site spec)	51.5 or 1,550 g/kg negligible
	Metal working (formulation)	20.1 mg/kg
	Metal working (use)	5.1 or 23.2 mg/kg
	Rubber formulations	<0.073 mg/kg
	Paints and sealing compounds	negligible
	Leather formulation (A)	310 mg/kg
	Leather use (B)	385 mg/kg
	Textile applications	negligible

Toxicity
The short-chain chlorinated paraffins seem to be of low acute toxicity to fish, as 48 and 96 h LC_{50} is larger than 100 mg/L. A chronic toxicity of LC_{50} = 0.34 mg/L has been measured in a 60 day study and NOEC values of <0.040 and 0.28 mg/L has been observed for rainbow trout and sheepshead minnow.

For daphnids 24 h EC_{50}s between 0.3 and 11.1 mg/L have been observed with acute NOECs between 0.06 and 2 mg/L. Long term studies, 21 days, showed EC_{50}s from 0.101 to 0.228 mg/L while NOECs ranged from 0.005 to 0.05 mg/L.

For algae, 69 h. EC_{50}s between 0.043 and 3.7 mg/L have been observed with a marine algae being more sensitive than a freshwater algae. One NOEC of 12.1 µg/L has also been reported.

The observed toxicities have lead to these predicted no effect concentrations (PNECs) in the EU risk assessment.

Table 7: Predicted PNECs

Compartment	PNEC
Aquatic	0.5 µg/L
Marine/estuarine	0.7 µg/L
Microorganisms	6 mg/L
Sediment	0.88 mg/kg wet weight
Soil	0.80 mg/kg wet weight

Vulnerable use and vulnerable groups
Metal working (formulation and use), leather (formulation) and rubber formulation are all uses where risk is evaluated to be high, and can be considered as vulnerable uses. Sediment dwelling organisms can be considered a vulnerable group as the short chain chloroparaffins accumulate here.

Legal status
Short chain length chlorinated paraffins are classified as a dangerous substance within the meaning of the directive 67/548/EEC. The classification is:
Carcinogen category 3: R40, with the symbol Xn and dangerous for the environment with the symbol N. They are assigned the risk phrases R40 (Possible risk of irreversible effects) and R50/53 Very toxic to aquatic organisms, may cause long term adverse effects in the aquatic environment.

Conclusion
The PEC/PNEC ratios indicate a significant risk to freshwater aquatic organisms from some local sources: Metal working (formulation and use), leather (formulation). According to the EU risk assessment, measures should be taken to reduce the risk from these sources.

The PEC/PNEC ratios indicate a significant risk to sediment dwelling organisms from both local and regional sources. The local sources of concern are metal working (formulation and use), rubber formulation and leather. For paints, sealing compounds and textile applications the risk is negligible. More studies on releases and possibly toxicity are recommended before final conclusions are drawn.

For the terrestrial compartment, the PEC/PNEC ratios indicate a significant risk from both local and regional sources. Excepted are the use in rubber formulations, paints and sealing compounds and textile applications. However, the PNECs is not based on experiments with directly relevant organisms so more information is needed.

PEC/PNEC ratios indicate a risk for secondary poisoning from leather applications (use and formulation) and metal working. For other uses the ratios does not cause immediate concern.

Based on the risk assessment conclusions above, short chain chlorinated paraffins is expected to be of high exposure concern.

References

European Union risk assessment report on alkanes, C_{10-13}, chloro
European chemicals bureau (2000)

CYHALOTHRIN (CAS NO. 68085-85-8), LAMBDA-CYHALOTHRIN (CAS NO. 91465-08-6)

The substance was selected for evaluation in the expert meeting as it is a used plant protection product (PPP) on the Biocidal Active Substances list 2000 (Draft Version) and is a very persistent chemical. It belongs to the group of pyrethroid pesticides. Lambda-Cyhalothrin is the optical isomer of cyhalothrin and both isomers are used as pesticides. The use and exposure scenario described in this section applies to both isomers.

Chemical characteristics

Molecular formula cyhalotrin: C23-H19-Cl1-F3-N1-O3

MW = 449.86

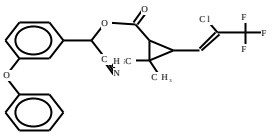


Table 1: Physical/chemical properties cyhalotrin

Parameter	Cyhalothrin	lambda-Cyhalothrin
Water solubility (mg/L, 25°C)	4·E-3(EHC) 5·E-3(SRC)	5·E-3 (EHC) 5·E-3(SRC)
Vapour pressure (mm Hg, 25°C)	7.5·E-9 (EHC) 1.5 E-9 (SRC)	1.5·E-9 (EHC)
log Kow	6.9 (EHC) 6.02-7.00 (SRC)	7.0 (EHC) 6.02-7.00 (SRC)
Henrys law constant (atm m3/mole)	1.48·E-6(SRC)	1.48 E-6 (SRC)
Koh (cm3/molecule sec)	3.15·E-11(SRC)	3.15 E-11 (SRC)
Biodegradation	Moderate	Moderate
BCF (L/kg)	1660-2240 (EHC) 1096 (SRC)	1096 (SRC)
Koc (L/kg)	4.76 E-5 (SRC)	4.76 E-5 (SRC)

Abiotic degradation
Cyhalothrin and lambda-cyhalothrin are rapidly hydrolysed under alkaline conditions but not in neutral or acidic media (EHC 99, 1990). The hydrolysis half-life of lambda-cyhalothrin was 7 days at pH 9 in an aqueous buffer solution whereas no hydrolysis was detected at pH 7 and below (EHC). A photodegradation half-life of 30 days was found for lambda-cyhalothrin in pH 5 buffer under exposure to sunlight, whereas cyhalothrin incubated in river water/sediment mixtures showed a photodegradation half-life of approximately 20 days following exposure to sunlight (EHC 99). In soil, a photodegradation half-life of less than 30 days has been measured for lambda-cyhalothrin when exposed to sunlight (EHC).

Biotic Degradation
Cyhalothrin is moderately persistent in the soil environment and biodegradation half-lives have been found to range between 4 and 12 weeks (Tomlin 1997 in HSDB). At 20º C, the half-lives of cyhalothrin were 22 days in a sandy loam soil and 82 days in a loamy sand soil under aerobic conditions and with an application rate of 100 g/ha. In the sandy loam soil, a slower degradation was observed with increased soil application rate (half-life: 42 days at 500 g/ha), decreased temperature (half-life: 56 days at 10º C) and under flooded (anaerobic) conditions (half-life: 74 days) (EHC 99, 1990). However, the principle degradative reactions identified were hydroxylation and hydrolysis in aerobic soils and hydrolysis in the flooded soil (EHC 99, 1990). In a different study, 30% cyhalothrin was mineralised to CO_2 after 5 weeks of incubation in a sandy loam soil (EHC 99, 1990).

Bioconcentration
The log K_{ow} value of 6.8-7.0 for cyhalothrin and lambda-cyhalothrin indicates a potential for bioaccumulation. Due to the low water solubility limited exposure to aquatic species is expected. In carp (*Cyprinus carpio*) exposed to cyhalothrin for 28 days, bioconcentration factors between approximately 500-4250 have been measured. Following the exposure period, cyhalothrin was rapidly metabolised with a biological half-life of 9 days (EHC). Cyhalothrin half-lives of approximately 1 and 7 days have been measured in daphnids and channel catfish, respectively (EHC 99, 1990). In general, the rapid metabolisation of cyhalothrin in animal systems indicates that bioaccumulation is not likely to present a risk.

Use, exposure and emissions
Cyhalothrin has been used for approximately 25 years to control a wide range of pests in both public and animal health (e.g. for control of parasites, flies, mosquitoes, cockroaches and ticks) but has also been employed in agriculture for control of pome fruit pests. lambda-Cyhalothrin is mainly used as an agricultural pesticide on a range of crops and is being developed for public health. No data are available on production levels (EHC). Occupational exposure to cyhalothrin and lambda-cyhalothrin may occur through inhalation of dust and dermal contact with this compound at workplaces where cyhalothrin is produced or used. Monitoring data indicate that the general population may be exposed to cyhalothrin via ingestion of food containing residues of this compound (HSDB). Cyhalothrin residues in crops are usually lower than 0.2 mg/kg (EHC 99, 1990). Residues of up to 0.5 ppm have been measured in apples, pears and oranges (Yess 1993 in HSDB).

Release to the environment
Release to the environment is an intended result of the use of cyhalothrin as a pesticide. Cyhalothrin may also be released from the production site (Budavari 1996 in HSDB).

Summary of environmental fate
After emission to soil, cyhalothrin is expected to sorb strongly to the soil surface (based on the estimated K_{oc} value of 180.000 L/kg) from where is removed by biodegradation and abiotic degradation processes. Studies have shown that cyhalothrin and its degradation products will not leach through soils and contamination of the groundwater is thus not expected (Stevens 1995 in ECH). Flooding of soil containing cyhalothrin has shown that cyhalothrin is not released into the water (Hamer 1985 in ECH). Cyhalothrin is thus immobilised in soil.

Due to the low water solubility and strong association with soil, cyhalothrin is not expected to be prevalent in surface waters. If released into water, cyhalothrin is expected to adsorb to suspended solids and sediment based upon the high estimated K_{oc} value. In the water, cyhalothrin will be removed by hydrolysis, photodegradation and biological transformation. Volatilisation from water surfaces may be an important fate process based upon this compound's estimated Henry's Law constant. Estimated volatilisation half-lives for a model river and model lake are 35 and 400 days, respectively. However, volatilisation from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column. The volatilisation half-life from a model pond is about 630 years when adsorption is considered (SRC in HSDB).
If released to air, cyhalothrin is expected to exist solely in the particulate phase (Bidleman 1988 and Tomlin 1997 in HSDB). Particulate cyhalothrin will be removed from the atmosphere by wet and dry deposition (SRC).

Vulnerable use and vulnerable groups
Due to the use in public health, cyhalothrin could impose a risk in homes and at workplaces where the compound is used to control pests. Workers involved in manufacturing and handling of cyhalothrin are expected to be the most vulnerable groups. Cyhalothrin is known to cause an effect described as “subjective facial sensation (SFS) which most likely arises from direct facial contact with the chemical. Taking the appropriate precautions when handling the substance, this risk of SFS can be minimised.

Environmental concentrations
Actual levels of cyhalothrin in the environment are not available, but considering the low use pattern and low application rates, environmental concentrations are expected to be low (ECH).

Conclusion
Cyhalothrin is a pesticide used for the control of pests in both residential, industrial and agricultural areas. The workers involved in the production of cyhalothrin and in spraying have the highest risk of exposure, but the general population is also exposed through food with residual cyhalothrin. It is assumed that the dietary exposure of the general population will not exceed the ADI of 0.02 mg/kg body weight. However, public health use of cyhalotrin against pests of cockroaches, flies and ticks suggests human exposure can not be excluded.
In the environment, cyhalothrin is removed by biological and abiotic degradation processes and is considered to be moderately persistent. Due to the low water solubility and strong sorption of the compound to soil and particulate matter, only limited exposure to soil and aquatic organisms is expected. Combined with the fast metabolisation of the compound in animal systems, the compound is not expected to bioaccumulate in living organisms. Due to its use, emission pattern and moderate persistence, cyhalothrin is categorised with high concern of exposure.

References

EHC, (1990). Environmental health criteria 99, Cyhalothrin, WHO, Geneva.

SRC, (2002). Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

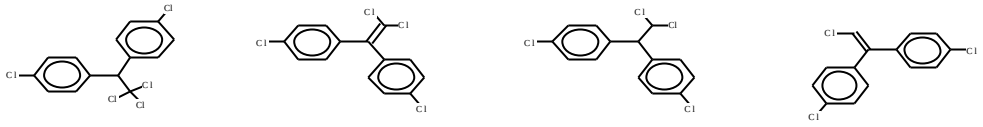
HSDB, (2002). Hazardous Substances Data Bank, a database of the national library of medicine's

TOXNET system, http://toxnet.nlm.nih.gov

DDT (CAS NO 50-29-3) AND DDT METABOLITES

This summary profile includes the DDT derivatives and metabolites o,p-DDT (789-02-6), p,p-DDD (cas no 72-54-8), p,p-DDE (cas no 72-55-9), p,p-DDMU (cas no 1022-22-6), o,p-DDD (cas no 53-19-0), o,p-DDE (cas no 3424-82-6), o,p-DDMU (cas no 14835-94-0), o,p-DDA-glycinat (cas no 65148-83-6), m,p-DDD (cas no 4329-12-8), 5-OH-o,p-DDT (65148-73-4), 5-MeO-o,p-DDT (65148-74-5), 5-MeO-o,p-DDD (65148-75-6), 5-MeO-o,p-DDE (65148-82-5), 4-MeO-o,p-DDT (65148-72-3), 4-MeO-o,p-DDE (65148-81-4), 3-MeO-o,p-DDE (65148-80-3), 3-OH-o,p-DDT (43216-70-2) and 1,1,1-trichloro-2,2-bis(4-chlorophenyl)ethane (2971-22-4)

Chemical characteristics



DDT C14-H9-Cl5
MW = 354.49
CAS 50-29-3

DDD C14-H8-Cl4
MW = 318.03
CAS 72-55-9

DDE C14-H10-Cl4
MW = 320.05
CAS 72-54-8

DDMU C14-H9-Cl3
MW = 283.59
CAS 1022-22-6

Table 1: Physical/chemical properties of DDT and its metabolites

Parameter	p,p-DDT	p,p-DDE	p,p-DDD	p,p-DDMU
Water solubility (mg/L, 25°C)	0.0031-0.0034[3] 0.0055[1]	0.04[1]	0.09[1]	0.305[1]
Vapour pressure (mm Hg, 25°C)	1.60 x 10-7 [1]	6.0 x 10-6[1]	1.35 x 10-6[1]	2.21 x 10-5[1]
log Kow	6.91[1, 3] 7.48[5] 5.44-6.91[3]	5.63 - 5.89[4] 6.51[1]	4.73 - 6.22[4] 6.02[1]	5.50[1]
Henrys law constant (atm m3/mole)	0.98 x 10-5[3,4] 1.53 x 10-5[1]	4.16 x 10-5[1]	6.60 x 10-6[1]	4.89 x 10-5[1]
Koh (cm3/molecule sec)	3.44 x 10-12[1]	7.43 x 10-12[1]	4.34 x 10-12[1]	2.08 x 10-11[1]
Biodegradation	Very slow	Very slow[1]	Very slow	Very slow
BCF (L/kg)	41750[1]	20540[1]	8618[1]	3448[1]
Koc (L/kg)	218776[1] 426580[3,4] 79432 – 1584893[2]	152500[1]	152500[1]	96600[1]

1) in SRC
2) in Gulden, 1998
3) in Fra97
4) in Gre96
5) in EHC83

All isomers of the compound DDT are white, crystalline, tasteless, almost odourless solids.
DDT, DDD and DDE are poorly to very poorly soluble in water (Gulden 1998). DDT is soluble in organic solvents and very soluble in animal fats (EHC83).

The compounds are lipophilic (log Kow 6-7) and known to accumulate in organisms. DDT and its metabolites are very persistent. On the basis of the log Koc (5.63) in combination with the poor solubility the compounds are primarily found in sediment (fra97).

Abiotic degradation
p,p'-DDT is not abiotically degraded in water. p,p'-DDT is dehydrochlorinated to p,'p'-DDE microbially and reduced to dechlorinated p,p'-DDD, converted in many steps to p,p'-DDA and further to p,p'-DDM (dichlorophenylmethane), p,p'-DBH (dichlorobenzohydrol) and p,p'-DBP (dichlorobenzophenone). Additional degradation products of p,p'-DDT are also known (Matsumura, 1985; Subba-Rao and Alexander in Gulden 1998). Biological degradation of p,p'-DDT is very slow. A half-life of 3 - 20 years has been estimated for soil and sediment. DDD and DDE are known to be even more persistent (Gulden, 1998). Humic material represents a major source of adsorptive capacity for DDT; the degree of sorption, however, is strongly connected with the degree of humification. Soil containing large

amounts of humic material may not adsorb DDT as greatly as other soils where humification is more advanced. Wheatley (1965) estimated half-times for the loss of DDT applied to soils. After surface application, 50% of DDT was lost within 16-20 days. The estimated time for the loss of 90% of surface-applied DDT was 1.5 to 2 years. With DDT mixed into the soil, 50% loss occurred in 5 to 8 years, and it was estimated that 90% of applied insecticide would be lost in 25-40 years (EHC83).

DDE may also undergo direct photolysis in the environment since it absorbs light greater than 290 nm. The reported atmospheric half-life in sunlight at 40 deg latitude was calculated to range from 0.9 days in summer to 6.1 days in winter. Particulate-phase DDE will be removed from the atmosphere by wet and dry deposition. If released to soil, DDE is expected to have no mobility based upon measured Koc values of 26,300 and 75,860. Volatilisation from moist soil surfaces is expected to be an important fate process based upon a Henry's Law constant of 4.16X10-5 atm-cu m/mole; however, adsorption may attenuate this process. DDE is not expected to volatilise from dry soil surfaces based on its vapour pressure. p,p'-DDE was less than 1% mineralised in flooded soils during a 42 day incubation period, suggesting biodegradation in soil surfaces is very slow. If released into water, DDE is expected to adsorb to suspended solids and sediment in water based upon the Koc data. Volatilisation from water surfaces is expected to be an important fate process based upon this compound's Henry's Law constant. However, volatilisation from water surfaces is expected to be severely attenuated by adsorption to suspended solids and sediment in the water column.

Estimated volatilisation half-lives for a model river and model lake are 2 and 18 days, respectively, if adsorption is neglected. The volatilisation half-life from a model pond is about 5 years when adsorption is considered. Biodegradation of DDE in water is expected to be very slow. No degradation of DDE exposed to ocean sediments in seawater under aerobic and anaerobic conditions was observed after a 12 month incubation period. The hydrolysis rate of DDE under environmental conditions is very slow, with a reported half-life of 120 years at 27 deg C and pH 3-5. Photolysis in sunlit surface water is expected to be an important fate process. Half-lives of 15 and 26 hours were reported for photolysis of DDE in water solutions irradiated at 310-410 nm. BCF values of 27,500 to 81,000 measured in fish, suggest that bioconcentration in aquatic organisms is very high. Although DDT is no longer registered for agricultural use in the US, the general population continues to be exposed to DDE due to its long persistence time. Although concentrations are continuously decreasing, monitoring data continues to show levels of DDT, DDD and DDE in environmental media.

Biotic degradation
The biodegradation half-lives in soil are 2- 15.6 years, in air 17.7 to 177 hours, in surface water 7 to 350 days and in ground water 16 to 31.3 years (Howard 91 in fra97).

As is well known, DDT is released into the air by volatilisation from soil surface and/or
adhered to the dust surface. It is considered that DDT is transported by adsorption to particles in the air (Japan, 1997). DDT is directly transferred into river system by drifting or moved with soil particles or dusts into river by erosion or rainfall. DDT is difficult to be released in water because of strong adsorption with soil particles (Japan). DDT is strongly adsorbed to soil particles. It leaches very poorly in soil (Japan, 1997). DDT is stable under most of the environmental conditions including biological and non-biological factors. One of the metabolites, DDE, is similarly or even more stable (Japan, 1997).

Microorganisms, plants, insects and birds produce many of the DDT metabolites found in mammals and humans (Smith, 1991 in Gulden, 1998). Species differences have been found. In mammals DDT is either first reduced to dechlorinated DDD, and finally converted to DDA or metabolised to DDE through the removal of HCI, this holds true primarily for p,p'-DDT. DDE is significantly more stable than DDT and its other metabolites. DDT is primarily excreted as DDA. o,p'-DDT and its metabolites are more rapidly eliminated from mammalians than p,p'-DDT and its metabolites. DDT is not intensively metabolised by fish. The metabolites p,p'-DDE and p,p'-DDD have been found in fish. It is possible, however, that a part of the metabolic activity seen in fish results from microbial activity.

Different organisms metabolise DDT via different pathways. Of the two initial metabolites, DDE is the more persistent, though not all organisms produce DDE from DDT. The alternative route of metabolism, via TDE leads to more rapid elimination (WHO, 1979). Much of the retained DDT and its metabolites are stored in lipid-rich tissues (EHC83). Because there is an annual cycle in lipid storage and utilisation in many organisms, there is also a related annual cyclic pattern in the handling of DDT (EHC83).

Bioconcentration
Because of high lipophilicity and hydrophobicity together with poor metabolism in living organisms, DDT and its stable metabolites are easily bio-accumulated in fat tissues of living organisms (Japan, 1997).

The physico-chemical properties of DDT and its metabolites enable these compounds to be taken up readily by organisms. Organisms can accumulate these chemicals from the surrounding medium and from food. In aquatic organisms, uptake from the water is generally more important, whereas, in terrestrial fauna, food provides the major source (EHC83).
The rates of accumulation into organisms vary with the species, with the duration and concentration of exposure, and with environmental conditions. In general, organisms at higher tropic levels tend to contain more DDT-type compounds than those at lower tropic levels (EHC83).

Experimental (dynamic flow system) bioconcentration factors of DDT in aquatic life (fish, daphnia and algae) are more than 10,000 for fish, 100,000 for daphnia and 5,000 - 60,000 for algae, respectively. Bioconcentration of DDT occurs by indirect incorporation from food or via environmental water (Japan, 1997).

Due to the high lipophilicity and persistence, DDT, DDD and DDE are concentrated in aquatic organisms and accumulate in the food chain. Bioconcentration factors of BCF = 1900 - 330,000 (p,p'-DDT), BCF = 64,000 (p,p'-DDE) and BCF = 2700 – 81,000 (p,p'DDE) have been measured in fish. Because of the differing metabolic stability of DDT isomers and metabolites, DDE, contributes in increasing proportion to the total DDT contamination based on time (after exposure) and increasing level within the food chain (Gulden 1998).

Concentration factors can be misleading with compounds such as DDT when exposure is high. The compound is readily taken up and retained at very low concentrations. At high concentrations, no more material can be taken up because a plateau has been reached. The only meaningful way to assess the capacity of organisms to take up and retain DDT is by looking over a wide range of exposure levels. The low concentration factor quoted in Table 2 for earthworms, for example, reflects the high exposure rather than a low capacity for uptake and retention of DDT, because concentration factors are simple ratios between "exposure" and final concentration in the organism (EHC83).

Concentration factors for fish are generally higher than for their invertebrate prey (Table 2). It is now generally agreed that most of the DDT taken into aquatic organisms comes from the water rather than from their food (Moriarty, 1975). Again, the concentration factors can be misleading. Aquatic organisms take in a small proportion of ingested DDT. However, they retain a large proportion of the DDT, which has been absorbed into the body from the food. There has been some controversy in the past over explanations for higher accumulations of DDT at higher tropic levels in aquatic systems. It now seems clear that this is not due primarily to biomagnification up food chains but rather to a tendency for organisms at higher tropic levels to accumulate more DDT directly from the water (EHC83).

Terrestrial organisms do not live in a uniform medium surrounded by a relatively constant concentration of a chemical. Even soil organisms live in a medium with very variable concentrations of DDT or its metabolites at different levels of the soil profile or patchy distribution of the chemical. Some terrestrial organisms could be directly exposed to DDT during application of the insecticide, but most will be exposed to what remains of the DDT after application. Therefore, higher terrestrial organisms will accumulate DDT mostly from their food. The data in Table 2 are taken from controlled laboratory investigations. There is ample evidence from the field that DDT does accumulate in many organisms in different media. There is similarly evidence that the residues of DDT or its metabolites persist in organisms for long periods after exposure has ceased (EHC83).

Table 2. Bioaccumulation of DDT[a] (EHC83)

Organism	Duration	Exposure (µg/litre)	Bioconcentration factor	Reference
Mosquito fish (Gambusia affinis)	3 days	2.0	344 [d]	Metcalf et al. (1973)
	3 days	0.9	217 [d]	
Rainbow trout (Salmo gairdneri)	12 weeks	0.176	21 363 [d]	Reinert et al. (1974)
	12 weeks	0.137	43 158 [d]	
	12 weeks	0.133	51 355 [d]	
Brook trout (Salvelinus fontinalis)	120 days	3 mg /kg	0.64 [d] diet	Macek & Korn (1970)
	120 days	0.003	8533 [d]	
Pinfish (Lagodon rhomboides)	14 days	0.1	40 000 [d]	Hansen & Wilson (1970)

	14 days	1.0	11 020 [d]	
Atlantic croaker (Micropogon undulatus)	14 days	0.1	12 500 [d]	Hansen & Wilson (1970)
	14 days	1.0	12 170 [d]	

Organism	Duration	Exposure (µg/litre)	Bioconcentration factor	Reference
Fathead minnow (Pimephales promelas)	14 days	45.6 mg/kg	1.17 [d]	Jarvinen et al.
	14 days	0.5	85 400 [d]	(1977)
	14 days	2.0	69 100 [d]	Jarvinen et al.
	112 days	45.6 mg/kg	1.33 [d]	(1977)
	112 days	0.5	93 200 [d]	Jarvinen et al.
	112 days	2.0	154 100 [d]	(1977)
Tilapia (Tilapia mossambica)	31 days	1.0	6800	Reinbold et al.
	31 days	10	10 600	(1971)
Green sunfish (Lepomis cyanellus)	31 days	1.0	3900	Reinbold et al. (1971)
	31 days	10	4020	
	15 days	0.1-0.3	17 500 [d]	Sanborn et al. (1975)
Chicken eggs fat	8 weeks	0.1	1.87 [d]	Foster et al.
	8 weeks	0.1	5.8 [d]	(1972)
Broiler hen fat	6 weeks	1.0	10.3 [d]	Kan et al. (1978)
White pelican (Pelecanus erythrorhynchos)	10 weeks	72	11.9 [d]	Greichus et al. (1975)
Double-crested cormorant (Phalacrocorax a. auritus)	9 weeks	0.95	236.3 [d]	Greichus & Hannon (1973)
American kestrel (Falco sparverius)	11-16 months	2.8	103.9	Wiemeyer (1972)
Mule deere muscle (Odocoileus heminonus) oral	30 days	5 mg/day	122.8 ug /kg [d]	Watson et al. (1975)

a Unless specified otherwise, bioconcentration factors are based on whole body (WB) measurements.

d Calculated on a wet weight basis .

Albone et al. (1972) investigated the capacity of river sediments, from the Severn Estuary, United Kingdom, to degrade DDT. p,p' -DDT (14C-labelled) was applied to sediments either in situ on the mud flats or in the laboratory. Sediment movement in the area of the in situ study was sufficiently small to neither bury nor expose the incubation tubes set into the mud. Incubation in situ over 46 days led to very little metabolism of DDT in the sediments. Some p,p' -TDE was produced, but the ratio of DDT to TDE was 13 : 1 and 48 : 1 in two replicate experiments. There was no production of extractable polar products; metabolism beyond TDE did not occur (EHC83). Incubation of the same sediments in the laboratory, over 21 days, led to much greater metabolism (ratios of 1 : 1.1 and 1 : 3.3, DDT to TDE, in replicate incubations) and the production of some unidentified, further breakdown products. Investigation of the microbial population of the sediment showed that some of the organisms were capable of degrading DDT; little metabolism appeared to take place in situ (EHC83).

The uptake and accumulation of DDT from the culture medium by microorganisms has been reviewed by Lal & Saxena (1982). All of the microorganisms studied showed some capacity to take up DDT from their growth medium, but the relative amount taken up varied greatly from species to species. Many species took up more than 90% of the DDT when exposed to concentrations ranging from 1 to 1000 µg/litre, whereas a few species took in only 0.5% of the available DDT. The concentration factors for DDT were variable but always high (EHC83).

Concentration factors are also variable in aquatic invertebrates. In all cases there is considerable uptake and retention of the DDT, though often as DDE or other metabolites rather than as the parent compound. The main point of interest is the ability of aquatic organisms to take up large amounts of the compound, over time, from water where DDT is present at very low concentrations, and to retain it (EHC83).

Eberhardt et al. (1971) applied radioactively labelled DDT, at a rate of 220 g/ha, to a freshwater marsh and followed the distribution of the compound and its metabolites. Concentration factors in ten species of plants varied between 5500 and 84 000. Various invertebrates showed high concentration factors: ramshorn snail (Planorbidae), 4700; backswimmer (Notonectidae), 10 000; crayfish (Orconectes immunis), 22 000; bloodworm (Tendipes), 25 000; and red leech (Erpobdella punctata), 47 000. Reporting earlier on the same study, over 15 months, Meeks (1968) showed that plants and invertebrates accumulated DDT to a maximum mainly within the first week after treatment, whereas

vertebrates required longer to attain maximum residues. Residues of DDT in the surface water and suspended particles had fallen below detectable levels within 1 month. Residues in sediments stabilised at about 0.3 mg/kg after 9 months (EHC83).

A rise in temperature results in increased uptake of DDT by fish (Reinert et al., 1974 in EHC83). Increasing salinity decreases DDT uptake significantly, but has no effect on the uptake of DDE or TDE by fish (Murphy, 1970 in EHC83).
Birds with the highest residues of DDT or its metabolites were either terrestrial predators feeding on other birds or aquatic predators feeding on fish (EHC83).

According to a model of gas/particle partitioning of semivolatile organic compounds in the atmosphere(1), DDT, which has a vapour pressure of 1.6X10-7 mm Hg at 25 deg C(2), will exist in both the vapour and particulate phases in the ambient atmosphere. Vapour-phase DDT is degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 5 days, calculated from its estimated rate constant of 3.4X10-12 cu cm/molecule-sec at 25 deg C determined from a structure estimation method. Particulate-phase DDT may be removed from the air by wet and dry deposition.

There are marked geographical differences throughout the United Kingdom, related to usage patterns of DDT (Cooke et al., 1982 in EHC83), and also marked seasonal changes in residues. These seasonal changes appear to relate more to physiological changes in body composition, which occur with climatic and breeding seasons, than to the environmental availability of pollutants.

Some, though very little, DDT was detected in black bears by Benson et al. (1974). There was no evidence that the area had been directly sprayed with DDT (EHC83).

Use, Exposure and emissions
A typical example of technical DDT had the following constituents: p,p' -DDT, 77.1%; o,p' -DDT, 14.9%; p,p' -TDE, 0.3%; o,p' -TDE, 0.1%; p,p' -DDE, 4%; o,p' -DDE, 0.1%; and unidentified products, 3.5% (EHC83).

In the production process o,p'-DDT is also formed as a by-product (15-20%) and in addition trace amounts of tris(4-chlorophenyl)methane (TCPM) is formed. TCPM-OH has been suggested to be a metabolite of TCPM (Buser 1995 in SEPA 1998). TCPM and TCPM-OH are both persistent and bioaccumulative as indicated by high concentrations of these compounds in biota at higher tropic levels (SEPA 1998).

DDT has been commercially produced since the early 1940s and was used intensively world-wide as an agricultural insecticide and in the effective fight against insects carrying e.g. malaria, typhus, yellow fever and sleeping sickness. The production and use of DDT was forbidden in most industrial countries in the late '60s (FRG: 1972). DDT is, however, still produced and used in tropical countries, in particular to combat malaria. DDT was used in the German Democratic Republic (GDR) until the late 1980s. It is estimated that by the end of the 1960s approximately two million tons of DDT were distributed over large areas. With the distribution of technical DDT, primarily p,p'-DDT (up to > 70%) and o,p'-DDT (up to > 20%), and in small quantities the corresponding DDD and DDE isomers were released into the environment (Gulden 1998). DDT was produced in 60000 tonnes/year in 1965 (EHC83).

DDT is forbidden in the EU. In Japan, after the registration as a pesticide in 1948, DDT had been used and sold as insecticide for agricultural and household use and as termite control agent. However, in 1971 it was prohibited to be used as insecticide for agricultural and household use in Japan because of long-term persistency in the environment. It was specified as Class I Chemical by Law concerning Examination and Regulation of Manufacture, etc. of Chemical Substance in 1981 and stopped manufacture, sale and use as termite control and all other uses (Japan, 1997). DDT has also been banned in Sweden for more than 20 years (SEPA 1998).
DDT is on Annex 1 and 2 of the EU council regulation 2455/92 which prohibits all plant protection products containing DDT as an active ingredient, to be used or placed on the market. DDT is also on the PIC list and in EC directives 76/769/EC and 79/117/EC. It is still permitted in Bhutan, Bolivia, Brazil, Ethiopia, Guinea, India, Kenya, Madagascar, Mexico, Nepal, the Philippines, Sudan and Slovenia (ISPRA, 2000).

The only information on stockpiles of DDT in the UN-ECE region is included below:

During negotiations for the POPs Protocol, the Russian Federation was the only UN-ECE country that requested that it be allowed to use DDT to control encephalitis. This continued need has not been

reconfirmed. In their response to the 2001 UN-ECE Questionnaire, Georgia stated that the use of DDT was banned. Georgia, however, reported that it is aware of, and attempting to control, the unsanctioned use of DDT in coastal areas, military zones, and in certain facilities in Georgia.

Table 3: Information on stockpiles of DDT in the UN-ECE region:

Country	Tons of DDT	Notes/Reference
Estonia	5.8	Response to July 2001 questionnaire
Latvia	172	Included in Estonian response to July 2001 questionnaire
Lithuania	80	Included in Estonian response to July 2001 questionnaire
Moldova	0.3 & 654.1	Response to July 2001 questionnaire reported the following: Inventory in year 2000, DDT stocks in stockpiles contain 0.300 tons. All forms of DDT in Vulcanesti pesticide dump site are 654.1 tons, including technical DDT - 107.5 tons; DDT-5.5% - 187.7 tons; DDT 30% - 318.9 tons; DDT-75% - 22.6 tons; DDT 15% - 3.1 tons; and DDT Paste - 14.3 tons.
Poland	400	Response to 2000 questionnaire

Vulnerable use and vulnerable groups

Because of their lack of degradation, their resulting widespread persistence in the environment, their high acute toxicity to organisms at the base of food chains, and their high potential for bioaccumulation, DDT and its metabolites should be regarded as a major hazard to the environment. DDT should not be used when an alternative insecticide is available (EHC83).

DDT still presents a risk to vulnerable groups.

Oral ingestion of food is the primary source of exposure for the general population. Ingestion of contaminated drinking water, inhalation of contaminated air and dermal contact with contaminated soil surfaces are also possible routes of human exposure.

Environmental concentrations

2,2-Bis(p-chlorophenyl)-1,1-dichloroethene (DDE) is an impurity in the formerly manufactured and used pesticide 2,2-bis(p-chlorophenyl)-1,1,1-trichloroethane (DDT), as well as a degradation product of DDT and therefore has been released to the environment as a result of the use of DDT as an insecticide. If released to air, a vapour pressure of 6X10-6 mm Hg at 25 deg C indicates DDE will exist in both the vapour and particulate phases in the ambient atmosphere. Vapour-phase DDE will be degraded in the atmosphere by reaction with photochemically-produced hydroxyl radicals; the half-life for this reaction in air is estimated to be 2 days.

Concentrations of DDT, DDD, and DDE in surface water are below the detection limit of 0.001 µg/l in 1991 and 1996 (fra97).

In the Fraunhofer report DDT (50-29-3) is measured in water with a median concentration of 0.0050 µg/l (mean 0.0057 µg/l) based on 1427 data from 47 stations (1221 data were above the determination limit). In sediment DDT (50-29-3) is measured with a median concentration of 5.5 µg/l (mean 150.64 µg/l) based on 1065 data from 57 stations (759 data were above the determination limit) (Fraunhofer, 1999).

DDT and its metabolites DDD and DDE were not found above detection limits of 10-50 ng/l in rivers in Germany (incl. Rhein, Neckar, Main, Donau, Inn, Satzach, Schmilka) in Baden-Württemberg (1992), Bayern (1994), Mecklenburg-Vorpommern (1993) and Sachsen (1994) (Gulden 1998).
In the Elbe River in Germany above (Zollenspieker) and below (Seemannshöft) the Hamburg harbour, 1993 measurements revealed no o,p'-DDE (8-10 water samples) (DL = 1 ng/1), o,p'-DDT only in 50% of the samples from Zollenspieker and o,p'-DDD in the majority of the samples. p,p'-DDT was found in almost every water sample, p,p'-DDD and p,p'-DDE in almost every sample above, but rarely below, the Hamburg harbor (Gulden, 1998).

In the German Elbe River from Schnackenburg (1991- 1993) and in the Weser River (1994) DDT and its metabolites rarely were found in detectable concentrations from max. 0.4 - 6 ng/l. Higher concentrations were measured in single cases in Thüringen (1995) and Sachsen-Anhalt (1995).

With a detection limit of 10 ng/l, the following measurements were made in Nordrhein-Westfahlen at 7 measuring stations (incl. Rhein , Sieg, Wupper, Ruhr, Lippe) some samples contained p,p'- and o,p'-DDT, -DDD and -DDE in typical concentrations of < 100 ng/l, in rare cases at higher concentrations (Wupper/Leverkusen-Rheindorf: p,p'-DDT up to 280 ng/l and o,p'-DDE up to 300 ng/1; Lippe/Wesel: o,p'-DDT up to 220 ng/l) (Gulden, 1998).

In 1994 in Brandenburg in Germany, at 5 stations samples were taken monthly (Schwarze Elster, Spree, Havel). P,p'-DDD and p,p'-DDE were found only in rare cases or just over the detection limit of 10 ng/l. In the majority of the cases, p,p'-DDT was not found in water measurable concentrations. Between October and November, however, in water from the Schwarze Elster at Liebenwerda and from the Spree at Cottbus, unusually high p,p'-DDT concentrations were found, 700-900 ng/l, and in November in water from the Havel at Potsdam even 1400 ng/l p,p'-DDT was measured (Gulden, 1998).

In 1994 no measurable concentrations (detection limit = 5 µg/kgDW) of DDT or its breakdown products were recorded from two measuring stations on the Rhine in Nordrhein-Westfahlen in Germany (Gulden, 1998).

In 1995 suspended particles from various rivers in Hessen were examined (20 measuring stations, detection limit = 1 - 5 µg/kg). o,p'-DDT was not detected at any station, in about 30% of cases o,p'-DDT at a max. of 4 µg/kg and o,p'-DDD with a max. of 85 µg/kg. p,p'-DDT (max. 88 µg/kg) was measured in 45% of the samples, p,p'-DDE (max. 68 µg/kg) and p,p'-DDD (max. 195 µg/kg) in about 95 to 75 % of the samples. The highest contamination was measured in the Schwarzbach River flowing into the Rhine (Gulden, 1998).

Samples taken from the ARGE Elbe from 8 measuring stations distributed along the Elbe River from Schmilka to Cuxhafen revealed the highest contamination near Magdeburg. The suspense particle concentration of DDT and its metabolites decreased strongly along the Elbe to Cuxhafen. p,p'-DDT (max. 980 µg/kg) was found at higher concentrations than o,p'-DDT (max. 503 µg/kg) at all measuring stations. In the lower Elbe, o,p'-DDD (max. 242 mg/kg) was found at higher concentrations than o,p'-DDT. In general contamination with p,p'-DDT was greatest, and among its breakdown products the concentration of p,p'-DDD (max. 443 µg/kg) was higher than that of p,p'-DDE (max. 90 µg/kg) (Gulden, 1998).

In measurements made by the IKSR and DKRR at 10 measuring stations distributed along the Rhein from Village-Neuf, to Kampen, the highest contamination was at Koblenz. The maximum values were significantly lower than measured in the Elbe near Magdeburg. In general p,p'-DDT was found at higher concentrations than o,p-DDT and p,p'-DDD and p,p'-DDE in approximately equal concentrations but significantly lower concentrations than p,p'-DDT (Gulden, 1998).

Results from studies on sediments in the Hamburg harbor (32 measuring stations) were published by Gotz et al. in 1990. p,p'-DDD was found in all samples, p,p'-DDT, p,p'-DDE and o,p'-DDD in almost all samples, and in 50-70% of the cases o,p'-DDT and o,p'-DDE were additionally found. In general p,p'-DDT was found in the highest concentrations, its metabolites (p,p'-DDD, p,p'-DDE) and o,p'-DDT in low concentrations. In the majority, DDT, DDD and DDE were measured in concentrations < 100 µg/kg, in individual cases p,p'-DDT, p,p'-DDD and o,p'-DDT in concentrations > 100 µg/kg. Very high concentrations (> 1000 µg/kg) were measured in sediment from the Müggenburger Canal in the vicinity of a former DDT production facility (Gulden, 1998).

In 1992 sediments from numerous rivers (103 measure stations) in Niedersachsen were tested. In the majority of cases, p,p'-DDT or its metabolites were found at concentrations >0.1 µg/kg, o,p'-DDT rarely in detectable concentrations, in 50% of the cases, however, its metabolite o,p'-DDD was found. The highest contamination with DDT and its metabolites (p,p'-DDD > 10 µg/kg) was found in the Weser River (Boffzen, Hajen, Petershagen) and in the Elbe River (Bleckede, Gorleben, Schnackenburg) (Gulden, 1998).

Sediments from the Elbe and its tributaries shortly before their junction with the Elbe, were studied in 1992 and sediments from the most important tributaries in 1994, by the GKSS Geesthacht. The metabolites p,p'-DDE, p,p'-DDD and o,p'-DDD were present in most samples at concentrations > 0.5 mg/kg, p,p'-DDT in about 50% of the cases and o,p'-DDE only in isolated cases, o,p'-DDT was not studied. In the Elbe River, high contamination (> 10 µg/kg) was found with DDT, DDD and DDE in the upper segment (Schmilka, Torgau) near Tangermünde and Lauenburg, the highest contamination (DDD > 100 µg/kg) near Dessau and Breithagen above Magdeburg. Of the tributaries, the Zwickauer Mulde, which flows into the Elbe near Dessau, and the white Elster near Leipzig were most contaminated. In general p,p'-DDE was found at lower concentrations than p,p'-DDD. In two cases (Elbe/Schmitka, Mulde/Trebsen) the concentration of p,p'-DDT was higher than that of its breakdown products DDD and DDE. This suggests an emission of DDT recently (Gulden 1998).

Based on the environmental monitoring data by the Japanese Environmental Agency, DDT and its analogue levels in water in Japan are below detection limit (<0.0003 ppb - <0.0001 ppb). In contrast, they are detected in bottom sediment (0.029 ppm in maximum) (Japan, 1997).

For example, according to the environmental monitoring in 1995 by the Environmental Agency, the level of such compounds in water was: p,p'-DDT 0.00001 ppm; p,p'-DDE 0.00001 ppm; and dieldrin 0.00001 ppm (less than detectable limit in all samples). The residues of DDT were detected in 7 out of 930 samples (30 kinds) of imported agricultural products, namely in pumpkin (detected/tested: 1/42), celery (2/8), wheat (1/27), soy beans (2/33), and immature peas (1/9). The maximum residue was 0.004 ppm as compared with the tolerance of 2 ppm (Japan, 1997).

DDT is very highly accumulative and is accumulated in human fat tissues and mother's milk, and is detected in fat tissues and blood of foetuses and new-borns whose levels are, however, lower than those in mothers. No recent data on human monitoring for DDT residues are found in Japan (Japan, 1997).

Table 4. Occurrence in the environment of DDT

Compartment	Year	Substance	Location	Concentration	Unit	Reference (source)
Water	1992		Rivers and lakes Netherlands	0	µg/l	Gre96 (phernambucq 96 in fra97)
Water	1992		North-sea coast Netherlands	0	µg/l	Gre96 (phernambucq 96 in fra97)
Water	1992		Wadden-sea Netherlands	0	µg/l	Gre96 (phernambucq 96 in fra97)
Water	1991 and 1996		Eijs, Harvss, ljmdn, Lobptn, Schaar in the Netherlands	<0.001d	µg/l	(riza in fra97)
Water		p,p'-DDT		<0.001	µg/l	Mtc in DHC99
Water	1974	p,p'-DDT	Japan	Not detected in 55 samples (dl 2 –100)	Ppt	Japan, 1997
Water	1994	p,p'-DDT	Japan	Not detected in 17 samples (dl 10)	Ppt	Japan, 1997
Suspended matter	1994	p,p'-DDT	N-Rhein-West in Germany	< 5 (dl)	µg/kg	Gulden, 1998
Suspended matter	1995	p,p'-DDT	Hessen Germany	<1 - 88	µg/kg	Gulden, 1998
Suspended matter	1993	p,p'-DDT	Elbe Germany	<0.1 - 980	µg/kg	Gulden, 1998
Suspended matter	1994	p,p'-DDT	Rhine-IKSR Germany	<1 – 96	µg/kg	Gulden, 1998
Suspended matter	1994	p,p'-DDT	Rhine-DKRR, Germany	<2 -96	µg/kg	Gulden, 1998
Sediment	1974	p,p'-DDT	Japan	0.8-7.3	Ppb	Japan, 1997
Sediment	1994	p,p'-DDT	Japan	0.082-20	Ppb	Japan, 1997
Wildlife biota	1995		Mussels ESD	0.7 av	µg/kg ww	RIKZ in fra97
Wildlife biota	-		Cod liver	8 (min) 47 (max)	µg/kg	De boer, 95 in fra97
Wildlife biota	1995		Mussels ESD	53 av	µg/kg fat	RIKZ in fra97
Wildlife biota	1996		Mussels ESD	0.1 av	µg/kg ww	RIKZ in fra97
Wildlife biota	1996		Mussels ESD	8 av	µg/kg fat	RIKZ in fra97
Wildlife biota	1995		Mussels WRS	0.3 av	µg/kg ww	RIKZ in fra97

Compartment	Year	Substance	Location	Concentration	Unit	Reference (source)
Wildlife biota	1995		Mussels WRS	17 av	µg/kg fat	RIKZ in fra97
Wildlife biota	1996		Mussels WRS	0.4 av	µg/kg ww	RIKZ in fra97
Wildlife biota	1996		Mussels WRS	25 av	µg/kg fat	RIKZ in fra97
Wildlife biota		p,p'-DDT	Molluscs, fish	<10	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDT	Birds, cormorant eggs	<10-9180	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDT	Birds, cormorant eggs	<0.2-171	µg/kg ww	IVM in DHC99
Wildlife biota		o,p'-DDT	Molluscs, fish	<10	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDT	Birds, cormorant eggs	<10-4840	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDT	Birds, cormorant eggs	<0.2-282	µg/kg ww	IVM in DHC99
Wildlife biota		o,p'-DDE	Molluscs	47-132	µg/kg fat	IVM in DHC99
Wildlife biota		o,p'-DDE	Molluscs	0-300	µg/kg fat	MTC in DHC99
Wildlife biota		o,p'-DDE	Fish	<10-600	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDE	Birds, cormorant eggs	6650-130000	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDE	Birds, cormorant eggs	388-4460	µg/kg ww	IVM93 in DHC99
Wildlife biota		pp'-DDD	Molluscs	40-160	µg/kg fat	MTC in DHC99
Wildlife biota		pp'-DDD	Molluscs	<10	µg/kg fat	IVM in DHC99
Wildlife biota		o,p'-DDD	fish	<10	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDD	Birds, cormorant eggs	<10-500	µg/kg fat	IVM in DHC99
Wildlife biota		p,p'-DDD	Birds, cormorant eggs	<0.2-29	µg/kg ww	IVM93 in DHC99
Wildlife biota		SDDT*	Baltic herring Sweden	4250	ppb lw (lipid wt)	Jansson et al 1993 in sepa98
Wildlife biota		p,p'-DDE	Fin whales (Balaenoptera physalus)	260	ppt lw	Aquilar and Borrell 1994 in sepa98
Wildlife biota		o,p'-DDT	Fin whales (Balaenoptera physalus)	390	ppt lw	Aquilar and Borrell 1994 in sepa98
Wildlife biota		o,p'-DDT	Brain of Bald eagles in lake superior	0.05 and 0.18	ppm ww	Kozie and Anderson 1991 in sepa98
Wildlife biota		p,p'-DDE	Brain of Bald eagles in lake superior	1.5 and 16	ppm ww	Kozie and Anderson 1991 insepa98

Compartment	Year	Substance	Location	Concentration	Unit	Reference (source)
Wildlife biota		sDDT*	Ringed seal blubber	230	ppm lw	Jansson 1993 in sepa98
Wildlife biota	1974	p,p'-DDT	Fish, Japan	0.9-1.3	ppb	Japan, 1997
Wildlife biota	1994	p,p'-DDT	Fish, Japan	1-50	ppb	Japan, 1997
Wildlife biota	1994	p,p'-DDT	Shell-fish, Japan	Not detected in 30 samples (dl 1 ppb)	ppb	Japan, 1997
Wildlife biota	1974	p,p'-DDT	Birds, Japan	1 (dl) detected in 5/5 samples	ppb	Japan, 1997
Humans		DDE*	Mother milk in Sweden	251**	ppb lw	Lundgren and Noreen 1998 in sepa98
Humans			Mother milk in Mexico	14000 (mean value) (500-162000)	ppb lw	Waliszewski 1995 in sepa98
Sediment	1974	p,p'-DDT	Japan	0.8-7.3	ppb	Japan, 1997

d.l= detection limit
* sDDT= sum of DDT, DDE and DDD.
Lw= lipid weight
** declined from 3200 ppb lw sDDT in 1972 to 250 ppb lw sDDT in 1992.

In the European COMMPS program European environmental concentration of DDT and its metabolites was determined in water and water sediment:

Table 4: Occurrence of DDT and its metabolites in the European environment

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
Water								
53-19-0	o,p -DDD	0.0218	0.0013	0.0062	0.0090	4	87	47
72-54-8	p,p -DDD	0.0483	0.0019	0.0089	0.0161	7	121	48
72-55-9	p,p-DDE	0.0443	0.0031	0.0125	0.0108	11	125	38
789-02-6	o,p-DDT	0.0036	0.0006	0.0012	0.0012	5	36	11
50-29-3	p,p-DDT	0.0066	0.0050	0.0057	0.0068	47	1427	1221
Sediment								
53-19-0	o,p -DDD	36.61	6.71	25.76	38.81	52	819	527
72-54-8	p,p -DDD	165.86	7.50	55.52	100.93	55	924	794
72-55-9	p,p-DDE	23.15	4.21	10.62	12.15	72	1284	1016
3424-82-6	o,p-DDE	6800.00	4.23	1625.09	2219.8	25	183	133
789-02-6	o,p-DDT	93.80	6.77	108.35	391.94	30	590	355
50-29-3	p,p-DDT	145.55	5.50	150.64	727.63	57	1065	759

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

Conclusion
DDT is a insecticide used against malaria. Although it is forbidden in the EU, the USA and Japan, it is still used in some countries. Because it is very persistent, bioaccumulative and can be redistributed as a consequence of long range air transport it is still found in the environment. Hence, there still is a high concern for exposure.

References
DHC99: Dutch Health Council. Endocrine-disrupters in the Netherlands (1999/07)

EHC83: WHO, 1989, Environmental Health Criteria 83, DDT and its Derivatives- Environmental aspects, IPCS series.

Fra97: Franse & de Voogt, 1997 Oestrogene verbindingen in het Nederlands milieu, MTC report.

Fraunhofer-Institute, 1999. Revised Proposal for a List of Priority Substances in the Context of the Water Framework Directive (COMMPS Procedure). Declaration ref.: 98/788/3040/DEB/E1

Gre96: Greve, 1996 (Dutch Health Council)

Gülden, M., et al, (1998), Endocrinically active chemicals and their occurrence in surface waters, UBA-FB 97-068, Research report 102 04 279

ISPRA, 2000, Exedim database on internet.

Japan, 1997. A Study on Hormone-Like (Hormone-Mimic) Effects of Exogenous Substances, Shortened English Version. Japan Chemical Industry Association. Japan Chemical Industry Ecology-Toxicology and Information Center.

SEPA, 1998. Olsson, P-E, et al, 1998, Endocrine disruption chemicals, Swedish Environment Protection Agency, report no. 4859.

DELTAMETHRIN (CAS NO 52918-63-5)

Deltamethrin, chemical name ; (1R,3R)-3-(2,2-dibromoethenyl)-2,2-dimethylcyclopropane carboxylic acid (S)-alpha-cyano-3-phenoxybenzyl ester, belonging to the group of pyrethroid pesticides
Trade names include Othrin, Butoflin, Crackdown, Striker, Butox, Decis, Decamethrin, Esbecythrin; FMC 45498, NRDC 161 and RU-22974;

Chemical characteristics

Molecular formula deltamethrin: C22-H19-Br2-N1-O3

MW = 505.21

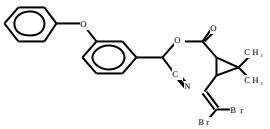


Table 1: Physical/chemical properties of deltamethrin

Parameter	Deltamethrin
Water solubility (mg/L, 25°C)	0.0002 (SRC) 0.002 (EHC 97 1990)
Vapour pressure (mm Hg, 25°C)	9.3 x 10-11 (SRC) $2{\cdot}10^{-6}$ Pa (EHC 97 1990)
log Kow	6.2 (SRC)
Henrys law constant (atm m3/mole)	3.09 x 10-7 (SRC)
Koh (cm3/molecule sec)	2.35 x 10-11 (SRC)
Biodegradation	Moderate-slow
BCF (L/kg)	248-907 (Muir 1985 in HSDB) 265.5 (SRC)
Koc (L/kg)	108000 (SRC) 460000-1630000 L/kg (Tomlin 1994)

Abiotic degradation

Photolysis seems to be an important process in the degradation of deltamethrin in water. Photolysis half lives of 1 to 5 days have been measured in distilled and natural waters (Maguire 1990 in HSDB). Hydrolysis, at least at low and neutral pH, does not seem to be important (Bowman 1987 in EHC 97 1990). At pH=7 and pH=8, hydrolysis half lives of 36 and 3.6 years, respectively, have been estimated (Mill 1987 in HSDB). At pH=9, a DT50 of 2.5 d has been measured (Tomlin1994).

Biotic Degradation

Deltamethrin is degraded biologically in soil and soil half lives of 5-15 weeks have been measured in a wide range of soils. Experiments have shown that biotic processes are the main mechanism in the degradation of deltamethrin in soil (HSDB). Activated sludge was used to degrade deltamethrin and 63.4 % was degraded after 9 hours (Cole 1982 in HSDB).

Bioconcentration

Experiments have shown lower bioconcentration factors than could be predicted from log Kow. This may be due to fast metabolism and reduced bioavailability (EHC 97 1990). BCF for fathead minnow of 248-907 have been measured after 24 hours (Muir 1985 in HSDB).

Use, exposure and emissions

Deltamethrin is used as a pesticide for protection of cotton, fruits and vegetables, cereals, corn and soybean. It is also used to protect stored commodities, in forestry, in public health (e.g. Chagas disease control in South America and malaria) and in animal facilities and against cattle infestation (EHC 97 1990).

Release to the environment

Release to the environment is an intended result of the use of deltamethrin as a pesticide. Deltamethrin may also be released from the production site.

Summary of environmental fate

After emission to water, deltamethrin is expected to sorb very strongly to suspended particles and sediments. Volatilisation from the water surface is, although attenuated by sorption, expected to be important. In a model river, volatilisation half-lives were estimated at 30 hours (SRC in HSDB), but volatilisation from surface micro-layer may be faster (HSDB). Besides volatilisation, deltamethrin will be removed from the water by photolytic and biological degradation and in alkaline waters, hydrolysis.

After application to soil, deltamethrin is expected mainly to be immobilised at the surface due to strong sorption. Here it will be degraded by microorganisms and sunlight. Evaporation of deltamethrin is expected to be very low from dry soil surface but higher from moist soil. Half-lives of 11 to 46 days in soil have been measured (Hill 1983 in HSDB). Long half lives have been measured at low temperatures (10°C) (EHC 97 1990).

If released to air, deltamethrin is expected to be found solely in the particulate phase, which will be removed from the atmosphere by dry and wet deposition (HSDB).

Environmental concentrations
In the Vemmenhog catchment of southern Sweden, sprayed with deltamethrin, average concentrations of 20 µg/kg dry weight was found in the sediment (Kreuger 1999 in HSDB). No further environmental concentrations have been found.

Vulnerable use and vulnerable groups
Workers involved in production of deltamethrin and workers involved in using the pesticide may be more exposed than the general population.

Conclusion
Deltamethrin is used as a pesticide on food crops and cotton. Deltamethrin is expected to be biodegradable and moderately bioaccumulative. Human exposure is expected through consumption of contaminated crops. Even more precarious is the use of deltamethrin in public health (Chagas disease and malaris in South America). As both wildlife and humans are exposed to deltamethrin, it is considered to be of high concern.

References
EHC 97 (1990). Environmental health criteria 97 deltamethrin, WHO, Geneva.

SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

2,4 DICHLOROPHENOXY-BUTYRIC ACID (= 2,4-DB) (CAS NO 94-82-6)

Chemical name: 4-(2,4-dichlorophenoxy)-butyric or butanoic acid
Trade names include Butirex, Butormone, Butyrac, Butoxone, Embuton, Embutax
2,4-DB belongs to the group of chlorophenoxy herbicides.

Chemical Characteristics

Molecular formula 2,4-DB: C10-H10-Cl2-O3

(MW = 249.09)

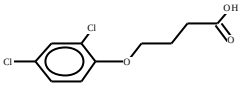


Table 1: Physical/chemical parameters 2,4-DB

Parameter	**2,4-DB**
Water solubility	46 ppb at 25°C (SRC) 0.062 g/l (pH = 5), 4.39 g/l (pH = 7), 454.8 g/l (pH = 9) at 20°C (SANCO)
Vapour pressure (mm Hg, 25°C)	3.5X10-6 (SRC) 7.1X10-7 (SANCO)
log Kow	3.53 (Jafvert in HSDB) pH 5 : log P_{ow}= 2.94 pH 7 : log P_{ow}= 1.35 pH 9 : log P_{ow}= -0.25
Henrys law constant (atm m3/mole)	2.16E-013 cm3/molecule-sec at 25°C (SRC)
Koh (cm3/molecule sec)	2.29 x 10-9 (SRC) 3.14 x 10-10 (SANCO)
Biodegradation	Yes / fast
BCF (L/kg)	70-280 (SRC)
Koc (L/kg)	370 (SRC) 320-407 (SANCO)

White to light brownish crystals, slightly corrosive to iron and a faint phenolic odour. Due to the production process, 2,4-DB may be contaminated with different dioxins. 2,4-DB is readily soluble in acetone, ethanol, and diethyl ether, but only slightly soluble in benzene, toluene, and kerosene (Hartley in HSDB).
2,4-DB has a pKa of 4.95 at 25°C; therefore it will exist predominantly in the dissociated form at pH = 5 and higher. Based upon an estimated vapour pressure of 3.5 x 10-6 mm Hg, 2,4-DB can exist in both the vapour and particulate phase in the ambient atmosphere. It will degrade rapidly in the vapour phase by reaction with photochemically activated hydroxyl radicals. Physical removal of particles by wet or dry deposition will also occur (SRC). The Koc value of 320 – 407 L/kg predicts 2,4-DB to be a compound with a moderate soil-mobility (Jafvert in HSDB). Based on the values of the Henrys law constant and vapour pressure as well as the observed rapid biodegradation, volatilisation from wet (or dry) soil surfaces as well as surfacewaters will not be an important fate process.

Abiotic degradation
When heated to decomposition it emits toxic fumes of hydrogen chloride (Sax in HSDB). Since phenoxyalkanoic acids have ultraviolet absorption maxima in water between 280 and 290 nm, there is a potential for direct photolysis in sunlight (Smith in HSDB). When released to the atmosphere, vapour phase 2,4-DB will rapidly degrade through photolysis, estimated photolysis half-lives for different environmental compartments are depicted in the table below (SANCO).

Table 2: 2,4-DB Half-lives in different environmental compartments

Compartment	**Abiotic TD50 (photodegradation)**	**Biotic TD50**	
		2,4-DB	**2,4-D**
Atmosphere	9-24 hours	-	-
Water		12.2-12.6 days*	**
pH = 5	5.1 days		
pH = 7	17.2 days		
pH = 9	6.9 days		
Soil	33.5 days	1-4 days	2.3-17.1 days

* mean value of different field studies under different pH conditions
** not detected

2,4-DB has no functional groups susceptible to hydrolysis; distilled water solutions and field studies showed no degradation during 50-day stability experiments (SANCO, SRC).

Biotic Degradation
In released to soil or water, microbial degradation of the herbicide 2,4-DB will be the major environmental fate process. Microbial degradation occurs through beta-oxidation mechanisms that yield (2,4-dichlorophenoxy)acetic acid (2,4-D) (Gutenmann in HSDB).
Under aerobic soil conditions 2,4-DB is rapidly degraded by soil organisms (DT50 = 1-4 days), at day 118 almost 50% of the applied 2,4-DB was completely mineralised to CO2 (SANCO). In anaerobic soils degradation takes place at lot slower, soil TD50 values can go up to around 70 days.
If released to water, 2,4-DB divides itself between the water (65%) and sediment phase (35%). The metabolite 2,4-D however could solely be detected in the sediment. Although microbial degradation is suspected to be most important degradation process, exposure to sunlight (abiotic degradation) may be of significant importance.

Bioconcentration
Based upon BCF values ranging from 70-280 L/kg (SRC) 2,4-DB might accumulate in the environment. Observed high rates of biodegradation, however, indicate that accumulation will be lower than predicted on BCF solely. Rapid biodegradation together with the fact that 2,4-DB is only applied once per season (and not directly to surfacewater) result in a low risk of bioaccumulation. However, estimated Koc values and results from leaching studies indicate that 2,4-DB has moderate mobility in soils. Therefore, leaching to groundwater may occur.

Use, exposure and emissions
2,4-DB is used as a herbicide against broad-leaved weeds, especially in grassland and barley (SANCO). It is applied as an ester that rapidly degrades into 2,4-DB on moist soil or as 2,4-DB sodium salt directly to the terrestrial environment using a tractor mounted boom (WSSA in HSDB).
Exposure to chlorophenoxy herbicides may occur through inhalation, skin contact or ingestion via 2,4-DB treated crops. The predominant route of occupational exposure appears to be absorption of spills or aerosol droplets through skin during production, formulation, application or disposal (IARC in HSDB).

Vulnerable use and vulnerable groups
2,4-DB could present a risk to agricultural workers using the herbicide or working the herbicide treated areas afterwards. Occupational predominantly arises from inhalation or dermal contact and is reported during production, formulation, application or disposal (IARC in HSDB). The general population might be at risk as a consequence of ingestion of contaminated food.
Furthermore, animals that live in the treated area or consume the sprayed crops might also be at risk.

Release to the environment
Release to the environment is an intended result of the use of 2,4-DB as a herbicide against broad-leaved weeds, especially on grassland and barley-fields.

Summary of environmental fate
2,4-DB released to the atmosphere is rapidly cleared through either deposition or photolysis. When emitted to soil it undergoes rapid biodegradation to CO2 via the metabolite 2,4-D. An estimated Koc value indicates moderate mobility and possible leaching to the groundwater compartment. In water, 2,4-DB divides between the water (65%) and sediment (35%) compartment. Again biodegradation takes places rapidly. Volatilisation from either soil, vegetation or surfacewater will be of no significant importance.

Environmental concentrations
Environmental concentrations of 2,4-DB in soil, water, air or organisms are not frequently reported due to rapid biodegradation. The SANCO profile did not contain any monitoring data of 2,4-DB in either of these compartments.

In a total of 454 water samples drawn from the collected river mouths of the Grand Saugeen and Thames rivers in Ontario, Canada between January 1981 and December 1985, 3 samples contained amounts of 2,4-DB up to 2.7 ug/l. During a monitoring programme of several hundred farm wells for pesticides used by farmers in agricultural regions of Ontario, no 2,4-DB was detected in any of the wells at an detection limit of 0.1 ug/l (Frank in HSDB).

As part of the Food and Drug Administration's Market Basket Survey of ready-to-eat foods, 2,4-DB was detected at a level of 0.025 ppm in a dairy product collected from a Los Angeles grocery store;

2,4-DB was classified as a pesticide that was infrequently found in American foods. In a compilation of three federal monitoring programs for fiscal years 1970-1976 (FDA's Market Basket Survey, FDA's Monitoring Program for 33,000 domestic and 18,000 raw agricultural commodities, and USDA's National Residue Program), 2,4-DB was detected in only two vegetable samples (Duggan in HSDB).

Toxicity

Observed toxicities in different species have led to the following Predicted Effect Concentrations (PECs) for 2,4-DB and its metabolite 2,4-D in different environmental compartments after a single application of 1800 g a.s/ha

Table 3: PEC values for 2,4-DB in different environmental compartments (single appl. of 1800 g/ha)

PEC per compartment in	**2,4-DB**	**2,4-D**
Soil	1.8 (mg/kg)	1.6
Sediment	0.021 (mg/kg)	*
Surface water	16.62 (ug/l)	*
Groundwater	< 0.001 (ug/l)	< 0.001 (ug/l)
Air	1.6 x 10-10 9(g/m3)	*

* no information

Conclusion

2,4-DB is a fungicide used as a post-emergency control herbicide. Workers involved in the production or usage of 2,4-DB have the highest risk of exposure, however the general population could also be exposed through consumption of 2,4-DB treated foods. Neither 2,4-DB nor its metabolites accumulate in the environment due to their high rate of biodegradation, therefore there is only medium exposure concern. 2,4-DB or its degraded products are only seldomly detected in the environment. Ecotoxicological risks for birds, aquatic species, algae, sediment dwelling organisms, bees, other arthropod species, earthworms and soil microorganisms are acceptable.

References

HSDB Hazardous Substances Data Bank, a database of the library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

SANCO Document 2001 on 2,4-DB

SRC, Syracuse research corporation PhysProp on-line database, http://esc.syrres.com (October 2002)

DICYCLOHEXYL PHTHALATE (DCHP) (CAS NO 84-61-7)

Dicyclohexyl phthalate, chemical name 1,2-Benzenedicarboxylic acid dicyclohexyl ester, belongs to the group of phthalates.
Trade names include Morflex 150

Chemical characteristics

Molecular Formula DCHP: C20-H26-O4

MW = 330.43

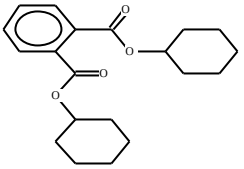


Table 1: Physical/chemical properties of DCHP

Parameter	DCHP
Water solubility (mg/L, 25°C)	0.04 (SRC) 4.0 (Yalkowsky 1992 in HSDB)
Vapour pressure (mm Hg, 25°C)	7.0 x 10-4 (HSDB) 8.68 x 10-7 (SRC)
log Kow	6.2 (SRC)
Henrys law constant (atm m3/mole)	1.0 x 10-7 (SRC)
Koh (cm3/molecule sec)	2.4 x 10-11 (SRC)
Biodegradation	slow
BCF (L/kg)	1.2 x 10+4 (SRC)
Koc (L/kg)	5.6 x 10+4 (SRC)

Abiotic degradation
Hydrolysis half lives in water has been estimated to be 12 and 1.2 years at pH 7and 8 respectively and hydrolysis is thus not expected to be an important degradation process in water (SRC in HSDB). In air, reaction with hydroxyl radicals causes half-lives of about 16 hours (SRC in HSDB).

Biotic Degradation
Dicyclohexyl phthalate at 100 mg/L reached 68.5 % of its theoretical BOD in four weeks when activated sludge was used as inocculum (Sasaki 1978 in HSDB).

Bioconcentration
An estimated BCF of $1.2 \cdot 10^4$ indicates that bioconcentration in aquatic organisms would be high. However, studies have shown that phthalate esters can be metabolised and this would reduce the bioconcentration somewhat (SRC in HSDB).

Use, exposure and emissions
Dicyclohexyl phthalate is used as a plasticiser for nitrocellulose, chlorinated rubber, polyvinyl acetate, polyvinyl chloride and other polymers (Lewis 1993 in HSDB). It is also used in alkyd resins, paper finishes and printers ink (Ullmans in HSDB).

Release to the environment
Dicyclohexyl phthalate may be released to the environment from production sites and from sites where it is used in the production of polymers. Furthermore it may be released from degrading polymers, at landfill sites, and possibly from the incineration of polymers. There may also be some release during the use of dicyclohexyl phthalate containing polymers.

Summary of environmental fate
After emission to water, dicyclohexyl phthalate is expected to sorb to suspended particles and sediments and to volatilise from the water surface. A river and a lake model showed volatilisation half-lives of 1.1 and 14 days respectively (SRC in HSDB). Models have shown that if maximal sorption is taken into account, volatilisation half lives for a 2 meter deep pond increases from 12 days (no sorption) to 75 months (US EPA 1987 in HSDB). Dicyclohexyl phthalate is expected to biodegrade in water and sediment, at least under aerobic conditions.

After emission to soil, dicyclohexyl phthalate is expected not to leach but to remain at the soil surface from where it is expected to evaporate, if the soil is moist. Dicyclohexyl phthalate is not expected to

volatilise from dry soil surfaces (HSDB). Dicyclohexyl phthalate is expected to be degraded by micro-organisms in soil.

After emission to air, dicyclohexyl phthalate is expected to be found in solely the vapour phase where it will be degraded by reactions with hydroxyl radicals (HSDB).

Environmental concentrations
Very few data has been found on the environmental concentration of dicyclohexyl phthalate. The only data reported in HSDB concerns the detection of dicyclohexyl phthalate in groundwater below a landfill site in Oklahoma. Here, dicyclohexyl phthalate was found in a concentration of 0.2 µg/L (Dunlop 1976 in HSDB).

Vulnerable use and vulnerable groups
No vulnerable groups or vulnerable uses have been identified.

Conclusion
Dicyclohexyl phthalate is used as a softener and plasticiser in commonly used plastics. Although dicyclohexyl phthalate is expected to be biodegradable and only transiently bioaccumulative, human exposure is expected through food (leaching from food packages) and for example plastics in baby toys. DCHP is categorised as high exposure concern.

References
HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov

DIETHYL PHTHALATE (DEP) (CAS NO 84-66-2)

Diethyl phtalate, chemical name 1,2-benzenedicarboxylic acid diethyl ester, belongs to the group of phthalates

Chemical characteristics

Molecular formula DEP: C12-H14-O4

MW = 222.24

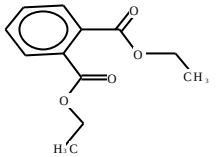


Table 1: Physical/chemical properties of DEP

Parameter	DEP
Water solubility (mg/L, 25°C)	1000 (Yalkowsky 1992 in HSDB) 1080 (SRC)
Vapour pressure (mm Hg, 25°C)	2.1 x 10-3 (Hinckley 1990 in HSDB)
log Kow	2.47 (Hansch 1995 in HSDB)
Henrys law constant (atm m3/mole)	6.1 x 10-7 (SRC)
Koh (cm3/molecule sec)	3.5 x 10-12 (SRC)
Biodegradation	moderate
BCF (L/kg)	14.57 (SRC) 15-117 (Howard 1997)
Koc (L/kg)	126 320-1726 (HSDB)

Abiotic degradation
Hydrolysis half-lives in water has been estimated to be 1058 and 110 days at pH 7and 8 respectively and hydrolysis is thus not expected to be an important degradation process in water (HSDB). In air, reaction with hydroxyl radicals causes half-lives of about 22-110 hours (Howard 1997, SRC in HSDB).

Biotic Degradation
Aerobic degradation half-life in natural fresh water has been estimated to be 3 days while anaerobic half-life was estimated as 28 days (Capel 1995 in HSDB). Degradation observed under anaerobic conditions corresponded to a half-life of 5 days (Parker 1994 in HSDB). Electrolytic respirometer experiments have shown that diethyl phthalate is readily biodegradable under aerobic conditions (Tabak 1992, Tabak 1990, Desai 1990, all in HSDB). This is supported by a large number of experimental findings, referenced in Howard (1997).

Bioconcentration
A measured BCF for sunfish of 117 (Veith in HSDB) and 15-16 for mullet (Shimada 1983 in Howard 1997) indicates that bioconcentration in aquatic organisms would not be high. Studies have shown that phthalate esters can be metabolised and this would reduce the bioconcentration (HSDB).

Use, exposure and emissions
Major uses of diethyl phthalate are in MFR celluid, as solvent for cellulose acetate in MFR varnishes, as fixative for perfumes and for denaturing alcohol. Furthermore, it find use as a wetting agent, in insecticidal sprays, as a camphor substitute, in mosquito repellents, as a dye carrier and as a plasticiser in polystyrene (Merck 1983, Lewis 1993, SRI both in HSDB).

Release to the environment
DEP may be released to the environment from manufacturing and processing plants. It may also be released by incineration of plastic products containing DEP. Furthermore, it may be released directly by the use of DEP-containing insecticidal sprays and mosquito repellent (Howard 1997).

Summary of environmental fate
After emission to water, diethyl phthalate is expected only to volatilise slowly from the water surface. A river and a lake model showed volatilisation half-lives of 89 and 652 days respectively (SRC in HSDB). DEP is expected to sorb moderately to suspended particles and sediment. In the water, DEP is expected to biodegrade under aerobic conditions whereas abiotic degradation is expected to be slow (Howard 1997). Under anaerobic conditions, in sediment, very slow degradation may occur (Howard 1997).

After emission to soil, diethyl phthalate is not expected to evaporate from moist surfaces but volatilisation from dry soil surfaces may be important (Howard 1997). Mobility in the soil is estimated to be low to medium (HSDB). In the soil, DEP is expected to undergo aerobic degradation.

After emission to air, diethyl phthalate is expected to be found primarily in the vapour phase, where it will react with hydroxyl radicals and degrade.

Environmental concentrations
Diethyl phthalate has been found in the Po and Lambro rivers in Italy (Cremonesi 1990 in HSDB). In the Rhine, concentrations of 0.04-0.08 µg/L were measured (Ritsema 1989 in HSDB). In rivers of Manchester UK, an average concentration of 0.5 µg/L was measured (Law 1991 in HSDB). In Mersey River concentrations between 0 and 141 ng/L has been observed (Preston 1989 in HSDB).

In the Irish sea concentrations of 0-430 ng/1000 m^3 were measured (Law 1991 in HSDB).
In the Yssel river in the Netherlands, diethyl phthalate was measured in the sediment in concentrations of 0.2-0.8 mg/kg. In the US, diethyl phthalate was found in Chesapeake bay sediments in concentrations of 42 ng/g (Giam 1984 in HSDB).

In urban air in the US, concentrations of 0.40-0.52 µg/m^3 have been measured (Shields 1987 in HSDB) and in Antwerp, Belgium 2.1 to 5.9 ng/m^3 was found (Cautreels 1977 in Howard 1997). In areas remote from industry, 0.1-0.8 ng/m^3 has been measured (Giam 1984 in HSDB, Cautreels 1977 in Howard 1997)

Vulnerable use and vulnerable groups
Workers involved in the production of DEP and users of insecticidal sprays, insect repellents and perfumes (Howard 1997).

Conclusion
DEP is used in consumer products as for example fixator in perfumes, desinfective soaps and insect repellents, therefore human exposure is inherent on its use. Furthermore, DEP is detected in different environmental compartments including fish. The substance is ranked as high exposure concern.

References
HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

Howard, P.H. (ed.) (1997) Handbook of environmental fate and exposure data for organic chemicals. Lewis publishers

EPICHLORHYDRIN (CAS NO 106-89-8)

Epichlorhydrin, chemical name 3-Chloro-1,2-epoxypropane, belongs to the group of bisphenols.

Chemical characteristics

Molecular formula epichlorhydrin:C3-H5-Cl1-O1

MW = 92.53

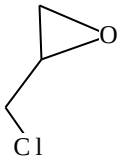


Table 1: Physical/chemical properties of epichlorohydrin

Parameter	Epichlorhydrin
Water solubility (mg/L, 25°C)	6.59 x 10+4 (Yalkowsky 1992 in HSDB)
Vapour pressure (mm Hg, 25°C)	16.4 (Daubert 1989 in HSDB) 4.8-17 hPa (20°C) (IUCLID)
log Kow	0.45 (Deneer 1988 in HSDB)
Henrys law constant (atm m3/mole)	3.0 x 10-5(SRC)
Koh (cm3/molecule sec)	4.4 x 10-13(Atkinson 1989 in HSDB)
Biodegradation	fast
BCF (L/kg)	3.2 (SRC)
Koc (L/kg)	4.49 (SRC) 123 (HSDB)

Abiotic degradation
Hydrolysis half-life in water has been measured to be 8.2 days in distilled water. In simulated seawater, half-life was 5.3 days (Mabey 1978 in HSDB). In very alkaline water (pH 12)and very acidic water (pH 2.5), half lives were 3.3 and 2.6 days respectively. Hydrolysis is thus expected to be an important degradation process in water. In air, reaction with hydroxyl radicals causes half lives of about 36 days (Atkinson 1989 in HSDB). Direct photolysis seems unimportant (IUCLID 2000).

Biotic Degradation
Test results have shown that epichlorohydrin can be rapidly degraded to 3-chloro-1,2-propanediol in pure cultures. Complete degradation however is not assured and experiments show degradations between 3 and 67% of theoretical BOD. Acclimatisation seems to improve degradation (CITI 1992, Neilson 1990, Krijgsheld1986, Matsui 1988 all in HSDB). Shell Nederland reports that 75% was removed after 48 hours in a OECD 301-A “ready biodegradability” study (old version) (IUCLID 2000).

Bioconcentration
An estimated BCF value of 3 indicates that bioconcentration in aquatic organisms would be low (HSDB).

Use, exposure and emissions
In 1984, the major uses of epichlorohydrin were as raw material for unmodified epoxy resins, for a number of glycerol and glycidol derivatives and for epichlorohydrin elastomers (CPS 1984 in HSDB). It is not known whether these still are the principal uses. According to the HSDB, epichlorohydrin is also used as an insect fumigant, as a sporicide, as a solvent for natural and synthetic resins, gums, cellulose esters and ethers, paints, varnishes, nail enamels and lacquers and in cement for celluloid. Epichlorhydrin is also used as a, as a stabiliser in chlorine containing materials, as cross linking agent, as heat stabiliser for plastics and for other applications (HSDB).

Release to the environment
Epichlorhydrin may be released from production sites and from its varied industrial use. A major release may be from the use as a fumigant. Certain polymers may contain unpolymerised epichlorohydrin that may be released to the environment during the use of the polymer e.g. in water purification (IUCLID 2000).

Environmental fate
After emission to water, epichlorohydrin is expected to volatilise from the water surface. A river and a lake model showed volatilisation half lives of 19 hours and 12 days respectively (SRC in HSDB). In the water phase, epichlorohydrin is expected to hydrolyse.

After emission to soil, epichlorohydrin is expected to evaporate from the soil surface whether dry or wet. (HSDB). As the mobility is high, it may also infiltrate into the soil with risk of reaching the groundwater (HSDB). In the soil, epichlorohydrin is expected to hydrolyse and biodegrade.

After emission to air, epichlorohydrin is expected to be found only in the vapour phase, where it will react with hydroxyl radicals and degrade (HSDB). Photolysis is not expected to be important (IUCLID 2000).

Environmental concentrations
Epichlorhydrin have been observed in river sediment near an epichlorohydrin manufacturing plant in the Netherlands (DeLeer 1985 in HSDB). According to the US-EPA concentrations larger than 0.05 mg/m^3 can be detected in air in the vicinity of production and processing plants (IUCLID 2000). No available information on background concentrations have been found.

Vulnerable use and vulnerable groups
The most vulnerable group is workers involved in epoxy fabrication or in fabrication of other polymers with epichlorohydrin.

Conclusion
Although epichlorohydrin is readily biodegradable and not bioaccumulative, human exposure to epichlorohydrin can be expected as a consequence of its use in consumer goods. Therefore, epichlorohydrin has a high exposure concern profile.

References
HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

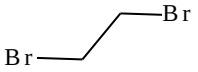
IUCLID (2000) International Uniform Chemical Information Database, European communities, European chemicals bureau

ETHYLENE DIBROMIDE (EDB) (CAS NO 106-93-4)

Ethylene dibromide, chemical name 1,2-dibromoethane, belongs to th egroup of “other pesticides”.

Chemical characteristics

Molecular formula ethylene dibromide: C2-H4-Br2



MW = 187.86

Parameter	Ethylene dibromide
Water solubility (mg/L, 25°C)	4.15 (Howard 1997)
Vapour pressure (mm Hg, 25°C)	11.2 (Call 1957 in Howard 1997)
log Kow	1.96 (Hansch 1995 in Howard 1997)
Henrys law constant (atm m3/mole)	6.67 x 10-4 (Howard 1997)
Koh (cm3/molecule sec)	2.5 x 10-13 (Atkinson 1989 in HSDB)
Biodegradation	Moderate - fast
BCF (L/kg)	1-14.9 (HSDB) 6.45 (SRC)
Koc (L/kg)	14-160 (HSDB) 43.8 (SRC)

Abiotic degradation
Uncatalysed hydrolysis of ethylene dibromide is very slow, but in natural aquifers half-lives of 1-2 months has been observed, probably due to the presence of HS (Barbash 1989 in HSDB). In air, reaction with hydroxyl radicals causes half lives of about 67 days (Howard 1997, Atkinson 1989 in HSDB). Ethylene dibromide is not expected to photolyse in ambient conditions (HSDB).

Biotic Degradation
A review of data showed that ethylene dibromide is readily biodegraded in the environment (Pignatello 1990 in HSDB) and it also degraded readily in primary sewage sludge under both aerobic (within days) and anaerobic conditions (within weeks) (Jex 1985 in HSDB).

Bioconcentration
An estimated BCF of 1-14.9 indicates that bioconcentration in aquatic organisms would be expected to be low (Kawasaki 1980, CITI 1992 both in HSDB).

Use, exposure and emissions
Ethylene dibromide was previously used as a lead scavenger in leaded gasoline, but with the much reduced use of leaded gasoline, this use has decreased. It is also used in the manufacturing of dyes, pharmaceuticals, polymers and as a general solvent for resins, waxes, gums and dyes (Howard 1997, HSDB). Earlier it has been used as a fumigant for citrus, grain and soil (HSDB), buy this use has been discontinued (Howard 1997). Algae have been observed to produce ethylene dibromide naturally (Howard 1997).

Release to the environment
Releases to the environment may be expected from accidental spills of leaded gasoline and from the exhaust from vehicles running on leaded gasoline. Furthermore, minor releases may be expected from the use of ethylene dibromide as a solvent in industrial production (HSDB and Howard 1997).

Summary of environmental fate
After emission to water, ethylene dibromide is expected to volatilise from the water surface. It is not expected to sorb to sediment particles. A river and a lake model showed volatilisation half-lives of 2.6 hours and 6.0 days respectively (HSDB). Biotic degradation and hydrolysis will also remove ethylene dibromide from the water phase.

After emission to soil, ethylene dibromide is expected to infiltrate with water due to high mobility and to evaporate from the soil surface. In the soil, degradation at different rates have been reported, with soil half lives ranging from 1.5 to 18 weeks, slowest in aquifers (Pignatello 1990, Cohen 1984, both in HSDB).

After emission to air, ethylene dibromide is expected to exist as a vapour in the atmosphere where it is degraded by reaction with hydroxyl radicals.

Environmental concentrations
In air near highways in the US, concentrations were around 11 μg/m^3 (IARC 1977 in HSDB). In air of areas remote from industry, concentrations between 0-9 ppt (Brodzinsky 1982 in HSDB). In surface water near industry, concentrations of 1.05-1.13 ppb have been measured. Ethylene dibromide was only found in concentrations above 1 ppb in samples from 2 out of 204 sites in 14 heavily industrialised river basins in the US (Going 1995 in HSDB).

Ethylene dibromide has been observed in a large number of wells in the US and in groundwater receiving infiltrating water from the surface where ethylene dibromide has been used as a fumigant (HSDB).

No further data have been found. Present environmental concentrations can be expected to be lower than the concentrations of the past as the use of leaded gasoline and the use of ethylene dibromide as a fumigant largely have been abandoned.

Vulnerable use and vulnerable groups
No vulnerable groups have been identified but uses that can cause pollution of groundwater may be considered vulnerable.

Conclusion
Ethylene dibromide is detected in the environment, therefore human and wildlife exposure is expected. However, ethylene dibromide is biodegradable and not bioaccumulative. Furthermore, it is solely released in the environment from accidental spills of leaded gasoline and diesel exhaust from vehicles on leaded gasoline. Whereas the use of leaded fuels is strongly diminished, it is expected that at present, the exposure of wildlife and humans to ethylene dibromide is restricted. Diethyl bromide has been categorised having only moderate exposure concern. The use of EDB as an industrial solvent has been assumed to take place in a closed system.

References
Howard, P.H. (ed.) (1997) Handbook of environmental fate and exposure data for organic chemicals. Lewis publishers, Boca Raton USA.

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

FENARIMOL (CAS NO 60168-88-9)

Fenarimol, chemical name alpha-(2-chlorophenyl)-alpha-(4-chlorophenyl)-5-Pyrimidinemethanol; Trade names include Rubigan 4AS; Rigidin; Bloc; EL 222; Tebulan; Rimidin. Fenarimol belongs to the group of pyrimidine and pyridine fungicides

Chemical characteristics

Molecular formula C17-H12-Cl2-N2-O1

MW = 331.2

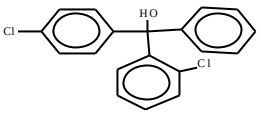


Table 1: Physical/chemical properties of fenarimol

Parameter	Fenarimol
Water solubility (mg/L, 25°C)	14 (USDA pest. prop. database in SRC 2002)
Vapour pressure (mm Hg, 25°C)	$2.25 \cdot 10^{-7}$ mm Hg 25°C, (SRC)
log Kow	3.60 (SRC)
Henrys law constant (atm m3/mole)	$7 \cdot 10^{-9}$ (SRC)
Koh (cm3/molecule sec)	$3.94 \cdot 10^{-12}$ (SRC)
Biodegradation	Very slow
BCF	118 (PMEP 2002)
Koc	760 (ARS 2002)

Abiotic degradation

In air, the rate of reaction between fenarimol and hydroxyl radicals have been estimated to be $5.35 \cdot 10^{-11}$ $cm^3 \cdot molecule^{-1}$ s^{-1} at 25°C (Meylan 1993 in SRC 2002). This corresponds to an atmospheric half-life of 98 hours when anticipating a hydroxyl concentration of $5 \cdot 10^5$ molecule$\cdot$ cm^{-3}.

In the ARS pesticide database (2002), a photolysis rate of 28 $days^{-1}$ is given for water. This corresponds to a half-life of 0.6 hours. Photolysis in soil was much slower with a rate of 0.0052 d^1 (ARS 2002) corresponding to a half-life of 133 days.

The rate of Hydrolysis of fenarimol in water is given as <0.023 d^1 at pH 5-9 (ARS 2002). This corresponds to a half-life of less than 30 days. However, ARS (2002) states that there was no sign of hydrolysis in soil in 30 days.

Biotic Degradation

Field dissipation half-lives has been reported as 165-360 days and half life in soil has been given as 840 days (ARS 2002). Biotic degradation can thus be expected to be very slow and the PMEP (2002) homepage states that fenarimol does not biodegrade under aerobic or anaerobic conditions.

Bioconcentration

Judged from a log Kow of 3.6, fenarimol would be expected to bioaccumulate. However, according to Tomlin (1994), fenarimol is rapidly excreted by mammals upon oral administration. Thus, excretion may reduce the bioaccumulation. A BCF of 113 was given at the PMEP (2002) homepage fact sheet.

Use, exposure and emissions

Fenarimol is a systemic fungicide used to control powdery mildews in pome fruit, stone fruit, strawberries, vines, cucumbers, aubergines, peppers, tomatoes, roses and other ornamentals and beet (Tomlin 1994). Fenarimol in also used on turf, lawns and golf courses (PMEP 2002).

Release to the environment

Release to the environment is an intended result of the use of fenarimol as a pesticide. Fenarimol may also be released from the production site.

Summary of environmental fate

After release to soil, fenarimol is expected to sorb to soil and to photo degrade on the surface of soil. It is not expected to leach much into groundwater and no significant evaporation from dry or wet soil surfaces is expected. The pesticide is expected to have a long half-life in soil.

After release to water, fenarimol is expected to sorb to suspended particles and sediment. It is expected to be photolysed rapidly when in the upper layer of the water, but removal from the deeper layers and sediment phase may be slow due to slow biotic degradation and hydrolysis.

After release to the atmosphere, fenarimol will react with hydroxyl radicals (half-life 98 hours) and will photolyse. It is not known if fenarimol will exist in the particulate phase or in the vapour phase.

Environmental concentrations
There is no data on environmental concentrations of fenarimol, but it can be expected that the pesticide can be found in soil where it has been applied as it is not biodegradable and as photo degradation is of limited effect inside soils. Likewise, it may be found in sediments of receiving waters as it sorbs strongly.

Vulnerable use and vulnerable groups
No vulnerable groups or uses have been identified, but workers involved in the production and use of epichlorohydrin may be expected to see increased exposure.

Conclusion
Fenarimol is of high concern as human exposure is expected via air, groundwater and food and as the pesticide is rather persistent and bioaccumulative. Furthermore, wildlife in and around areas where fenarimol is used as a pesticide will be exposed to fenarimol.

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

ARS (2002) ARS pesticides properties database http://wizard.arsusda.gov/acsl/

PMEP (2002) The Pesticide Management Education Program at Cornell University Homepage, Fenarimol (rubigan) chemical fact sheet 2/85

FENITROTHION (CAS NO 122-14-5)

Fenitrothion, chemical name dimethyl O-(3-methyl-4-nitrophenyl) phosphorothionate, belongs to the group of organophosphorous pesticides.
Trade names include Kotion, Dybar, Novathio, Nuvanol, Cytel, Arbogal, Agriya 1050, Agrothion, Sumithion, Fenitox, Metathion, Bayer 41831, Bayer S-5660, Nitrophos, Cyfen and Folithion

Chemical characteristics

Molecular formula fenitrothion: C9-H12-N1-O5-P1-S1

MW = 277.23

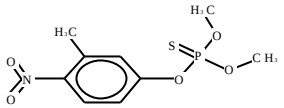


Table 1: Physical/chemical characteristics of fenitrothion

Parameter	Fenitrothion
Water solubility (mg/L, 25°C)	14 (EHC 133 1992) 38 (SRC)
Vapour pressure (mm Hg, 25°C)	6 x 10-6 (EHC 133 1992) 5.4 x 10-5 (SRC)
log Kow	3.3 (Hansch 1995 in SRC 2002)
Henrys law constant (atm m3/mole)	9.3 x 10-7 (SRC)
Koh (cm3/molecule sec)	6.0 x 10-11 (SRC)
Biodegradation	moderate
BCF (L/kg)	20-450 continuous exposure (EHC 133 1992) 69.34 (SRC)
Koc (L/kg)	864.6 (SRC) 2000-7150 (ARS 2002)

Abiotic degradation

Fenitrothion hydrolyses in water but hydrolysis rate depends strongly on temperature. At pH 5-9 the hydrolysis half-lives are 4-8 days at 45°C, 17-61 days at 30°C and 200-630 days at 15°C (EHC 133 1992).

Hydrolysis seems to be slightly faster at high pH with half-lives of 100-101 days measured at 25°C (Ito 1988 in (EHC 133 1992)). DT50 hydrolysis has been estimated as 108.8 d (pH 4), 84.3 d (pH 7), 75 d (pH 9) at 22°C (Tomlin 1994)

Fenitrothion photolyses in water and soil when exposed to sun light. In distilled water and solutions at pH of 3, 7 and 9 the photolysis half lives were 10, 50, 20 and 6 hours, respectively (Miyamoto 1977a in (EHC 133 1992)). In soil, half lives of 85 days and 182 days have been measured for fenitrothion in a soil with and without artificial irradiation (Dykes 1988 in (EHC 133 1992)). In air, half-lives of 24 and 61 minutes have been measured at 85-90°C in the absence or presence of ozone respectively (Addison 1981 in (EHC 133 1992)).

Biotic Degradation

Several micro-organisms can degrade fenitrothion (EHC 133 1992). Experiments with ring labelled fenitrothion have showed half-lives of 2-5 days in upland conditions. After one year, 60-70% of initial radiocarbon had been collected as CO_2, the remainder was incorporated in the organic matter of the soil (Mikami 1985 in EHC 133 1992). Sterilisation reduced degradation in another experiment indicating biotic degradation (Adhya 1981 in EHC 133 1992).

Bioconcentration

Fenitrothion is bioconcentrated in fish and other aquatic organisms, but is rapidly metabolised and excreted when water concentrations drop. With continuous exposure, BCFs of 20-450 have been measured for fish (EHC 133 1992).

Use, exposure and emissions

Fenitrothion is mainly used in agriculture for controlling chewing and sucking insects on rice, cereals, fruits, vegetables, stored grains, cotton, and in forest areas. It is also used for the control of flies, mosquitoes, and cockroaches in public health programmes and/or indoor use (EHC 133 1992).

Release to the environment
Release to the environment is an intended result of the use of fenitrothion as a pesticide. fenitrothion may also be released from the production site.

Summary of environmental fate
After emission to water, fenitrothion is expected to sorb moderately to suspended particles and sediments. Volatilisation from the water surface is expected to be small as Henrys law constant is small. In a model study, a volatilisation half-life of 93 days was calculated (Marshall 1977 in (EHC 133 1992)). However, very fast volatilisation was observed from the surface of a pond after spraying the surface (Maguire 1980 in (EHC 133 1992)). Besides volatilisation, fenitrothion will be removed from the water by hydrolysis and photolytic and biological degradation. Half-life in water is less than 24 hours in the presence of sunlight (EHC 133 1992).

After application to soil, fenitrothion is expected to sorb at the surface from where it is removed by hydrolysis, photodegradation and biological degradation. In soils with low organic content, some infiltration may take place (EHC 133 1992). Only little evaporation is expected from soil surfaces.

Environmental concentrations
Concentrations in streams in sprayed areas have been measured after spraying and fenitrothion concentrations of up to 64 μg/L have been registered. In all reported cases concentrations in water dropped sharply within few hours or days (EHC 133 1992).

After spraying, concentrations in soil reached 0.13-0.23 mg/kg within 1-8 days (Ohmae 1981 in (EHC 133 1992)) and similar concentrations were found in other cases. After continued spraying for five years, there was no build up in the soil and concentrations in soil were continuously <0.005 mg/kg 45 days after spraying (Yule 1974 in (EHC 133 1992)).

According to the COMMPS monitoring data, fenitrothion was found in 395 aquatic phase samples from 37 sampling stations. Average concentration was 0.0168 μg/L.

Vulnerable use and vulnerable groups
No vulnerable groups were identified, but workers involved in production and use may be exposed. The general population is exposed via food (EHC 133 1992).

Conclusion
The organophosporous pesticide fenitrothion is used on food crops, is readily biodegradable and moderately bioaccumulative. Environmental concentrations in water and sediment are reported. Human exposure might be expected through ingestion of treated crops or contaminated water. Because fenitrothion is readily biodegradable human exposure is less likely to occur. More important however is indoor use against flies, cockroaches and mosquitoes and use in public health programmes. All together, human exposure is expected and hence fenitrothion is categorised as a high exposure concern compound..

References
EHC 133 (1992). Environmental health criteria 133 Fenitrothion, WHO, Geneva.

SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

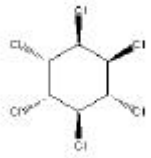
Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

ARS (2002) ARS pesticides properties database http://wizard.arsusda.gov/acsl/

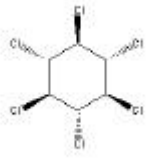
HEXACHLOROHEXANES (HCHS) (CAS NO 608-73-1)

Although this group theoretically contains alpha HCH, beta HCH and gamma-HCH, most data are derived from lindane (Gamma HCH).

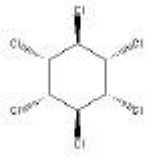
Chemical characteristics
Alpha, Beta and Gamma HCH are 3 isomers of hexachlorocyclohexane (MW = 290.83)



Alpha HCH
CAS 319-84-6



Beta HCH
CAS 318-85-7



Gamma-HCH (Lindane)
CAS 58-89-9

Table 1: Physical/chemical properties of lindane.

Parameter	Lindane (Gamma HCH)
Water solubility (mg/L, 25°C)	0.24-7.3 (SRC) 6.94-7.6 (fra97; gre96) 8.52 (cefic 57)
Vapour pressure (mm Hg, 25°C)	3.52 x 10-5 (SRC) 4.4 x 10-3 Pa at 24°C (>99.5%)
log Kow	3.5 (Cefic, 1999) 3.7 (fra97; gre96; riwa 1998) 3.72-4.14 (SRC)
Henrys law constant (atm m3/mole)	0.2 Pa.m3/mole (fra97; gre96) 5.14 x 10-6 (SRC)
Koh (cm3/molecule sec)	5.73 x 10-13
Biodegradation	Slow
BCF (L/kg)	307.5
Koc (L/kg)	2.97 (gre96) (teunissen 96b in fra97)

Lindane is poorly soluble in water but has a relatively low log Kow value. Therefore lindane accumulates poor to medium in organisms. Lindane will be primarily found in the water phase and not bound to the sediment. Lindane has a low volatility from water (fra97).

Abiotic degradation
Lindane can be considered to be hydrolytically and photolytically stable. In an aquatic environment Hydrolytic half-lives were determined to be 35 days (pH = 9). The major degradation products were identified as pentachlorocyclohexane (amounted to about 7% maximum after 30 days), 1,2,4-trichlorobenzene and 1,2,3-trichlorobenzene (amounted to about 4% maximum after 30 days)
In a sediment/water study where lindane was added to the system under stirring a DT_{50} (sediment) of 135 days was found under aerobic conditions and of 162 days under anaerobic conditions.

Published atmospheric half-life times vary markedly and are in the range of 4.6 to >11 000 days. The atmospheric stability of lindane is confirmed by the fact that its long-range transport is proven. Photodegradation in water and soil are expected to be of little importance.

Biotic degradation
All HCHs are persistent compounds, alpha- and beta HCH being more persistent than their gamma relative. Biodegradation to pentachlorocyclohexane and subsequently tetra-, tri- and dichlorocyclohexanes occurs but is a slow fate process. The first dehydrochlorination step leading to pentachlorocyclohexane is considered to be the rate limiting factor
On the basis of field testing in Europe it has been established that in most cases lindane DT_{90} <1 year. However under certain conditions persistence of lindane can occur in soil. In the case of one tested site in Europe dissipation of lindane was prolonged significantly: DT_{50} >290 days and DT_{90} >1 year. Additionally in two studies conducted in California lindane showed persistence in soil: DT_{50} >90 days and DT_{90} >1 year.
Based on biodegradation rates, bioaccumulation of lindane in soil is likely to occur.

Bioconcentration
The BCF of lindane in algae is 240 (average), in mussels it varies from 150 to 350, in rainbow trout from 1200 to 2000 and the log BCF in vegetation is –0.41 (fra97). Bioaccumulation of lindane in fatty tissues are observed. Especially organisms higher in the food chain feeding on fish and mussels might be exposed to high concentrations of lindane. (Jansson 1993 in sepa98).

Use, Exposure and emissions
Lindane is an insecticide which acts by contact, ingestion and fumigation. It has been widely applied especially in agriculture, horticulture and forestry against a wide range of phytophagous and soil-inhabiting insects, in seed treatment and as ectoparsiticide for livestock. Lindane is also used as a biocide in the preservation of wood and leather, as an indoor applicant, and medical- or veterinary treatment.

Use of lindane is restricted to seed treatment and treatment of soil with subsequent incorporation into the top soil layer. All other uses, especially foliar spraying, are not supported by CIEL. The use restrictions to seed and soil treatment were self-imposed and voluntarily proposed by CIEL in order to minimise the evaporation of Lindane (CEFIC, 1999). Nevertheless, if not applied properly lindane may be transported by long-range transport (SEPA, 1998). Furthermore, the crude product with higher levels of alpha and beta-HCH is still often in used in the developing countries.

Lindane is still in use as a therapeutic drug in the treatment of parasitic infections e.g. scabies.

The quantities of Lindane used world-wide have been reduced to a third during the last years. The production rate of gamma-HCH (Lindane) of CIEL- quality (purity >99.5 %) is about 900 metric tonnes per year (CEFIC, 1999).
In the Netherlands 29 tonnes lindane was used in 1985, 24.3 tonnes in 1988, 21 tonnes in 1991 and 19 tonnes in 1994 (Ordelman et al., 1993). The emission is 14 tonnes/year in 1994 (gre96).

Vulnerable use and vulnerable groups
Lindane is used on seeds and soil before culturing and hence not directly used on food crops. HCH could however present a risk to agricultural workers applying the herbicide. Assumed is that these workers take the necessary precautions using the substance.

Since animals metabolise the gamma-isomer effectively, it is unlikely to be found in meat or eggs unless lindane was directly applied to livestock or their food. On the contrary, the beta-isomer is metabolised slowly. It tends to become incorporated into food chains including the rice straw-cow-human chain in Japan.

The substance has been proposed for adoption in the priority list because of specific concern for drinking water suppliers (EUREAU) (fraunhofer report, 1999).

Release to the environment
Release to the environment is an intended result of the use of lindane as an insecticide, biocide and therapeutic drug in both humans and livestock.

After 1992 the permission for the use of lindane are strongly reduced. Most applications involve seed- or soil treatments with incorporation. Due to the volatility of lindane and its observed long atmospheric half-lives contamination of sensitive areas as a consequence of long range air transport can not be prevented. Foliar and soil surface applications of lindane are very limited within the European Community, but use of lindane in other parts of the world might be redistributed to remote areas (even Europe). Erosion of lindane gives the most important contribution to the emission of lindane (>65%). Monitoring results indicate that contamination of the environment with HCH is mainly due to lindane usage within Europe (*Weiss*, 1998; *Simonich and Hites*, 1995). Long range transport of HCH solely seems to be only an additional source. Therefore a significant change of the environmental lindane concentrations as they are shown in monitoring studies of the recent years is not expected.

Summary of environmental fate
When released in the atmosphere lindane is very stable. Half lives of over 11.000 days are reported. Through long range air transport lindane might be redistributed to remote areas. The latter is the main reason for the restricted use of lindane in Europe right now. Lindane is solely applied using techniques where volatilisation is as low as possible. However, volatilisation of water and soil can not be prevented completely. Without precautions, lindane losses from soil surface within 24 hours would be up to 90 % of the initially applied amount. Evaporation from plant surfaces is even faster. Up to 86% of the initial amount is lost after 6 hours. The evaporation process from soil stops if the upper surface layers dry out. Evaporation from soil is reduced when lindane is incorporated into the soil. Under

laboratory conditions lindane losses within 24 hours by evaporation after incorporation were between 2 and 4 % and up to 13 % when a 1.5 cm uncontaminated soil layer was brought above the sprayed soil
When accidentally applied to water or incorporated into soil, lindane is expected to absorb strongly to particulate matter and sediment. Leaching to the groundwater compartment will not be an important fate process. Lindane is persistent, biodegradation to less chlorinated cyclohexanes take place but is very slow.

Environmental concentrations
In the Fraunhofer report (1999) lindane is measured in water with a median concentration of 0.0083 µg/l (mean 0.0168 µg/l) based on 11666 data from 546 stations (8260 data were above the determination limit). In sediment lindane is measured with a median concentration of 3.19 µg/l (mean 9.15 µg/l) based on 953 data from 53 stations (689 data were above the determination limit).

Lindane is found in freshwater in 1992 and 1993, in rain water in 1988, 1989, 1990/91 and 1992 and in shallow/deep ground water. No measurements have been done in marine water (Ordelman, 1996).

Occurrence in the environment of lindane

Compartment	Year	Location	Concentration average (max.)	Unit	Reference (source)
Water	1993	Lakes and rivers	0.01 (0.01)	µg/l	Gre96
Water		North-sea coast	0.03 (0.05)	µg/l	Gre96
Water		Wadden-sea	0.01 (0.01)	µg/l	Gre96
Water	1996	Eijs	0.01	µg/l	Riza in fra97
Water	1991	Harvss	0.006	µg/l	Riza in fra97
Water	1996	Harvss	0.005	µg/l	Riza in fra97
Water	1996	Ijmdn	0.005	µg/l	Riza in fra97
Water	1991	Lobptn	0.003	µg/l	Riza in fra97
Water	1996	Lobptn	0.003	µg/l	Riza in fra97
Water	1992	VLSB	0.00815	µg/l	Riza in fra97
Water	1993	VLSB	0.00415	µg/l	Riza in fra97
Water	1994	VLSB	0.0048	µg/l	Riza in fra97
Water	1995	VLSB	0.0045	µg/l	Riza in fra97
Water	1992	NWK	0.00405	µg/l	Riza in fra97
Water	1993	NWK	0.00255	µg/l	Riza in fra97
Water	1994	NWK	0.002	µg/l	Riza in fra97
Water	1995	NWK	0.00185	µg/l	Riza in fra97
Water		Rhine	Max. 0.02	µg/l	6 riwa, 1998
Water		Rhine	<0.1	µg/l	22 riwa, 1998
Water		Meuse	<0.1	µg/l	22 riwa, 1998
Water		Dutch waterway (boezemwater)	0.04	µg/l	6 riwa, 1998
Water		Twente Kanaal	0.01	µg/l	87 riwa, 1998
Water		Ijsselmeer	<0.1	µg/l	22 riwa, 1998
Water		Haringvliet	<0.1	µg/l	22 riwa, 1998
Water	Oct. 1988	Yonne	19	ng/l	53 riwa, 1998
Water	Jan. 1988	Yonne	11	ng/l	53 riwa, 1998
Water	March 1991	Yonne	36	ng/l	53 riwa, 1998
Water	1984-1985	France Seine	0.01-0.05	µg/l	24 riwa, 1998
Water	1988	Germany Rhine Koblenz	0.001-0.012	µg/l	24 riwa, 1998
Sediment	Sept.1986	Yonne	22	µg/kg	53 riwa, 1998
Sediment	Oct. 1988	Yonne	<0.01	µg/kg	53 riwa, 1998
Suspended matter	1992	Salt waters	4.85 av	µg/kg	Riza in fra97
Suspended matter	1991	Salt waters	0.0041 av	µg/l	Riza in fra97
Suspended matter	1991	Salt waters	5E+11 Av	µg/l	Riza in fra97

Compartment	Year	Location	Concentration average (max.)	Unit	Reference (source)
Wildlife biota	1994	Red eel	199 av.	µg/kg fat	De boer 95 in fra97
Wildlife biota	1995	Driehoeksmossel	92 av.	µg/kg fat	Pieters 95 in fra97
Wildlife biota	1992	Cod liver North-sea	37 av.	µg/kg fat	Teunissen 95 in fra97
Wildlife biota	Sept.1986	Yonne mollusc	67-110	µg/kg	53 riwa, 1998
Wildlife biota	June 1987	Yonne mollusc	76	µg/kg	53 riwa, 1998
Wildlife biota	Oct.1988	Yonne mollusc	36	µg/kg	53 riwa, 1998
Wildlife biota	Apr. 1991	Yonne fish	45	µg/kg	53 riwa, 1998
Wildlife biota		Red eel	7-84	µg/kg ww	Rivo in DHC99
Wildlife biota		mollusc	0.009-0.1	mg/kg fat	Ivm in DHC99
Wildlife biota		fish	<0.02-8.4	µg/kg ww	Ivm in DHC99
Wildlife biota		Fish eel	0.02-0.2	mg/kg fat	Ivm in DHC99
Wildlife biota		Cormorant egg	5-58	µg/kg ww	Ivm in DHC99
Wildlife biota		Cormorant egg	0.1-1.4	mg/kg fat	Ivm in DHC99
Humans		Italian human milk	180	ppb lw beta HCH	Larsen 1994, johanssen 1994 in sepa98)
Humans		Norwegian human milk	33	ppb lw beta HCH	Larsen 1994, johanssen 1994 in sepa98)
Humans		Adipose tissue from Iran	730	ppb lw beta HCH	Burgaz 1995 in sepa98
Humans		Adipose tissue from Iran	18	ppb lw alpha HCH	Burgaz 1995 in sepa98

d.l= detection limit

In the European COMMPS program European environmental concentration of HCHs were determined in water and sediment:

Table 3: Occurrence of HCHs in the European environment according COMMPS

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
water								
319-84-6	HCH, alpha- isomer	0.0248	0.0036	0.0094	0.0082	77	1974	1190
319-85-7	HCH, beta- isomer	0.0378	0.0064	0.0129	0.0080	44	1226	751
58-89-9	HCH, gamma- isomer (lindane)	0.0370	0.0083	0.0168	0.0279	546	11666	8260
sediment								
319-84-6	HCH, alpha- isomer	76.96	2.67	19.42	31.23	27	594	398
319-85-7	HCH, beta- isomer	62.80	3.08	42.26	143.64	27	822	528
58-89-9	HCH, gamma- isomer (lindane)	10.96	3.19	9.15	15.57	53	953	689

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

Toxicity
Observed toxicities in different species have led to the following Predicted Effect Concentrations (PECs) for lindane after single application of 1.5 kg a.i/ha

Table 4: PEC values for lindane after single application of 1.5 kg a.i/ha

PEC per compartment (mg/kg)	1 meter spray distance	20 m spray distance
Surface water	0.02	0.0005
Sediment	0.133	0.0033

Conclusion
CEFIC, 1999 reports that the Lindane isomer B-HCH, which is a contaminant in the production of gamma HCH, may be of relevance regarding interference with the endocrine system, especially, that it might mimic an oestrogen. Furthermore they report that there are indications that not Lindane itself is, is an in vitro endocrine modulator (CEFIC, 1999). Therefore it should be checked in greater detail whether, the observed endocrine effects might have been caused by the B-HCH isomer.

Although no information available, there might be a concern for the use of drinking water.

Due to the persistent character of lindane and its potential to distribute through the environment, there is a high exposure concern for wildlife. Lindane is used on seed and soil before culturing. Lindane is inherently biodegradable, bioaccumulates and is found wide spread in the environment, in fish (food) and mother milk. Lindane is also found in human tissues. Furthermore production- and agricultural workers handling lindane might be exposed. Also its application as a therapeutic drug leads to human exposure. The substance is prioritised as having high concern.

References
Bruhn, T., et al, (1998), Umweltforschungsplan des bundesministeriums für umwelt, naturschutz und reaktorsicherheit. Einstufung von Schadstoffen als endokrin wirksame Substanzen. Forschungsbericht 216 02 001/08.

CEFIC57: CEFIC, 1999. Information provided to the expert meeting on endocrine disrupters: Response to European Crop Protection Association Elaboration of a List of Chemicals for Further Assessment in Relation to Endocrine Disruption prepared by SCC GmbH on behalf of CIEL

Fra97: Franse & de Voogt, 1997 Oestrogene verbindingen in het Nederlands milieu, MTC report.

Fraunhofer-Institute, 1999. Revised Proposal for a List of Priority Substances in the Context of the Water Framework Directive (COMMPS Procedure). Declaration ref.: 98/788/3040/DEB/E1

Gre96: Greve, (1996). (Dutch Health Council). Hormoon-verstorende stoffen in Nederland. Gebruik, emissie, milieuconcentraties en fysisch/chemische karakteristieken

Orde96, Ordelman, H.G.K., & Schrap S.M., (1996) Watersysteemverkenningen 1996. Een analyse van de problematiek in aquatisch milieu. Bestrijdingsmiddelen. RIZA nota 95.059.

RIWA (1998), Xeno-oestrogenen en drinkwater(bronnen).

SEPA, 1998. Olsson, P-E, et al, 1998, Endocrine disruption chemicals, Swedish Environment Protection Agency, report no. 4859.

Monograph prepared in the context of inclusion of following active substance in Annex I of the Council Directive 91/414/EEC

IOXYNIL (CAS NO 1689-83-4)

Ioxynil, chemical name 4-hydroxy-3,5-diiodobenzonitril or 4-hydroxy-3,5-diiodophenylcyanide belongs to the group of hydroxynitril herbicides.
Trade names include Actril, Actrilawn, Bantrol, CA 69-15, Certrol, Iotox, Iotril, Joxynil, Mate, M&B 8873, Loxynil, Totril, Trevespan.

The parent compound ioxynil is applied as an ester (CAS 3861-47-0 = ioxynil octanoate = 4-cyano-2,6-diiodophenyl octanoate) which only serves as a vesicle for the active phenolic compound. When applied the octanoate rapidly degrades into the active phenol.

Chemical characteristics

Molecular formula ioxynil: C7-H3-I2-N1-O1

MW = 370.92

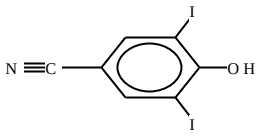


Table 1; Physical/chemical parameters of ioxynil

Parameter	Ioxynil
Water solubility (mg/L, 25°C)	50 (SRC)
Vapour pressure (mm Hg, 25°C)	1.38 x 10-7 (SRC) 2.04 x 10-6 Pa at T = 25°C (SANCO)
log Kow	3.43 (SRC) 0.90 at pH = 6.5 (Hansch in HSDB)
Henrys law constant (atm m3/mole)	5.48 x 10-6 (SRC) 9.55 x 10-6 (SANCO 2.16 x 10-13 (SRC)
Koh (cm3/molecule sec)	2.16 x 10-13 (SRC)
Biodegradation	Yes/fast
BCF (L/kg)	3 (SRC) 29 (SANCO)
Koc (L/kg)	75 (using log Kow = 0.90, HSDB) 182-276 (SANCO)

Ioxynil is a non-corrosive, white crystalline powder with a faint phenolic odour. If released in the atmosphere it will exist in both vapour and particulate phases, based on an estimated vapour pressure of 1.38 x 10-7 mm Hg at T = 25°C. If released to soil ioxynil is expected to be moderately adsorbed (Koc 182-276 L/kg). Due to its low vapour pressure volatilisation of ioxynil from soil surfaces or vegetation is very low, respectively 0.47% and 0.2%. Volatilisation from surfacewater is very low as well, based upon an estimated Henrys law constant of 5.48E-010 atm-m3/mole and rapid degradation in water sediments..

Abiotic degradation
In the atmosphere, ioxynil exists in both a particulate and a vapour phase. Vapour-phase ioxynil is rapidly degraded by reaction with photochemically produced hydroxyl radicals (DT50 < 8 hours). Under oxidising conditions, small amounts of iodine may be released from ioxynil Particulate ioxynil is removed by both wet and dry deposition (SANCO).
In aquatic environments, photodegradation of ioxynil is not expected to play a significant role due to the rapid degradation and absorption to sediment of ioxynil octanoate. In soil no photodegradation takes place (SANCO).

Biotic Degradation
In the environment ioxynil octanoate is rapidly degraded to the active phenolic ioxynil compound, which on its turn is degraded to 3,5-diiodo-4-hydroxy-benzamide and 3,5-diiodo-4-hydroxy-benzoic acid respectively. Also small amounts of free iodine may be released from ioxynil resulting in 3-iodo-4-hydroxybenzamide. In biological systems the ultimate benzoic acid is eventually degraded to catechols and CO2 (mineralisation of phenylring).
Under aerobic soil conditions ioxynil is rapidly degraded into its metabolites, illustrated by its DT50 values below. Mineralisation of the phenylring (and absorption to the humic fraction) is significant after 48 days (27.5%) and reaches 66 % after 128 days. Degradation under anaerobic conditions is slower but similar (TD50 ioxynil octanoate = 14 days) (SANCO; Hsu in HSDB).

In an aquatic environment, biodegradation is even more rapid than in soil. Ioxynil octanoate rapidly adsorbs to the sediment. Within one day 52% of ioxynil octanoate is converted to its active substance. Mineralisation of the phenylring reaches 85% after 60 days.

Table 2: Half-lives of ioxynil and its metabolites for different environmental compartments

DT50 (days)	Ioxynil octanoate	Ioxynil	"Benzamide"	"Benzoic acid"
Soil	10	2.5	7.7	2
Water	1	4	-*	-*
Air	0.3	-*	-*	-*

* Not given because concentrations are insignificant for the compartment involved.

Bioconcentration

SANCO reports a BCF for ioxynil of 29 and even 135 for ioxynil octanoate. Therefore, risk for bioconcentration has to be considered. However, residues were rapidly eliminated (> 98% within 90 h) after termination of the exposure to Ioxynil octanoate. Ioxynil and its metabolites do not bioaccumulate in tissues, body fluids and milk. The risk of bioconcentration can be considered as low. The latter is in agreement with the estimated BCF of 3.0 which was calculated for ioxynil, using a log Kow of 0.90 (SRC).

Use, exposure and emissions

The contact herbicide ioxynil is used for post-emergence control of a wide range of annual broad-leaved weeds, especially young seedlings of Polygonacae, Compositae and Borginaceae, in winter- and spring cereals, onions, garlic, leeks, shallots, flax, kiwi, sugar canes, grasses, lawns and newly sown turf (Tomlin in HSDB). The active compound is an inhibitor of the second light reaction of photosynthesis and uncouples oxidative phosphorylation of respiration. It therefore acts as both electron transport inhibitor and uncoupling agent (SANCO). Typical application rates (expressed as phenol equivalent) are 0.350-0.450 kg/ha for cereals and 0.180-0.630 kg/ha for shallots). Ioxynil is an applied through tractor-mounted sprayer with ground-directed boom.

The general population may be exposed to ioxynil through ingestion of contaminated food. Occupational exposure would be by inhalation or dermal contact.

Vulnerable use and vulnerable groups

Ioxynil could present a risk to agricultural workers applying the herbicide or working the fields. However, assuming these workers take the necessary precautions using the substance there is no indication that ioxynil presents a specific risk to them. In a worst case situation (spraying a shallot field 0.630 kg/ha) exposure of agricultural workers (as a percentage of AOEL) is depicted below:

Table 3: Exposure of agricultural workers to ioxynil using different protection methods.

Method of appliance	Exposure	% AOEL
No gloves	0.0230 mg/kg/day	230% AOEL
Gloves only when mixing/loading	0.0135 mg/kg/day	135% AOEL
Gloves only during spray application	0.0122 mg/kg/day	122% AOEL
Gloves during spray application and mixing/loading	0.0043 mg/kg/day	43% AOEL

Since ioxynil formulations are applied at times at which it is not necessary to enter crops shortly after spraying, field workers also are at low risk.

Because ioxynil is used as a herbicide on food crops this could mean a certain risk. However, ioxynil is metabolised quickly in the environment and most of the time sprayed only once per growing season. Therefore, in harvested crops no detectable amounts of ioxynil were found (SANCO). Typical ioxynil pre-harvesting intervals (PHI) for different crops are depicted below

Table 4: PHI values for ioxynil treated crops

Crop	PHI (days)
Spring- and winter cereal	60
Grass and cereals for grazing	21

Garlic, leeks, onions and shallots	14

Release to the environment
Release to the environment is an intended result of the use of ioxynil as a post-emergency control herbicide in variety of cereals, crops, grasses or newly sown turf.

Summary of environmental fate
Ioxynil emitted in the atmosphere is supposed to be rapidly cleared through deposition or hydroxyl radical mediated photodegradation. When emitted in soil, ioxynil moderately absorbs to soil particles. It shows little mobility due to its Koc and its rapid degeneration to benzamide and benzoic acid metabolites. Therefore, ioxynil leaching to the groundwater compartment is of no importance. Volatilisation from either wet (or dry) soils is not an important fate process due to a low vapour pressure and Henrys law constant. In an aquatic environment ioxynil degradation is even faster than in soil.

Environmental concentrations
Environmental concentrations of ioxynil (ioxynil octanoate or phenolic ioxynil) in air, water, soil or organisms are just seldomly reported. The SANCO profile contained no monitoring data of ioxynil in either, soil, surfacewater, groundwater or air.

Despite its use in the area, ioxynil was not detected in either surface water or groundwater collected from the Granta catchment, United Kingdom in 1985-1988 (detection limit 0.06 ug/l)
(Clark in HSDB)

In 2% of the analysed surfacewater samples from the Anglian water region in the United Kingdom (1987) ioxynil was detected up to a level of 0.09 ug/l (Croll in HSDB).

None out of 54 samples of soil water and only 2 out of 56 surface water samples from the Bolbro Beak in Denmark (1989-1991) contained solely small amounts of ioxynil (0.05 ug/l). In another Danish region (Hojvads Rende) 1 out of 38 soil water samples, 0 out of 20 drainage water samples and 7 out of 47 surfacewater samples contained small amounts of ioxynil up to a maximum of 0.7 ug/l (Mogensen in HSDB).

Toxicity
Observed toxicities in different species have led to the following Predicted Effect Concentrations (PECs) for ioxynil and its major metabolites after single application of 844 g ioxynil octanoate / ha shallot field.

Table 5: Ioxynil PEC values (single application of 844 g ioxynil octanoate / ha shallot field)

PEC per compartment (mg/kg) or (ug/l)	**Ioxynil octanoate**	**Ioxynil**	**"benzamide"**	**"benzoic acid"**
Soil	1.13	0.84	0.09	0.17
Sediment**	0.02	0.0039	*	*
Surface water**	11.25	1.69	*	*
Ground water	*	*	*	*
Air	*	*	*	*

**Drift at 1 m

Conclusion
Ioxynil is used as a herbicide against broad-leaved weeds on food crops. Ioxynil is readily biodegradable and not bioaccumulative. Although human exposure through herbicide treated crops might be expected, extensive basket case studies have proved otherwise. Wildlife on the other hand might be exposed through appliance directly in the field. Ioxynil is categorised as medium exposure concern chemicals..

References
HSDB Hazardous Substances Data Bank, a database of the library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

SANCO Document 2001 on Ioxynil

SRC, Syracuse research corporation PhysProp on-line database, http://esc.syrres.com (October 2002)

4-ISOOCTYLPHENOL (CAS NO 11081-15-5)

4-Isooctylphenol belongs to the group of alkylphenoles.

Chemical characteristics

Molecular formula 4-Isooctylphenol: C14-H22-O1

MW = 206.33

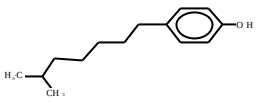


Table 1: Physical/chemical parameters 4-isooctylphenol

Parameter	4-isooctylphenol
Water solubility (mg/L, 25°C)	3.599 (SRC)
Vapour pressure (mm Hg, 25°C)	1.7 x 10-4 (SRC)
log Kow	5.42 (SRC)
Henrys law constant (atm m3/mole)	1.3 x 10-5 (SRC)
Koh (cm3/molecule sec)	50.3 x 10-12 (SRC)
Biodegradation	Moderate
BCF (L/kg)	129-297(Tsuda et al 2000) 2997 (SRC)
Koc (L/kg)	27670 (SRC)

Abiotic degradation
4-octylphenol may photodegrade indirectly in natural water through the reaction with photo excited Fe(III) (Brand et al 2000). The same can be expected for 4-isooctylphenol. In air, a rate of $50.3 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1} has been predicted (EPIWIN) for the reaction between 4-isooctylphenol and atmospheric hydroxyl radicals, leading to a half-life of 0.213 days (12 hour day). 4-isooctylphenol is not expected to hydrolyse.

Biotic Degradation
The aerobic degradation (to CO_2) half-life of nonylphenol has been measured as 20 days (Staples et al 1999). Nonylphenol has a structure very similar to iso-octylphenol and similar half-lives of iso-octylphenol can be expected. The octylphenol metabolites octylphenoxyacetic acid and octylphenoxyethoxyacetic acid were shown both to be readily biodegradable using the OECD 301 B (modified Sturm method) (Staples et al 1999). The same can be expected for the iso-octyl metabolites. Although branching may affect biodegradability, the difference between biodegradability of iso-octylphenol and octylphenol is expected to be small, as the branching in the iso-octylphenol is limited.

Bioconcentration
For 4-tert-octylphenol, environmental BCFs was determined by Tsuda et al (2000). BCF values for three kinds of fish were 129-297 whereas laboratory BCF value was 261 for Killifish (Tsuda et al 2000). This BCF predicted for 4-isooctylphenol from a log Kow of 5.42 was 2997 (EPIWIN) which does seem high. If a correction factor for long alkyl chains is used, as was done for 4-octylphenol, the estimated BCF value becomes 300, which seems more reasonable.

Use, exposure and emissions
9004-87-9 Ethoxylated iso-octylphenol has been used as an inert ingredient in pesticide formulations (NCAP 2002). It can also be expected to occur, together with other phenoloctylisomers, in the production of octylphenolethoxylates. Octylphenol is furthermore used as plasticiser, antiflex cracking agent and fungistat (NCM 1996).

The major source of octylphenol in the environment is most likely octylphenol based surfactants (octylphenolethoxylates) which degrades to octylphenol. Octylphenolethoxylates comprise 15-20% of the alkylphenolethoxylate consumption (Staples et al 1999).

Release to the environment
In Europe, 4-isooctylphenol will mainly arise from the degradation of isooctylphenolethoxylate in the anaerobic processes of sewage treatment plants and elsewhere, e.g. anaerobic sediment and anaerobic sewage system. Isooctylphenolethoxylate itself is expected mainly to be released to wastewater after being used for cleaning purposes.

According to a wwtp model, 86.4 % of the 4-isooctylphenol that enters a wwtp will be removed with the sludge due to strong adsorption (EPIWIN) while the remainder more or less leaves with the effluent as degradation is estimated to be slow (EPIWIN).

The sludge may be applied to agricultural land, incinerated, stored or used for other purposes.

Summary of environmental fate
After emission to water, 4-isooctylphenol is expected to sorb to suspended particles and sediment. Little volatilisation from water surfaces can be expected. In a model river, volatilisation half-life was 82 hours and in a model lake it was 1019 hours = 42 days (EPIWIN). In the water, and aerobic parts of the sediment iso-octylphenol is expected to biodegrade, with half-lives somewhat larger than 20 days, based on data for 4-nonylphenol.

After emission to soil, which will mainly occur with the application of sludge, 4-isooctylphenol is expected to remain strongly sorbed to the sludge. This will reduce the volatilisation which is thus expected to be small and leaching is also expected to be minimal. In the soil, 4-octylphenol is expected to be degraded by microorganisms. No data on the rates are available.

After emission to air, which will mainly occur as a result of volatilisation, 4-isooctylphenol in the vapour phase will react rapidly with hydroxyl radicals and degrade. Atmospheric half-lives of 3 hours (light) has been estimated (EPIWIN).

Environmental concentrations
In eight rivers flowing into Lake Biwa, Japan, 4-tert-octylphenol was detected in 23 out of 48 samples, in concentrations of ND-0.09 µg/L. Lowest concentrations of nonylphenolethoxylates were observed in winter, supposedly because the degradation of alkylphenolethoxylates in waste water treatment plants was slow at low temperatures (Tsuda et al 2000). In Canadian waters near highly industrialised sites, concentrations of octylphenol from not detected to 0.084 µg/L was found (Staples et al 1999). A survey of 22 European estuaries showed sediment concentrations of octylphenol from not detected to 2.2 µg/kg.

Octylphenol was found in the sediment of the Great Lakes in concentrations of 0.002-23.7 µg/g (Gray et al 1999).

Vulnerable use and vulnerable groups
No vulnerable uses or vulnerable groups have been identified.

Conclusion
4-isooctylphenol is used as raw material in the manufacturing of e.g. surfactants, detergents and wetting agents. It is also used as plasticiser, stabiliser in fuels, adhesive in rubbers and intermediate in several bactericides and pesticides. It will mainly arise in wastewater from degradation of octylphenolethoxylates after being used as a cleaning agent. Octylphenoles are inherently biodegradable and expected to be bioaccumulative. Because environmental levels have been detected and human exposure is expected through consumer goods containing octylphenoles it is prioritised as high exposure concern.

References
Gray, M.A.; Niimi, A.J.; Metcalfe, C.D. (1999)
Factors affecting the development of testis-ova in medaka, oryzias latipes, exposed to octylphenol.
Environmental toxicology and chemistry, Vol. 18, No. 8, pp. 1835-1842.

Tsuda, T.; Takino, A.; Kojima, M.; Harada, H.; Muraki, K. and Tsuji, M. (2000)
4-nonylphenols and 4-tert-octylphenol in water and fish from rivers flowing into Lake Biwa.
Chemosphere, Vol 41, pp. 757-762

Brand, N.; Mailhot, G.; Sarakha, M.andBolte, M. (2000)
Primary mechanism in the degradation of 4-octylphenol photoinduced by Fe(III) in water-acetonitrile solution.
Journal of photochemistry and photobiology A: Chemistry, Vol. 135, pp. 221-228

Staples, C.; Williams, J.B.; Blessing, R.L. and Varineau, P.T. (1999)
Measuring the biodegradability of nonylphenol ether carboxylates, octyl ether carboxylates, and nonylphenol.
Chemosphere, Vol. 38, pp. 2029-2039

NCAP 2002, Northwest coalition for alternatives to pesticides.
http://www.pesticide.org

NCM (1996), Nordic Council of Ministers
Chemicals with estrogen-like effects
TemaNord 1996:580

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

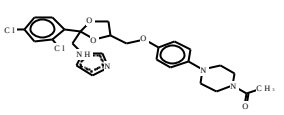
EPIWIN v.3.10. Environmental property estimation programme package. Office of pollution prevention and toxics, US EPA. 2000.

KETOKONAZOLE (CAS NO. 65277-42-1)

Ketokonazole, chemical name cis-1-acetyl-4-(4-((2-(2,4-dichlorophenyl)-2-(1H-imidazol-1-ylmethyl)-1,3-dioxolan-4-yl)methoxy)phenyl)piperazine, belongs to the group of piperazine fungicides (triazines and triazoles).
Trade names include Fungarest; Fungarol; Ketoderm; Ketoisdin; Orifungal M; Panfungol; Fungoral; Nizoral

Chemical characteristics

Molecular structure Ketokonazole: C26-H28-Cl2-N4-O4



MW = 531.44

Table 1: Physical/chemical properties ketokonazole

Parameter	Ketokonazole
Water solubility (mg/L, 25°C)	0.0866 (SRC)
Vapour pressure (mm Hg, 25°C)	6.4 x 10-14 (SRC)
log Kow	4.35 (SRC)
Henrys law constant (atm m3/mole)	5.59 x 10-20 (SRC)
Koh (cm3/molecule sec)	2.36 x 10-10 (SRC)
Biodegradation	recalcitrant
BCF	446 (SRC)
Koc	4589 (SRC)

Abiotic degradation
No data regarding abiotic degradation of ketokonazole.

Biotic Degradation
No data regarding biodegradation of ketokonazole (Stuer-Lauridsen 2002). Ketokonazole is estimated to be recalcitrant in the environment (EPIWIN 2000).

Bioconcentration
A bioconcentration factor of 446 has been estimated, suggesting that the compound is potentially bioaccumulative in aquatic organisms. Likewise, the high log Kow value indicates that the compound is hydrophobic and is likely to accumulate in lipid tissues.

Use, exposure and emissions
Ketokonazole is a broad-spectrum antifungal agent administered to humans (and animals) in tablets (200 mg ketokonazole), in shampoo (containing 2% ketokonazole) and in cream (2% ketokonazole) for the treatment of fungal diseases (Rxlist 2002). In the body, 20-70% is adsorbed from the gastrointestinal tract. Ketokonazole is metabolised in the liver (Dadlnet.dk 2002). In a specification of drugs used in Denmark in 1997, ketokonazole was listed as no. 25 of the drugs used most in Denmark (based on number of defined daily doses) (Stuer-Lauridsen 2002). Besides its intended use as a drug, exposure to the general population is not expected.

Release to the environment
Ketokonazole is mainly expected to reach the environment as a result of its therapeutic use as a drug. Following treatment, ketokonazole is metabolised in the liver and excreted via the urine and bile, only a few percent is excreted in unchanged form via urine and bile (Rxlist 2002). Ketokonazole not taken up from the dietary system may be released with faeces to waste water. Ketokonazole used in shampoos will also be released with wastewater. Ketokonazole may also be released to the environment via medical industries that produce or distribute the compound. Due to the high costs and stringent demands regarding quality and environmental standards in the medical industry, it is however assumed that release from production sites is low (Stuer-Lauridsen 2002).

Summary of environmental fate
After release to wastewater, ketokonazole is expected to sorb to suspended particles. The fate in wastewater treatment plants is not known, but the relatively high Kow indicates that if ketokonazole is not degraded it will most likely sorb to sludge and will thus be removed from the water together with the sludge. If released to surface water, ketokonazole is expected to sorb to suspended particles and sediment. No volatilisation from water will take place, as Henrys law constant is extremely small. In

conclusion, the major parts of ketokonazole released are expected to end up in sludge. Further release to the environment may thus happen via disposal of sludge, e.g. distribution in agriculture, incineration, deposition at landfills etc.

Environmental concentrations
No data regarding environmental concentrations of ketokonazole have been found.

Vulnerable use and vulnerable groups
Ketokonazole is a therapeutic drug purposely used for treatment of fungal infections. If administered correctly, no vulnerable groups are identified.

Conclusion
Ketokonazole is used as an antifungal drug and applied as a tablet, shampoo or cream. Human exposure in people taking ketokonazole in their treatment against fungal diseases is inevitable. Ketokonazole is prioritised as high exposure concern. Wildlife might be exposed as well as a result from release through wastewater (shampoo), faeces or accidental spills. However, environmental levels are not reported

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

EPIWIN v.3.10. Environmental property estimation programme package. Office of pollution prevention and toxics, US EPA. 2000.

Stuer-Laudirsen F, Hansen L, Birkved M, Kjølholt J, Mikkelsen S. 2002. Litteraturudredning vedrørende human medicin i miljøet [Literature study regarding human medicine in the environment]. Environmental Project No. 661. Danish Environmental Protection Agency. Copenhagen, Denmark.

RxList (2002), RxList monographs, www.rxlist.com

Dadlnet.dk (2002). Directions for the use of antimycotics for the treatment of superficial mycosis, www.dadlnet.dk/klaringsrapporter/2000-02/2000-02-11b.htm

MANCOZEB (CAS NO 8018-01-7)

Mancozeb, chemical name [1,2-ethanediylbis[carbamodithioato](2-)]manganese mixture with [1,2-ethanediylbis [carbamodithioato] (2-)] zinc (9CI) [ethylenebis(dithiocarbamato)] manganese mixture with [ethylenebis(dithiocarbamato)]zinc (8CI), belongs together with e.g. maneb, zineb and metiram to the group of ethylene-bisdithiocarbamate pesticides (EDBCs)
Trade names include Dithane, Dithane-Ultra, Fore, Green-Daisen M, Karamate, Mancofol, Mancozeb, Mancozin, Manzate 200, Manzeb, Manzin Nemispor, Nemispot, Policar, Riozeb, and Zimaneb

Chemical characteristics

Molecular formula mancozeb: $(C4\text{-}H6\text{-}N2\text{-}S4)_x(Zn)_y$

MW = 271,3

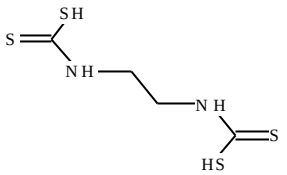


Table 1: Physical/chemical properties of mancozeb

Parameter	Mancozeb
Water solubility (mg/L, 25°C)	2-20 (SANCO) 1.14 x 10+5 (SRC)
Vapour pressure (mm Hg, 25°C)	1.33 x 10-5 Pa (SANCO) 7.5 x 10-8 (SRC)
log Kow	0.11-1.8 (SANCO) 0.62 (SRC) 0.14-0.15 (metabolite ETU, SANCO)
Henrys law constant (atm m3/mole)	5.9 x 10-9 (SANCO) 4.6 x 10-9(SRC)
Koh (cm3/molecule sec)	2.12 x 10-10 (SRC)
Biodegradation	Fast
BCF	3.2 L/kg (SRC)
Koc	363 –2334 L/kg (SANCO) 1000 L/kg (HSDB) 2.6-146 L/kg (metabolite ETU, SANCO)

Mancozeb is a non-corrosive, greyish yellow powder with a musty odour, which is practically insoluble in organic solvents (Willoughly in HSDB).

Abiotic degradation
Mancozeb is stable under normal, dry storage conditions but decomposes at temperatures of 192-204 °C. Thermal decomposition products may include very toxic fumes of sulfoxides, zinc oxide, and nitroxides (Lewis in HSDB). EBDC residues in or on the outside of foods convert readily to ethylenethiourea (ETU), a known teratogen and suspected carcinogen, during commercial processing and cooking (DHC99)
Mancozeb is susceptible to photolysis. It has a photolysis rate constant greater than 5.5/day in air which equates to a half-life of less than 3 hours (US Department of Agriculture in HSDB). The soluble disodium salt ion absorbs at 285 nm with molar absorbance of 6 x 10+4 in water. Maximum absorbances are detected at 281 and 310 nm (NaOH, 10%, pH 9.8) in UV-B. Three major decomposition products were observed: Ethylene thiourea (ETU), ethylene bisisothiocyanide sulphide (EBIS) and ethylene urea (EU) (SANCO) Mancozeb rapidly degrades in the environment by photolysis (Tomlin in HSDB).
Mancozeb is unstable in the presence of strong acids, strong alkalis and most polar solvents. Due to the presence of hydrolysable groups mancozeb is degraded by hydrolysis and oxidation in the presence of moisture and oxygen. The latter and not photolysis appears to be the major decomposition route (SANCO). Mancozeb has a hydrolysis rate constant of 0.46, 0.30 and 1.04 per day at pH 5,7 and 9 respectively. This equates to half-lives of 36 days at pH = 5, 55 hours at pH = 7 and 16 hours at pH = 9. The same major decomposition products were observed; ETU, EU and EBIS, of which the teratogen and supposed carcinogen ETU is hydrolytically stable (SANCO).

Biotic Degradation
EBDCs are generally unstable compounds. Through photolysis but especially through hydrolysis and oxidation mancozeb (but also related products as metiram, maneb and zineb) are rapidly and spontaneously degraded to metabolites including ETU, EBIS, EU ethylene thiuram disulphide (ETD), ethylene thiuram monosulphide (EMS) and sulphur. Mancozeb is of low persistence and strongly

bound to soil particles. Due to the presence of hydrolysable groups mancozeb-decomposition probably is an important fate process in wet environments (Hartley in HSDB). Therefore, contamination of groundwater is not expected. However, mancozeb may enter surface waters if erosion of contaminated soil occurs. Lab studies indicate a soil half life (expressed as DT50 values) of 1 – 3 hours for mancozeb, 7.2-24 hours for ETU and 4.8-7.6 days for EU under aerobic conditions at 20 °C. Under anaerobic conditions mancozeb has a DT50 of 11 days.
Field studies in wet aerobic soils on the other hand predict longer biodegradation half-lives for mancozeb, varying from 2 to 40 days (Halfon in HSDB; Tomlin in HSDB). After 100 days 31-52 % mancozeb, 32-58% ETU and 47% EU is mineralised (SANCO). Mancozeb is readily degraded by soil microorganisms, eventually releasing its ethylene C-atoms as CO2. Plants extensively metabolise mancozeb, terminal metabolites are natural metabolites especially those derived from glycine (US Department of Agriculture in HDBC).

Bioconcentration
An estimated BCF of 3.2 was calculated for mancozeb, using a log Kow of 1.33 and. This BCF suggests that the potential for bioconcentration in aquatic organisms is low. Since mancozeb is of low mobility and is known to hydrolyse rapidly in aqueous environments, bioconcentration or biomagnification in aquatic organisms or greater systems is unlikely to occur (SRC in HSDB).

Use, exposure and emissions
Mancozeb is a leaf and soil fungicide used in the control of a wide variety of fungal diseases (e.g. blight, leaf spot , rust, downy mildew, scab, shot-hole, damping off diseases, needle cast, black leg etc) in field crops, fruits, nuts, vegetables, flowers, seeds, ornamentals, etc. It is applied foliar or as a seed treatment (Kirk in HSDB). Major crops treated with mancozeb are potatoes, tomatoes, apples, pears, onions, lettuce, roses and whets. In 1996, 3465 tons of mancozeb were used world-wide (Halfon in HSDB).

Occupational exposure to mancozeb may occur through inhalation of powder formulations and dermal contact with this compound at workplaces where mancozeb is produced or used. Breathing zone concentrations of mancozeb during spraying a potato field was near or below the detection limit, 0.01-0.04 mg/cu m (Nilsson in HSDB). However, during preparation and filling of the spraying liquid, the concentration was 0.22 mg/cu m, on the average. The highest individual eight-hour time-weighted average exposure was 0.05 mg/cu m. Concentrations of mancozeb in 5 samples of factory workrooms were 0.042, 1.78, 1.25, 0.45, and 0.58 mg/cu m (Maini in HSDB). A field study in which exposure to mancozeb during application by airplane and airblast spraying techniques was monitored, found that mixer/loaders received the highest exposure followed by tractor driver applicators (Wang in HSDB). Pilots and home gardeners, in general experienced less exposure. NIOSH (NOES Survey 1981-1983) has statistically estimated that 7277 workers are potentially exposed to in the US. However, the NOES Survey does not include farm workers.
The general population may be exposed to mancozeb via ingestion of food and contact with fungicide products containing mancozeb. Mancozeb is detected in some food products due to its use as a commercial fungicide. (SRC in HSDB). An experiment was conducted to study Mancozeb residues after application to tomatoes. Mancozeb was applied at 6 lbs/acre to tomatoes. After nine days, the tomatoes were harvested and measured for residues. Tomatoes contained Mancozeb residues at 0.54, 0.19, and 0.10 ppm that had either not been washed, were washed for 10 mins, or were treated with hot acid for two minutes respectively (Marshall in HSDB). The US EPA said exposure to EBDCs may pose increased occupational health risks of cancer, birth defects and thyroid disorders to mixers, loaders and applicators handling these formulations. However, as part of a special review in july 1987 a basket study was performed to determine the actual level of EBDT residues on consumer purchased products. It was concluded levels were too low to affect human health.

Release to the environment
Release to the environment is an intended result of the use of mancozeb as a fungicide. Mancozeb has effectively been used against a broad spectrum of fungi as well as a means to protect fruits, vegetables, field crops, and ornamentals from foliar diseases and damping off.

Summary of environmental fate
The estimated low vapour pressure of 9.8 x 10-8 mm Hg at 25 °C indicates that mancozeb will exist solely in the particulate phase in the ambient atmosphere. Particulate-phase mancozeb will be removed from the atmosphere by wet and dry deposition. If released to soil, mancozeb is expected to have a low mobility based upon a Koc of 1000. Volatilisation of mancozeb from moist (or dry) soil surfaces or surfacewaters is not expected to be an important fate process based upon an estimated Henry's Law constant of 4.6 x 10-9 atm-cu m/mole and its low vapour pressure. If released into water, mancozeb is expected to adsorb to sediment and suspended solids (Lyman in HSDB). Generally all dithiocarbamates strongly absorb to soil particles and are rather unstable in the biological

environment. Especially by hydrolysis and in a lesser extent by photodegradation this class of compounds is converted to different toxic metabolites of which neurotoxin carbon disulphide and teratogen/carcinogen ETU give reason to major concern.

Vulnerable use and vulnerable groups
Because mancozeb is used as a herbicide on food crops this could mean a certain risk. However mancozeb is metabolised quickly in the environment. The EPA (see above) concludes that actual levels of mancozeb are too low to affect human health. Mancozeb could also present a risk to agricultural workers applying the herbicide. Assumed is that these workers take the necessary precautions using the substance. There is no indication that mancozeb presents a specific risk to vulnerable groups or creates high risk situations. However the metabolite ETU could present a risk but this substance is not evaluated as an endocrine disrupter. This substance should be researched, to find out if it could have endocrine effects.

Environmental concentrations
In the Netherlands, the mancozeb metabolite ETU was found in Flevoland in 46% of the measurements, up till 0.9 ug/l. Also carbon disulphide was incidentally detected up to 7.5 ug/l. Especially in areas with bulb cultivation high levels of ETU occur in groundwater (max 42 ug/l). In Flevoland rainwater maximum concentrations of 75 ug/l ETU and 226 ug/l carbon disulphide were detected. In 55% of the sediment samples taken, low amounts of carbon disulphide were found (Ordelman et al, 1999). However, the amounts of ETU and carbon disulphide detected are the result of the combined use of all dithiocarbamates and hence do not originate from mancozeb solely.

ETU has been confirmed in only 1 (16 ppb) of 1393 ground water samples in areas of heavy agricultural use of EBDC fungicides in the US, including areas where the wells have been subject to contamination with other agricultural chemicals or fertilisers (LOQ 0.1-25 μg/L) (EPA in HSDB).

After the application of mancozeb to a banana plantation in Costa Rica, concentrations in two canal streams were studied from February 16-March 31, 1994(1). Results indicated that canal water contained mancozeb concentrations ranging from 0.77-2.38 ug/cu cm in one canal and 0.50-4.00 ug/cu cm in the other (Mortensen in HSDB).

Ethylene bis-dithiocarbamate fungicides (including mancozeb) were found to be the most prevalent residue found on fruits and vegetables analysed in Switzerland in 1989-90. Out of 461 salads analysed in Geneva, 23 samples had levels of ethylene bis-dithiocarbamate fungicides exceeding tolerance values (Coryl in HSDB)

No mancozeb residues were found in FDA's Los Angeles surveillance samples, 1982-86 (18,435 total samples). In California's Priority Pesticide program for 1989 in which samples of crops that have been treated with targeted pesticides are analysed, no mancozeb was detected in all 4 samples of apples, the one sample of dried onion, and in 5 of 8 samples of grapes. The other three samples of grapes were within tolerance. While mancozeb residues were not mentioned as present in food in the FDA pesticide residue monitoring program for 1983-1986, the combined occurrence of six EBDCs was under 2% (Winter in HSDB).
The level of mancozeb in shellfish from Canadian estuaries was <1.6 ppm (Reish in HSDB)

Toxicity
Observed toxicities in different species have led to the following Predicted Effect Concentrations (PECs) for mancozeb and its major metabolites ETU, EBIS and EU in different environmental compartments when applied to orchards (single application 2.4 kg/ha; multiple application 2.4 kg a.i./ha 12 applications spaced in 7 days)

Table 2: PEC-values for Mancozeb and its major metabolites

Compartment	Compound	PEC single	PEC multiple
soil	mancozeb	1600	-*
Sediment**	-	-	-
Surface water	mancozeb	230	190
	ETU	43	62
	EBIS	47	39
	EU	28	89
Groundwater**	-	-	-
Air***	-	-	-

* Only single application due to the extremely rapid dissipation of mancozeb
** Not submitted, no major amounts of mancozeb or its metabolites are found in the sediment or groundwater (<0.005 ug/l)
*** Not submitted since mancozeb is a polymeric non volatile compound

Conclusion
Mancozeb is a fungicide used to prevent crop damage in the field and to protect deterioration in storage and transport. Workers involved in the production or usage of mancozeb have the highest risk of exposure, however the general population is also exposed through consumption of mancozeb treated foods. Mancozeb does not accumulate in the environment due to its relative instability. However, hydrolysis and photodegradation of mancozeb, as well as other EBDCs, result in the formation of more stable, less immobile and hazardous metabolites such as ETU and carbon disulphide.

Based on the toxic metabolite ETU mancozeb is classified as a substance of high exposure concern

References
DHC99, (1999). Dutch Health Council. Endocrine disrupters in the Netherlands

Extoxnet, (2002). Data Bank on pesticide information profiles (http://ace.ace.orst.edu/info/extoxnet/pips/mancozeb.htm)

HSDB, (2002). Hazardous Substances Data Bank, a database of the library of medicine's TOXNET system http://toxnet.nlm.nih.gov

Ordelman, H.G.K., et al, (1999). Watersysteemverkenningen 1996. Een analyse van de problematiek in aquatisch milieu. Dithiocarbamaten. RIZA nota 96.040

SANCO (2002. Document on Mancozeb

SRC (2002). Syracuse research corporation PhysPop on-line database, http://esc.syrres.com

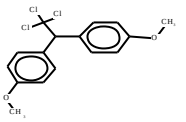
METHOXYCHLOR (CAS NO 72-43-5)

Methoxychlor, chemical name 1,1,1-trichloro-2,2-bis(p-methoxyphenyl)ethane, belonging to the group of methoxychlor and its derivatives.
Trade names include Marlate, Metox, Chemform, DMDT, Methoxy DDT, Maxie, Methoxcide, oms 466

Chemical characteristics

Molecular formula methoxychlor: C16-H15-Cl3-O2

MW = 345.66



Technical methoxychlor consist of up to 12 % of the o,p-isomer while the remainder is the p,p-isomer. It is the p,p-isomer that is the active compound. When not specified in literature, methoxychlor is taken to mean the p,p-isomer and data reported for methoxychlor in literature, and referred here, is expected to be valid for the p,p-isomer.

Table 1: Physical/chemical properties of methoxychlor

Parameter	Methoxychlor
Water solubility (mg/L 25°C)	0.1 mg/L (SRC)
Vapour pressure (mm Hg 25°C)	2.58 x 10-6 (SRC)
Log Kow	5.08 (SRC)
Henrys Law constant (atm cu3 m/mole)	2.03 x 10-7 (SRC)
Koh (cm3/molecule sec)	5.35 x 10-11 (SRC)
Biodegradation	slow
BCF (L/kg)	138-8300 (HSDB) 1628 (SRC)
Koc (L/kg)	22000-107000 (ARS) 42600 (SRC)

Abiotic degradation

Photolysis half-lives for methoxychlor in distilled water was 37 days, while in some river waters it was as little as 2-5 hours in sunlight (Menzie 1978 in HSDB). In other studies, half- lives in distilled water has been measured to be 270 days against only 8 days in aged tap water, previously holding fish (Murty 1986). 91.4 % of Methoxychlor in thin dry films was photodegraded in 12 days indicating that methoxychlor on e.g. soil surfaces may photodegrade (Nat´l Research Council Canada 1975 in HSDB). Hydrolysis half–lives of methoxychlor in water at pH 3-7 is estimated to be 367 days (Wolfe 1977 in HSDB). At pH 9, the hydrolysis half-life was estimated at 270 days (Park 1982 in HSDB). Methoxychlor is not expected to be oxidised in natural waters (Bomberger 1983 and Zepp 1976, both in HSDB)

In air, the rate of reaction between methoxychlor and hydroxyl radicals have been estimated to be $5.35 \cdot 10^{-11}$ cm^3 $molecule^{-1}$ s^{-1} at 25°C (Meylan 1993 in SRC 2002). This corresponds to an atmospheric half-life of 7 hours.

Biotic Degradation

In an aerobic die-away study with water from Santa Rosa sound, methoxychlor had a half-life of more than 25 days (Walker 1988 in HSDB). Half-lives of 7-29, 9.6-14.4, 4.8-29 and 7-14.4 days have been measured for four different freshwaters (Parish 1986 in HSDB). Studies have shown that anaerobic degradation in soils were faster than aerobic degradation: in flooded soils half-lives of 1 week to 2 months have been measured against more than three months for upland soils (Castro 1971 in HSDB). The same tendency was observed in sediment water systems, with the fastest degradation taking place under anaerobic conditions (Muir 1984 in HSDB). Field studies showed that methoxychlor is fairly persistent as it was still present in soil, one year after application (Golovleva 1984 in HSDB).

Bioconcentration

Bioconcentration factors of 8300 (Veith 1979 in HSDB) and 138 (Parrish 1977 in HSDB) have been measured for fathead minnow and sheepshead minnow respectively. The difference in BCF may reflect a difference in the ability to metabolise methoxychlor. A BCF of 16,360 has been predicted from water solubility (Kenaga 1980 in HSDB). Methoxychlor is thus expected to bioconcentrate strongly.

Use, exposure and emissions
Methoxychlor is an insecticide with contact and stomach action and it is used to control a wide range of insects, particularly chewing insects, in field crops, forage crops, fruit, vines, flowers, vegetables and in forestry. It is also used in animal houses, dairies, and in household and industrial premises (Tomlin 1994). In public health programmes, methoxychlor is used as 3% sprays, applied by air, for the control of sensitive mosquitoes (IPCS 2002).

Release to the environment
Release to the environment is an intended result of the use of methoxychlor as a pesticide. Methoxychlor may also be released from the production site. Releases of 0.5 kg of methoxychlor for each metric tonne produced have been reported (Sittig 1980 in HSDB).

Summary of environmental fate
After release to water, methoxychlor is expected to sorb to sediment and suspended particles and the majority (>90 %) of methoxychlor in a water sediment system will be found in the sediment and suspended particle phases (HSDB). Methoxychlor present in the sediment may be degraded relatively fast if the sediment is anaerobic. Half-lives of less than 28 days have been recorded for methoxychlor in anaerobic sediment-water systems (Muir 1984 in HSDB). Methoxychlor may also be removed from the water phase by photolysis whereas hydrolysis not is expected to be an important process at ambient pHs (HSDB). Methoxychlor is not expected to volatilise from the water surface (HSDB).

After release to soil, methoxychlor is expected to sorb strongly to soil particles. Methoxychlor will thus be rather immobile in the surface soil. Methoxychlor is neither expected to volatilise from moist soil surfaces nor from dry surfaces, as both vapour pressure and Henrys law constant are rather low (HSDB). Under aerobic conditions, methoxychlor is expected only to be removed slowly from the soil while removal is expected to be faster in anaerobic, e.g. flooded soil.

After release to air, methoxychlor is expected to exist both in the vapour phase and in the particulate phase. Vapour phase methoxychlor will degrade by reaction with hydroxyl radicals and a half-life of 7 hours has been estimated for this reaction (HSDB). Particulate methoxychlor will be removed from the atmosphere by dry and wet deposition (SRC in HSDB).

Environmental concentrations
Methoxychlor has been identified in 0.7-0.8 % of a large number of groundwater samples (HSDB) which indicates that methoxychlor may reach groundwater despite it's apparent low mobility. Concentrations of up to 0.01 ppb have been measured (Spalding 1980 HSDB). In 1974-75, concentrations of up to 0.02 ppb were measured in Lake Superior (Konasewich 1978 in HSDB). In 11 out of 15 samples taken in lake Ontario, methoxychlor was detected in concentrations of up to 0.086 ng/L (Biberhofer 1987 in HSDB). In Missouri River water, taken at five locations, concentrations of up to 6.4 ng/L were detected (Petty 1995 in HSDB) and in a tributary of Lake Michigan, concentrations of 2.9-89.1 ppt were found (Schacht 1974 in HSDB). In the revised proposal for a list of priority substances in the context of the water framework directive, methoxychlor is reported to have been found in concentrations above detection limit in only 1 sample. The concentration was 0.0006 µg/L.

In the European COMMPS program European environmental concentration of methoxychlor was determined in water:

Table 2: Occurrence of methoxychlor in the European aquatic environment

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
72-43-5	methoxychlor	0.0006	0.0006	0.0006	-	1	4	1

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

During a US national soils monitoring program, methoxychlor was detected in only 1 out of 1729 cropland soil samples in a concentration of 0.28 ppb. In apple orchards, methoxychlor was detected in soils at concentrations of 0-4 ppb. Methoxychlor in trace levels has been observed in sediments of the Delaware River estuary and James River near Hopewell, VA (HSDB). In a tributary of Lake Michigan, concentrations of 0.19-175.0 ppb were measured in the sediment (Schacht 1984 in HSDB).

Methoxychlor was detected in arctic air samples from Canada and Russia, in concentrations of 0.26-0.41 pg/m^3 (Hallsal 1998 in HSDB).

Vulnerable uses and vulnerable groups
Women may be at increased risk along with individuals who have liver kidney diseases or convulsive disorders. Developing foetuses and young children may be the most susceptible human population to the reproductive effects of methoxychlor (HSDB).

Conclusion
Methoxychlor is used as an insecticide used on food crops and flowers but is also applied in animal houses dairies and as a household spray. Methoxychlor is persistent and highly accumulative. Environmental levels of methoxychlor are detected in all compartments and biota. Humans might be exposed to through consumption of methoxychlor treated crops, contaminated drinking water and household use. Methoxychlor, and therefore its metabolites as well although environmental levels are not reported, is prioritised as a high exposure concern compound.

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council , Surrey, UK and the Royal society of chemistry, Cambrigde, UK.

ARS (2002) ARS pesticides properties database http://wizard.arsusda.gov/acsl/

IPCS (2002). Data sheets on pesticides no. 28, methoxychlor. WHO, IPCS INCHEM homepage http://www.inchem.org/documents/pds/pds/pest28_e.htm

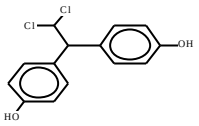
METHOXYCHLOR DERIVATIVES

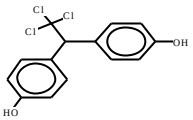
This summary concerns the three methoxychlor metabolites:

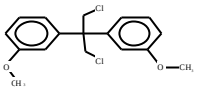
1,1-dichloro-2,2-bis(4-hydroxyphenyl)ethane (DHPE) Cas no: -
1,1,1-trichloro-2,2-bis(4-hydroxyphenyl)ethane (THPE) Cas no: 2971-36-0
1,3-dichloro-2,2-bis(4-methoxy-3-methylphenyl)propane (DMMPP) Cas no: 30668-06-5

There have been found no available data on these substances and thus, only predicted values of environmental properties are presented.

Chemical characteristics







DHPE
C14-H12-Cl2-O2
MW = 283.16

THPE
C14-H11-Cl3-O2
MW = 317.06

DMMPP
C17-H18-Cl2-O2
MW = 325.24

Table 1: Physical/chemical properties of DHPE, THPE and DMMPP

Parameter	DHPE	THPE	DMMPP
Water solubility (mg/L 25°C)	47	4.8	0.022
Vapour pressure (mm Hg 25°C)	2.4 x 10-8	1.7 x 10-8	7.4 x 10-8
Log Kow	3.62	4.55	6.37
Henrys Law constant (atm m3/mole)	1.9 x 10-10	$1.5 \cdot 10^{-9}$	1.6 x 10-6
Koh (cm3/molecule sec)	81.5 x 10-12	80.6 x 10-12	66.0 x 10-12
Biodegradation			
Fish BCF (L/kg)	123	631	15970
Koc (L/kg)	152500	220,300	156,700

All data estimated using EPIWIN

Abiotic degradation

The rate of DHPE reaction with hydroxy radicals in the atmosphere is estimated at $81.5 \cdot 10^{-12}$ $cm^3 \cdot molecule^{-1}$ s^{-1}, which corresponds to 1.574 hours. The estimated rates for THPE and DMMPP are very similar at $80.6 \cdot 10^{-12}$ and $66.0 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1} respectively, which corresponds to 1.592 and 1.943 hours in atmosphere with $1.5 \cdot 10^6$ OH-molecules/cm^3. Thus, DHPE, THPE and DMMPP are expected to be short-lived in the atmosphere (EPIWIN).

Biotic Degradation

No data on the persistence of these substances have been found. An estimation of biodegradability indicates that the three substances can be expected to be very persistent to biotic degradation in soil and water (EPIWIN).

Bioconcentration

High BCF values can be estimated by EPIWIN, with especially THPE and DMMPP being very bioaccumulative.

Use, exposure and emissions

DHPE and THPE are not expected to be used as such, but rather to be the result of the degradation/metabolism of methoxychlor. Methoxychlor is a pesticide and as such is spread in the environment as a result of its use (see methoxychlor summary).

The origin of DMMPP is not known.

Release to the environment

DHPE and THPE are released to the environment when methoxychlor, present in the environment, degrades. No source of release of DMMPP has been identified.

Environmental summary
If released to water, DHPE, THPE and DMMPP are expected to sorb to suspended particles and sediment. DHPE and THPE are not expected to volatilise. Volatilisation half-lives in a river has been estimated to at 131300 and 394199 years for DHPE and THPE respectively. For DMMPP, volatilisation half-life from a river is estimated at 103 days. No data on the degradation of the substances in water have been gained but it has been estimated that removal rates will be low (EPIWIN). The substances are thus expected to remain in the sediment for a long time.

If released to soil, the substances are expected to resist degradation and to persist for a long time. No or little leaching is expected, as the substances are believed to sorb very strongly to soil.

If released to the atmosphere, half-life is short. However, only DMMPP can be expected to reach the atmosphere.

Environmental concentrations
No measurements of environmental concentrations were found.

Vulnerable uses and vulnerable groups
Especially unborn and breastfeeding infants are vulnerable. The prevalence for infectious diseases is increased in childhood, when exposure to contaminants like methoxychlor take place in the period of pregnancy and breastfeeding (Richter-Reichhelm et al 2002).

Conclusion
Methoxychlor derivatives are of high exposure concern as they are expected to be both bioaccumulative and persistent in the environment. Because they result from the same use as methoxychlor itself, they are marked as high exposure concern.

References
EPIWIN v.3.10. Environmental property estimation programme package. Office of pollution prevention and toxics, US EPA. 2000.

Richter-Reichhelm, H.-B.; Althoff, J.; Schulte, A.; Ewe, S. and Gundert-Remy, U. (2002)

Workshop report. Children as special sub-populations: focus on immunotoxicity. Federal institute for health protection of consumers and veterinary medicine (BgVV), 15-16 November 2001, Ber**lin,** Germany. Arch Toxicol, vol. 76, pp. 377-382

METIRAM (METIRAM-COMPLEX) (CAS NO 9006-42-2)

Metiram, official IUPAC name is zinc ammoniate ethylene-bis(dithiocarbamate)-poly(ethylenethiuram disulphide), belongs together with e.g. maneb, zineb and mancozeb to the group of ethylene-bisdithiocarbamate pesticides (EDBCs)
Trade- or other names for metiram include arbatene, NIA 9102, Polyram, Polyram-Combi, and Zinc metiram (extoxnet).

Chemical characteristics

Molecular formula metiram: C8-H16-N5-S8-Zn1

MW = 504.12

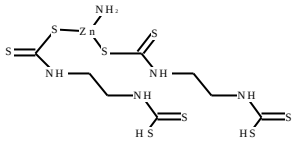


Table 1: Physical/chemical properties of metiram

Parameter	Metiram
Water solubility (mg/L 25°C)	<1 mg/L (SRC) 2 x 10-4 g/100 g water at 20°C (Extoxnet)
Vapour pressure (mm Hg 25°C)	1.44 x 10-13 mm (SRC)
Log Kow	0.3 (HSDB) 0.42 (SRC) 0.14-0.15 (metabolite ETU, SANCO)
Henrys Law constant (atm m3/mole)	1.25 x 10-16 (SRC)
Koh (cm3/molecule sec)	3.60 x 10-10 (SRC)
Biodegradation	fast
Fish BCF (L/kg)	3.2 (SRC)
Koc (L/kg)	1.0 x 10+5 (US Dept. Agriculture in HSDB) 5.0 x 10+5 (Extoxnet) 0.26 x 10+5 (SRC) 2.6-146 (metabolite ETU, SANCO)

Metiram is an odorous, non-corrosive, yellow powder, which is practically insoluble in both water and organic solvents (e.g. ethanol, acetone, benzene). It does solve (with decomposition) in pyridine.

Abiotic degradation
Metiram is stable at 30 °C but decomposes at temperatures of 140-156 °C. Thermal decomposition products may include toxic and corrosive fumes of ammonia, and toxic oxides of nitrogen and sulphur. EBDC residues in or on the outside of foods convert readily to ethylenethiourea (ETU), a known teratogen and suspected carcinogen, during commercial processing and cooking (829 in DHC99).
EDBCs are susceptible to photolysis. However, photodegradation of metiram is assumed to be of minor importance due to the lack of absorption in he environmental UV-spectrum (>290 nm) (Tomlin in HSDB)
Metiram is unstable to strong acids, strong alkalis, most polar solvents or a combination of heat and moisture. Both aqueous suspension and dimethylformamide solutions of metiram were found to decompose appreciably in about 2 hrs. When 300 ug of metiram was added in 1% aqueous solution of starch, 50% decomposition of metiram was observed in less than 6 hrs (Cullen in HSDB).

Biotic Degradation
Dithiocarbamates are generally unstable compounds. Metiram is probably similar in its environmental fate to closely related compounds such as zineb, maneb and mancozeb. It is of low persistence (soil half life of 20 days) and strongly bound to soil particles. Due to the presence of hydrolysable groups it undergoes rapid decomposition in the presence of moisture and/or oxygen. Metiram-decomposition probably is an important fate process in wet environments (Hartley in HSDB). Therefore, contamination of groundwater is not expected. However, metiram may enter surface waters if erosion of contaminated soil occurs. Breakdown of metiram occurs rapidly through hydrolysis and in a lesser extent through photodegradation. Important metabolites of all EBDCs are neurotoxin carbon disulphide, sulphur hydrogen, ethylenediisocyanate and ETU. The teratogen ETU is stable in water at pH 5-9 and degradation of this compound is not enhanced by sunlight. Moreover, other derivatives of thiourea, thiuram monosulphide, thiuram disulphide, and sulphur can be formed in the environment.

Bioconcentration
An estimated BCF of 3.2 L/kg, from its log Kow of 0.30 and a regression-derived equation, suggests the potential for bioconcentration in aquatic organisms is low (Franke in HSDB).
Expected is that most EDBCs will be metabolised rapidly in the environment and therefore will not spread to greater systems and will not bioaccumulate or biomagnify (Ordelman et al, 1999)
When metiram was applied to an orchard at a rate 20 lbs/acre, the maximum concentration of metiram on top soil was 6 mg/kg, but no metiram was detected beyond a depth of 2 inches in soil(1). It was concluded that metiram is biodegradable under the existing field conditions (Kuhr in HSDB).

Use, exposure and emissions
The EBDCs all are fungicides used to prevent crop damage in the field and to protect harvested crops from deterioration in storage or transport. Metiram is effective against a broad spectrum of fungi and is used to protect fruits, vegetables, field crops, and ornamentals from foliar diseases and damping off. For example scab on pome fruit, rust on currants and plums, downy mildew, red fire disease, black rot on vines, late blight on potatoes and tomatoes and leaf spot on celery and celeriac. In 1992 US EPA announced its intent to cancel the use of maneb, mancozeb and metiram for use on apricots, carrots, celery, collards, mustard greens, nectarines, peaches, rhubarb, spinach, beans and turnips. Nowadays in the U.S., use of metiram is limited to potatoes, roses and apples. Also in European countries EDBCs are intensively investigated and use is restricted (EPA in HSDB).

Occupational exposure to metiram may occur through inhalation of metiram powders and dermal contact with this compound at workplaces where metiram is produced or used. NIOSH (NOES Survey 1981-1983) has statistically estimated that 7277 workers are potentially exposed to in the US. However, the NOES Survey does not include farm workers. The general population may be exposed to metiram via ingestion of food and dermal contact with fungicide products containing metiram. Metiram is detected in some food products due to its use as a commercial fungicide (SRC in HSDB). The US EPA said exposure to EBDCs may pose increased occupational health risks of cancer, birth defects and thyroid disorders to mixers, loaders and applicators handling these formulations. However as part of a special review in july 1987 a basket study was performed to determine the actual level of EBDT residues on consumer purchased products. It was concluded levels were too low to affect human health.

Release to the environment
Release to the environment is an intended result of the use of metiram as a fungicide. Metiram has effectively been used against a broad spectrum of fungi as well as a means to protect fruits, vegetables, field crops, and ornamentals from foliar diseases and damping off.

Summary of environmental fate
The estimated low vapour pressure of 1.44 x 10-13 mm Hg at 25 °C indicates that metiram will exist solely in the particulate phase in the ambient atmosphere. Particulate-phase metiram will be removed from the atmosphere by wet and dry deposition. If released to soil, metiram is expected to be immobile based upon a Koc of 1.0X10+5. Volatilisation of metiram from moist (or dry) soil surfaces or surfacewaters is not expected to be an important fate process based upon an estimated Henry's Law constant of 1.25 x 10-16 atm m3/mole and its low vapour pressure. If released into water, metiram is expected to adsorb to sediment and suspended solids (Lyman in HSDB).
Generally all dithiocarbamates are rather unstable in the biological environment. Especially by hydrolysation and in a lesser extent by photodegradation this class of compounds is converted to different toxic metabolites of which neurotoxin carbon disulphide and teratogen/carcinogen ETU give reason to major concern.

Vulnerable use and vulnerable groups
Because metiram is used as a herbicide on food crops this could mean a certain risk. However metiram is metabolised quickly in the environment. The EPA (see above) concludes that actual levels of metiram are too low to affect human health. Metiram could also present a risk to agricultural workers applying the herbicide. Assumed is that these workers take the necessary precautions using the substance. There is no indication that metiram presents a specific risk to vulnerable groups or creates high risk situations. However the metabolite ETU could present a risk but this substance is not evaluated as an endocrine disrupter. This substance should be researched, to find out if it could have endocrine effects.

Environmental concentrations
In the Netherlands, the metiram metabolite ETU was found in Flevoland in 46% of the measurements, up till 0.9 ug/l. Also carbon disulphide was incidentally detected up to 7.5 ug/l. Especially in areas with bulb cultivation high levels of ETU occur in groundwater (max 42 ug/l). In Flevoland rainwater maximum concentrations of 75 ug/l ETU and 226 ug/l carbon disulphide were detected. In 55% of the

sediment samples taken, low amounts of carbon disulphide were found (Ordelman et al, 1999). However, the amounts of ETU and carbon disulphide detected are the result of the combined use of all dithiocarbamates and hence do not originate from metiram solely.

A mixture of ethylene-bisdithiocarbamate fungicides including metiram was detected in various vegetables collected in the United States during 1978-1982 (Yess in HSDB). A mixture of dithiocarbamate fungicide including metiram was detected in Ontario-grown cauliflower, cucumber and tomatoes collected during 1980-1985. A maximum concentration of 1 mg/kg (for the total dithiocarbamate fungicides expressed as zineb equivalent) was detected in a cauliflower composite sample. On the other hand, no metiram was detected in fruits including cherries and peaches produced in Ontario during 1980-1984(Franke in HSDB)

Ethylene bis-dithiocarbamate fungicides (including metiram) were found to be the most prevalent residue found on fruits and vegetables analysed in Switzerland in 1989-90. Out of 461 salads analysed in Geneva, 23 samples had levels of ethylene bis-dithiocarbamate fungicides exceeding tolerance values (Coryl in HSDB)

In a UK survey on apricots carried out by the Working Party of Pesticides Residues (WPPR) in 1996, the Acceptable Daily Intake (ADI) for ETU appeared to be exceeded. Researchers found 21% of 24 samples contained detectable residues of dithiocarbamates. Relatively high dithiocarbamate residues at 17 mg/kg were found in one sample. The WPPR report on the survey concluded that a risk assessment was carried out which indicated that the high dithiocarbamate residues detected would lead to a "small exceedance of the ADI" for a high level infant consumer of apricots. Because these levels are unlikely to occur the WPPR further concluded that no adverse effects on health would be expected from occasional exceedances of the ADI. However, clearly safety margins have been eroded.

Conclusion

Metiram is a fungicide used to prevent crop damage in the field and to protect deterioration in storage and transport. Workers involved in the production or usage of metiram have the highest risk of exposure, however the general population is also exposed through consumption of metiram treated foods. Metiram does not accumulate in the environment due to its relative instability. However, hydrolysis and photodegradation of metiram, as well as other EBDCs, result in the formation of more stable, less immobile and hazardous metabolites such as ETU and carbon disulphide.

Based on the toxic metabolite ETU mancozeb is classified as a substance of high exposure concern

References

DHC99 (1999). Dutch Health Council. Endocrine disrupters in the Netherlands

Extoxnet, (2002). Data Bank on pesticide information profiles (http://ace.ace.orst.edu/info/extoxnet/pips/metiram.htm)

HSDB, (2002). Hazardous Substances Data Bank, a database of the library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

Ordelman, H.G.K., et al, (1999). Watersysteemverkenningen 1996. Een analyse van de problematiek in aquatisch milieu. Dithiocarbamaten. RIZA nota 96.040

SRC (2002). Syracuse research corporation PhysPop on-line database, http://esc.syrres.com

METRIBUZIN (CAS NO. 21087-64-9)

Metribuzin, chemical name 4-Amino-6-(1,1-dimethylethyl)-3-(methylthio)-1,2,4-triazin-5(4H)-one; 4-Amino-6-tert-butyl-3-(methylthio)-1,2,4-triazin-5(4H)-one or 4-amino-6-tert-butyl-3-(methylthio)-1,2,4-Triazin-5(4H)-one, belongs to the group of triazines and triazoles.
Trade names include Bay 94337, Bayer 6159H, DIC 1468, Lexone, Salute, Sencor, Sencoral, Sencorex

Chemical characteristics

Molecular Structure metribuzin: C8-H14-N4-O1-S1

MW = 214.29

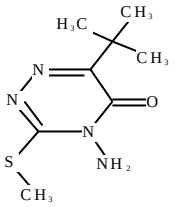


Table 1: Physical/chemical properties metribuzin

Parameter	Metribuzin
Water solubility (mg/L 25°C)	1050 (SRC) 1000 (ARS Pesticide Properties Database)
Vapour pressure (mm Hg 25°C)	4.35 x 10-7 (SRC)
Log Kow	1.7 (SRC)
Henrys Law constant (atm cu3 m/mole)	1.17·10-10 (SRC)
Koh (cm3/molecule sec)	1.82·10-11(SRC)
Biodegradation	
BCF (L/kg)	4.06 (SRC) 10 (Freitag 1985 in HSDB)
Koc (L/kg)	60 (Ahrens 1994 in HSDB) 1196 (SRC)

Abiotic degradation
Metribuzin is hydrolysed with a half-life of 90 days (Gustafson 1989 in HSDB). Photodegradation in water is rapid. A photolytic half-life of 4.3 hours in water, pH 6.6, has been reported (USEPA 2000 in HSDB). In soil, metribuzin had a photolytic half-life of 2.5 days in sandy loam at temperatures up to 31º C. Only Metribuzin at the soil surface will be affected by photolysis (USEPA 2000 in HSDB). The estimated vapour-phase half-life in the atmosphere is 21 hours as a result of reaction with photochemically produced hydroxyl radicals (SRC and Meylan 1993 in HSDB).

Biotic Degradation
Biodegradation is the major mechanism governing the removal of metribuzin in soil. Losses due to volatilisation or photodegradation are considered to be insignificant under field conditions (Stevens 1991 and Kidd 1991 in ECOTOXNET). Metribuzin is moderately persistent in soil with aerobic degradation half-lives ranging from 30-120 days depending on soil type, climate etc (Wauchope 1992 in ECOTOXNET). Under optimal conditions, degradation half-lives between 14-28 days have been measured (Ahrens 1994 in HSBD). A half-life of 172 was found in a sandy loam soil (Ahrens 1994 in HSDB). Under anaerobic conditions, half-lives of metribuzin in soil ranging from 112-439 days have been reported. Due to its high water solubility and poor binding properties, metribuzin is potentially leached from the soil to surface and ground water. A degradation half-life of 7 days has been measured in pond water (Tomlin 1994).

Bioconcentration
A bioconcentration factor of 10 has been measured in fish, suggesting that the potential for bioaccumulation in aquatic organisms is low (Freitag 1985 in HSDB). In addition, the low persistence in water and low log Kow value indicates that the substance is not likely to present a risk of bioaccumulation in the aquatic environment. In mammals it has been shown that 98% of orally administrated metribuzin is eliminated within 96 hours (Tomlin 1994).

Use, exposure and emissions
Metribuzin is used for control of a large number of grass and broadleaf weeds in agricultural crops, on turf, grass and on fallow lands. Uptake of Metribuzin in plants primarily takes place via the roots and to a lesser extent via the leaves. Metribuzin inhibits photosynthesis in susceptible plants. Occupational exposure to metribuzin may occur though inhalation and dermal contact during manufacturing and handling (incl. use) of the substance (HSDB). The general population may be exposed via residues in crops and contaminated drinking water (Duggan 1983, Wnuk 1988 and Frank 1990 in HSDB).

Release to the environment
Release to the environment is an intended result of the use of metribuzin as a pesticide. Metribuzin may also be released from the production site.

Summary of environmental fate
Following application to soil, biological degradation is expected to be the major mechanism of removal. As metribuzin is highly mobile in soil, leaching to surface water and ground water may be significant. If released to water, photo- and biodegradation will lead to a rapid removal of metribuzin. In water, metribuzin is likely to be found in the water column rather that in the sediment due to its poor binding properties. Volatilisation from water surfaces is not expected to be of significance (Lyman 1990 in HSDB).

If released to air, metribuzin will exist in both vapour and particulate phases. In the vapour phase, a photodegradation half-life of 21 hours has been estimated (SRC in HSDB). Particulate phase metribuzin will be removed from the atmosphere via wet and dry deposition (SRC in HSDB).

Vulnerable use and vulnerable groups
Workers involved in manufacturing and handling (incl. use) of the substance are expected to be the most vulnerable groups.

Environmental concentrations
In lake Eyre tributaries, which drain agricultural watersheds, average time weighted metribuzin concentrations ranges from 0.07-0.29 µg/l in the period 1983-1991 (Richards 1993 in HSDB). An average concentration of 0.029 µg/l was detected in 18 out of 174 lakes/reservoirs in the United States (USEPA 2000 in HSDB). In a Canadian river, average concentrations of 0.8-7.7 µg/l have been measured in different sets of samples (Frank 1990 in HSDB). In rural waste water treatment plant effluent, a maximum concentration of 1.2 µg/l was found in Germany between 1996-1997 (Nitschke 1998 in HSDB).

In a reconnaissance survey of mid-western streams in the United States, pre-application concentrations were below 1 µg/l and generally below the detection limit of 0.05 µg/l, whereas post-application concentrations 1.4, 1.2 and 0.5 µg/l in 1989, 1994 and 1995 respectively USEPA 2000 in HSDB).

In groundwater, metribuzin was found in 136 of 5010 sources with average metribuzin concentrations of 0.048 µg/l (USEPA 2000 in HSDB). Average concentration levels of 0.05-2.10 µg/l have been detected in groundwater in Iowa, Kansas, Maine, Minnesota and Wisconsin (Williams 1988 in HSDB). Metribuzin and two of its metabolites were detected in groundwater in Wisconsin in concentrations of 2.3 µg/l (parent compound) and 7.6 µg/l (total residues). More than two years after application, metribuzin residues were still detected in groundwater (USEPA 2000 in HSDB).

Metribuzin has been detected in drinking water in 27 out of 1814 Public Water Supplies from surface water sources in the United States at average concentrations of 0.097 µg/l. In drinking water from groundwater supplies, the average concentrations were 0.96 µg/l (USEPA 2000 in HSDB). In treated drinking water, metribuzin concentrations of 0.14-0.45 µg/l was detected in Iowa public water supplies, whereas a concentration of 0.89 µg/l was detected in an untreated drinking water sample (Wnuk 1988 in HSDB).

Conclusion
Metribuzin is a pesticide used for the control of pests in agriculture. The workers involved in the production of metribuzin and in spraying have the highest risk of exposure, but the general population is also exposed through food and drinking water containing metribuzin residues. In the environment, metribuzin is primarily removed via biological degradation and it not expected to bioaccumulate in living organisms. Due to its use (also in households), emission patterns and moderate persistence, metribuzin is a chemical with high exposure concern.

References
The ARS Pesticide Properties Database, http://wizard.arsusda.gov/acsl/ppdb.html

SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

HSDB (2002). Hazardous Substances Data Bank (2002). A database of the national library of medicine's TOXNET system, http://toxnet.nlm.nih.gov

ECOTOXNET, (2002). The EXtension TOXicology NETwork, A data base of toxicology and environmental chemistry information about pesticides, http://ace.ace.orst.edu/info/extoxnet/

Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council , Surrey, UK and the Royal society of chemistry, Cambrigde, UK.

NONACHLOR, TRANS- AND CIS- (CAS NO 3734-49-4)

Chemical name: 1,2,3,4,5,6,7,8,8-nonachloro-2,3,3a,4,7,7a-hexahydro-4,7-Methano-1H-indene belongs to the group of chlorinated cyclodiene insecticides.

Nonachlor is a mixture of two isomers:
trans-Nonachlor (CAS no 39765-80-5); 1,2,3,4,5,6,7,8,8-nonachloro-2,3,3a,4,7,7a-hexahydro-, (1alpha,2beta,3alpha,3aalpha,4beta,7beta,7aalpha)- 4,7-Methano-1H-indene and
Cis-nonachlor (CAS No 5103-73-1); 1,2,3,4,5,6,7,8,8-nonachloro-2,3,3a,4,7,7a-hexahydro- (1alpha, 2alpha, 3alpha, 3aalpha, 4beta, 7beta, 7aalpha)- 4,7-methano-1H-indene.

Chemical characteristics

Molecular formula: C10-H5-Cl9

MW = 444.23

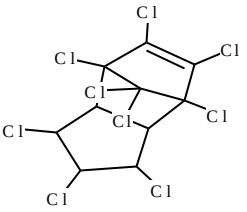


Table 1: physical/chemical properties of nonachlor

Parameter	Nonachlor
Water solubility (mg/L 25°C)	6.12 x 10-3 (SRC)
Vapour pressure (mm Hg 25°C)	1.00 - 2.16 x 10-6 (SRC)
Log Kow	6.08-6.35 (SRC)
Henrys Law constant (atm cu3 m/mole)	4.87 x 10-12 (SRC)
Koh (cm3/molecule sec)	2.06 x 10-4 (SRC)
Biodegradation	Recalcitrant (SRC)
BCF (L/kg)	15470 (SRC)
Koc (L/kg)	1.46 x 10+5 (SRC)

Nonachlor is a major constituent of technical chlordane and technical heptachlor (verschueren in HSDB). Technical grade heptachlor contains approximately 73% heptachlor, 22% *trans*-chlordane, and 5% nonachlor (Leber and Benya 1994, IARC 1979). Menzo (1980) report 7% nonachlor in chlordane. The ratio of cis- and trans congeners depends on the production process.

Abiotic degradation
If released in air nonachlor is expected to be stable to light and hence not sensible towards photodegradation.
If released to water nonachlor is not expected to undergo significant hydrolysis, oxidation or direct photolysis. Sensitised photolysis might be possible, however when released to water nonachlor rapidly absorbs to sediment and particulate matter and hence photolysis is severely impaired.

Biotic degradation
Little is certain about the environmental fate and degradation of cyclodiene insecticides (HSDB). QSAR calculations, however, predict that nonachlor and e.g. chlordane and heptachlor are recalcitrant in the environment (SRC). Stable epoxide degradation products, however, have been detected in the environment (HSDB). Reported soil and surface water half-lives of chlordane vary between 283 days to 2.3 years, groundwater degradation is even slower TD50 varies from 566 days to 7.8 years. Half-lives of nonachlor are expected to be similar to those of chlordane.

Bioconcentration
Nonachlor is highly persistent and expected to be highly bioaccumulative based on its calculated Kow and BCF. Observed bioaccumulation of chlordane in mother milk and biota predicts the same scenario for nonachlor. The epoxide degradation products of nonachlor are heavily bioconcentrated in lipids of aquatic wildlife, humans and foods.

Use, exposure and emission
Nonachlor is used as a constituent of chlordane. Chlordane (which solely lacks one of the chlorine atoms) has been used as a broad-spectrum insecticide for more than 35 years, mainly on non-agricultural crops and animals. Perhaps 600 million lb of these highly chlorinated, cyclic organic compounds have been dispersed into soil, air, water, & food of the USA during the last 30 yr (HSDB). Human exposure might occur through the ingestion of food. However since chlordane was not normally used on food crops, and overall use is prohibited nowadays, this appears not to be a

significant problem. Due to its persistent nature nonachlor might still be present in the environment, however it is expected to be present as an immobile sink.

Summary of environmental fate
Chlordane is applied as a spray. Due to limited volatility and high octanol-water partition, it is expected that nonachlor will be distributed to soil and sediment mainly. Calculations suggest low removal by degradation (SRC, Fugacity calculations). Nonachlor is expected to be highly immobile in soil and sediment, leaching to ground- and surfacewater is not expected.

Environmental concentrations
Cis- and trans-nonachlor have been detected in the Upper Bay (USA) at a concentration of 0.2 and 0.17-0.24 ppb, respectively (Waffle). Trans-nonachlor has been detected at low concentrations in fish in the Northern central USA in less than 10% of the tested samples (HSDB).

Vulnerable groups
Since chlordane is no longer used as an insecticide, there is no professional exposure. No other uses of nonachlor are reported. Because nonachlor is highly persistent (TD50 > 1 year) and bioaccumulative it might still be present in the environment. Chlordane was detected in biota, human tissue and mother milk and hence human exposure was likely. However, nonachlor is rarely detected and the largely immobile sinks of nonachlor that are still present in our environment are slowly fading away.

Conclusions
Nonachlor was used as a constituent of the insecticide chlordane, which was mainly used on non-crops and animals. The use of chlordane is prohibited in the EU, USA and Japan. Nonachlor is persistent and highly bioaccumulative. Due to limited volatility long-range air transport is not likely. Nonachlor will therefore generally be present as an immobile sink. Since chlordane is no longer used as an insecticide, the phase out of the sole use of the chemical results in a low exposure concern..

References
EHC 34 (1984), Chlordane environmental Health Criteria 34, International program on Chemical Safety (ICPS), WHO Geneva

HSDB (2002). Hazardous substances databank, a database of the national library of medicine's TOXNET system, http://toxnet.nlm.nih.gov

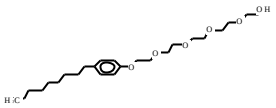
SRC (2002). Syracuse research corporation PhysPop on-line database, http://esc.syrres.com

NONYLPHENOLETHOXYLATE (CAS NO 9016-45-9)

Nonylphenolethoxylate (NPE) is part of the group of alkyl phenols ethoxylates (APEO). This specific compound is considered to be one of the most important compounds within the group. Nonylphenolethoxylate is produced via the a reaction of nonylphenol with ethylene oxide. The resulting product is not pure, but a mixture of nonylphenolethoxylates with a variable number of ethoxylate units (EO), ranging from zero (very low level) to over 100. Most common is nonylphenol with five ethoxylate units. Furthermore, polyethylene glycol can be found in most NPEO as an inert by-product (Groshart et al 2000).

Chemical characteristics

Molecular formula nonylphenolethoxylate:
C15-H24-O1-[C2-H4-O1]n



MW = 440.63 (n = 5)

Table 1: Physical/chemical properties of nonylphenol ethoxylate

Parameter	Nonylphenolethoxylate
Water solubility (mg/L, 25°C)	> 1000 mg/L (CITI in HSDB)
Vapour pressure (mm Hg, 25°C)	3.2 x 10-10 (Lyman 1986; SRC; both in HSDB)
log Kow	4.48 n = 5 (SRC)
Henry's law constant (atm m3/mole)	4.1x 10-12 (Meylan & Howard 1990 in HSDB)
Biodegradation	Yes/ primary
BCF (L/kg)	7-5000 (Groshart 2000)
Koc (L/kg)	2600-5200 (Groshart 2000)

Nonylphenolethoxylates are present as a pale yellow viscous liquid with a slight phenolic odour. NPE with 35 or 40 EO units are solids.

Abiotic degradation

Hydrolysis of NPEO is an important process in its degradation, resulting in the release of ethoxylate units. The main products are nonylphenol monoethoxylate and diethoxylate (Groshart et al 2000).
Photolysis of NPEO in the atmosphere is expected to be an important removal process, with short half-life times. It was found that photolysis in water is not an important mechanism for the removal of NPEO from water (Groshart et al 2000).

Biotic degradation

Primary degradation of NPEO is occurring, with nonylphenol diethoxylate as primary degradation product after 4 days; this degradation product was degraded for 50% after 28 days. Degradation scheme suggest both aerobic as anaerobic degradation to nonylphenol monoethoxylate and nonylphenol (Groshart et al 2000).
Biotic degradation in soil is fast after adaptation of 15-20 days. The mineralisation takes solely place at the nonyl chain (Groshart et al 2000).

Bioconcentration

Bioaccumulation of NPEO has been studied by Ahel et al (1993 in Groshart et al 2000). No clear BCF values can be presented, because biomagnification is also part of the process. Bioaccumulation factors ranged from 7 (nonylphenol diethoxylate for birds) to 3500-5000 (nonylphenol monoethoxylate in algae). On the whole, nonylphenol monoethoxylate bioaccumulates more strongly than nonylphenol diethoxylate, due to higher hydrophobicity (Groshart et al 2000).

Use, exposure and emissions

APEOs are used as nonionic surfactants, detergents and wide-range stabilisers. These chemicals are primarily used for industrial applications, covering more than 70 percent of the APEOs used in Europe. The industrial markets include leather processing, agricultural industry, chemical industry, textile industry and polymers industry. The non-industrial applications include institutional cleaning products, paints, lacquers and wetting agents for agricultural chemicals. NPEO is voluntarily banned from household cleaning products in the EU (Groshart et al 2000).
Total NPEO production within the European Union is estimated to be approximately 118,000 tonnes (Groshart et al 2000).

Some of the applications of NPEO cause emissions to the environment. Emissions to wastewater and surface water were extrapolated from use, using emission factors. For the EU it was estimated that annually 40705 tonnes and 3375 tonnes were emitted to wastewater and surface water, respectively. In wastewater treatment plants approximately 90-95% of the NPEO is removed (Groshart et al 2000).

Release to the environment
As was shown in the emissions paragraph, many of the applications of NPEO lead to the emissions to surface and wastewater.

Summary of environmental fate
NPEO have high water solubility and low vapour pressure. Emissions to the aquatic environment are expected to stay in the water phase. NPEO with low number of EO units are rather hydrophobic, whereas NPEO with high numbers of EO units are highly soluble in water. Due to hydrolysis, the amount of ethoxylate units will be diminished to one or two. These compound will sorb to all solid particles, resulting in some removal from the water phase. In soil low mobility and relatively high biodegradability is expected.

Environmental concentrations
NPEO has been detected in fresh water in Switzerland, the UK, the USA and the Netherlands, as is presented in table 2. Furthermore it was found in fresh water sediments. as is presented in table 3.

Table 2: Nonylphenol ethoxylates in fresh water (µg/l) (table from Groshart et al 2000)

Surfacewater	**Year**	**NPnEO**	**NPnEC**	**Reference**
River Glatt	Switzerland			
- range in surfacewater	1984	3-110	2-115	Ahel et al., 1994
Various rivers	United Kingdom			
River Aire	1995	15-76	-	Blackburn et al., 1999
River Mersey	1995	6-11	-	Blackburn et al., 1999
River Tees	1995	76	-	Blackburn et al., 1999
Various rivers	United States			
- range in surfacewater	1990	0.13- 1.8	-	Naylor,1992
Various surfacewaters	The Netherlands			
Kanaal Gent-Terneuzen	1997	0.14	-	LOES, 1999

NPnEO : Nonylphenol ethoxylate with n ethoxylate groups
NPnEC : Carboxylic acid of NPnEO formed by oxidation of the terminal hydroxyl group
n = 1, 2

Table 3 Nonylphenol ethoxylates in fresh water sediments (µg/kg ds) (Table from Groshart et al 2000)

Surfacewater	**Year**	**NPnEO**	**NPnEC**	**Reference**
River Glatt	Switzerland			
- at effluent discharge	1984	11600	6800	Ahel et al., 1994
- average value	1984	7600	4500	Ahel et al., 1994
River Rhine	Germany			
Average value	1987	1500	-	TemaNord, 1996
Various surfacewaters	The Netherlands			
Nieuwe Waterweg	1997	8100	-	LOES, 1999
Noordzeekanaal Amsterdam	1997	5700	-	LOES, 1999
Kanaal Gent-Terneuzen	1997	2980	-	LOES, 1999

NPnEO : Nonylphenol ethoxylate with n ethoxylate groups
NPnEC : Carboxylic acid of NPnEO formed by oxidation of the terminal hydroxyl group
n = 1,2

Vulnerable use and vulnerable groups
Large differences in emission factors were observed for the various applications of NPEO. Therefore applications with high emission potentials on surface water (as opposed to wastewater) are vulnerable uses. These applications include pulp and paper industry, leather industry processing and industrial and institutional cleaning (Groshart et al 2000).

Conclusions

Nonylphenol ethoxylate is a chemical that is used in high quantities in a large variety of applications. The vast majority of these applications are industrial. However, NPEO is also present in consumer goods, e.g. paint. NPEO is primarily degraded. However, NPEO with few ethoxylate units have been detected in the environment.

Therefore, the concern for exposure for nonylphenol ethoxylates is high.

References

EPIWIN, calculation method of EPISUITE, USEPA

Groshart et al, Chemical study on alkylphenols, 2000, National Institute for Coastal and Marine Management/RIKZ, RPS BKH, Delft, The Netherlands

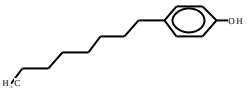
HSDB Hazardous Substances Data Bank, http://toxnet.nlm.nih.gov, visited November 2002.

4-OCTYLPHENOL (CAS NO 1806-26-4)

4-Octylphenol belongs to the group of alkylphenols.

Chemical characteristics

Structural formula 4-octylphenol: C14-H22-O1



MW = 206.33

Table 1: Physical/chemical properties of 4-Octylphenol

Parameter	4-Octylphenol
Water solubility (mg/L 25°C)	3.1 (SRC) 12.6 (Shiu et al 1994)
Vapour pressure (mm Hg 25°C)	9.8 x 10-5(Hinckley 1990 in HSDB)
Log Kow	4.12 (Shiu et al 1994) 5.50 (SRC)
Henrys Law constant (atm cu3 m/mole)	4.50 x 10-6 (SRC) 4.85 x 10-6 (Shiu et al 1994)
Koh (cm3/molecule sec)	5.03 x 10-11 (SRC)
Biodegradation	Moderate
BCF (L/kg)	129-297(Tsuda et al 2000) 341.4 (SRC)
Koc (L/kg)	3500-18000 (Johnson et al 1998) 33010 (SRC)

Abiotic degradation
4-octylphenol may photodegrade indirectly in natural water through the reaction with photo excited Fe(III) (Brand et al 2000). In air, a rate of $50.3 \cdot 10^{-12}$ cm^3 $molecule^{-1}$ s^{-1} has been predicted (EPIWIN) for the reaction between 4-octylphenol and atmospheric hydroxyl radicals, leading to a half-life of 0.213 days (12 hour day). 4-octylphenol is not expected to hydrolyse.

Biotic Degradation
The aerobic degradation (to CO_2) half-life of nonylphenol has been measured as 20 days (Staples et al 1999). Nonylphenol has a structure very similar to octylphenol and similar half-lives of octylphenol can be expected. The octylphenol metabolites octylphenoxyacetic acid and octylphenoxyethoxyacetic acid were shown both to be readily biodegradable using the OECD 301 B (modified Sturm method) (Staples et al 1999).

Bioconcentration
For 4-tert-octylphenol, environmental BCFs was determined by Tsuda et al (2000). BCF values for three kinds of fish were 129-297 whereas laboratory BCF value was 261 for Killifish (Tsuda et al 2000). This is slightly higher than a BCF value of 29.7 predicted from a log Kow of 4.12 (EPIWIN).

Use, exposure and emissions
4-octylphenol is used in manufacture of nonionic surfactants, as plasticiser, antioxidant, fuel oil stabiliser and as an intermediate for resins, fungicides, bactericides, dyestuffs, adhesives and rubber chemicals (Hawley 1977 in HSDB). The major source of octylphenol in the environment is most likely octylphenol based surfactants (octylphenolethoxylates) which degrades to octylphenol. Octylphenolethoxylates comprise 15-20% of the alkylphenolethoxylate consumption (Staples et al 1999).

Release to the environment
In Europe, 4-octylphenol in the environment will mainly arise from the degradation of octylphenolethoxylate in the anaerobic processes of sewage treatment plants and elsewhere, e.g. anaerobic sediment and anaerobic sewage system. Octylphenolethoxylate itself is mainly released to wastewater after being used for cleaning purposes.

According to a sewage treatment plant (STP) model, 87.5 % of the 4-octylphenol that enters a STP will be removed with the sludge due to strong adsorption (EPIWIN) while the remainder more or less leaves with the effluent as degradation is estimated to be slow (EPIWIN).
The sludge may be applied to agricultural land, incinerated, stored or used for other purposes.

Summary of environmental fate
After emission to water, 4-octylphenol is expected to sorb to suspended particles and sediment. Little volatilisation from water surfaces can be expected. In a model river, volatilisation half-life was 98 hours and in a model lake it was 1193 hours = 49 days (EPIWIN). In the water, and in aerobic parts of the sediment, octylphenol is expected to biodegrade, with half-lives somewhat larger than 20 days. Indirect photolysis may be important.

After emission to soil, which will mainly occur with the application of sludge, 4-octylphenol is expected to remain strongly sorbed to the sludge. This will reduce the volatilisation which is expected to be small and leaching is also expected to be minimal. In the soil, 4-octylphenol is expected to be degraded by microorganisms. No data on the rates are available but for nonylphenol in soil, 80% was removed the first month while nonylphenol still could be detected after 322 days (NCAP 2002).

After emission to air, which will mainly occur as a result of volatilisation, 4-octylphenol is expected to be found primarily in the vapour phase, where it will react rapidly with hydroxyl radicals and degrade. Atmospheric half-lives of 3 hours (light) has been estimated (EPIWIN).

Environmental concentrations
In eight rivers flowing into Lake Biwa, Japan, 4-tert-octylphenol was detected in 23 out of 48 samples, in concentrations of ND-0.09 µg/L. Lowest concentrations of nonylphenolethoxylates were observed in winter, supposedly because the degradation of alkylphenolethoxylates in waste water treatment plants was slow at low temperatures (Tsuda et al 2000). In Canadian waters near highly industrialised sites, concentrations of octylphenol from not detected to 0.084 µg/L was found (Staples et al 1999). A survey of 22 European estuaries showed sediment concentrations of octylphenol from not detected to 2.2 µg/kg (Staples et al 1999). Octylphenol was found in the sediment of the Great Lakes in concentrations of 0.002-23.7 µg/g (Gray et al 1999).

In the COMMPS list, 15 samples of sediment were reported to have an average concentration of 1.31 µg/L.

Vulnerable use and vulnerable groups
No vulnerable uses or groups have been identified.

Conclusion
4-octylphenol is used as raw material in the manufacturing of e.g. surfactants, detergents and wetting agents. It is also used as plasticiser, stabiliser in fuels, adhesive in rubbers and intermediate in several bactericides and pesticides. It will mainly arise in wastewater from degradation of octylphenolethoxylates after being used as a cleaning agent. Octylphenoles are inherently biodegradable and expected to be bioaccumulative. Because environmental levels have been detected and human exposure is expected through consumer goods containing octylphenoles it is prioritised as high exposure concern.

References
Gray, M.A.; Niimi, A.J.; Metcalfe, C.D. (1999)
Factors affecting the development of testis-ova in medaka, oryzias latipes, exposed to octylphenol.
Environmental toxicology and chemistry, Vol. 18, No. 8, pp. 1835-1842.

Tsuda, T.; Takino, A.; Kojima, M.; Harada, H.; Muraki, K. and Tsuji, M. (2000)
4-nonylphenols and 4-tert-octylphenol in water and fish from rivers flowing into Lake Biwa.
Chemosphere, Vol 41, pp. 757-762

Brand, N.; Mailhot, G.; Sarakha, M.andBolte, M. (2000)
Primary mechanism in the degradation of 4-octylphenol photoinduced by Fe(III) in water-acetonitrile solution.
Journal of photochemistry and photobiology A: Chemistry, Vol. 135, pp. 221-228

Staples, C.; Williams, J.B.; Blessing, R.L. and Varineau, P.T. (1999)
Measuring the biodegradability of nonylphenol ether carboxylates, octyl ether carboxylates, and nonylphenol.
Chemosphere, Vol. 38, pp. 2029-2039

NCAP 2002, Northwest coalition for alternatives to pesticides.
http://www.pesticide.org

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

EPIWIN v.3.10. Environmental property estimation programme package. Office of pollution prevention and toxics, US EPA. 2000.

Shiu, W.-Y.; Ma, K.-C.; Varhanícková, D. and Mackay, D. (1994)
Chlorophenols and alkylphenols: A review and correlation of environmentally relevant properties and fate in an evaluative environment
Chemosphere, Vol. 29, No. 6, pp. 1155-1224

Johnson, A.C.; White, C.; Besien, T.J. and Jürgens, M.D. (1998)
The Sorption potential of octylphenol, a xenobiotic oestrogen, to suspended and bed-sediments collected from industrial and rural reached of three English rivers.
The science of the total environment, Vol. 210/211, pp. 271-282

P-BENZYLPHENOL (CAS NO 101-53-1)

Other common names used for p-benzylphenol include 4-Hydroxydiphenylmethane, 4-Benzylphenol, alpha-Phenyl-p-cresol and 4-(phenylmethyl)-phenol. It belongs to the group of phenylhydroxyphenylmethanes.

Chemical characteristics

Molecular formula: C13-H12-O

MW 184.2372

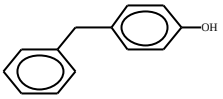


Table 1: Physical / chemical properties of p-benzylphenol

Parameter	p-benzylphenol
Water solubility (mg/L,25 ºC)	73.2 (SRC)
Vapour pressure (mm Hg, 25 ºC)	6.85 x 10-5 (SRC)
Log K_{OW}	3.47 (SRC)
Koh (m^3/molecule-sec at 25 ºC)	4.65 x 10-11(SRC)
Henry's law constant (atm-m3/mole)	4.99 E-8 (SRC)
Biodegradation	Yes (SRC)
Fish BCF	93.73 (SRC)
K_{OC}	1.82 x 10+4 (SRC)

P-benzylphenol is a powder at room temperature. Release to soil will lead to adsorption, based on the high K_{OC}. Volatilisation from water is expected to be low, based on a low Henry's law constant. Because bioconcentration is only moderate, will tend to stay in the water, and being degraded there. The high K_{OC} predicts that adsorption to suspended matter is an important mechanism for removal from the water compartment.

Abiotic degradation
The substance is rapidly degraded in air by hydroxyl radicals with an estimated half-life of 2.7 hours.

Biotic degradation
Calculations with BIOWIN predict readily biodegradability; modelling with the MITI model forecasts a low probability of ready biodegradability (EPI). However, p-benzylphenol is expected to be low accumulative (Nikunen 1990)

Use, exposure and emissions
The intended use of this chemicals has not precisely been derived. It is used in plastics as a germicide, antiseptic, preservative and in organic synthesis (Nikunen).

Summary of environmental fate
It is expected in multimedia fate modelling calculations that p-benzylphenol will partition to soil and water. In these compartments the calculated half-live is 360 hours.

Vulnerable groups and use
Due to its use in plastics p-benzylphenol might be present in food packaging and consumer goods (partly) consisting of plastic. For example babies chewing on plastic toys might be a vulnerable group.

Environmental concentrations
No data could be found on the environmental presence of p-benzylphenol

Conclusion
Little is known about this compound, even its use remains a bit unclear. However, p-benzylphenol might be used in plastics and hence human exposure might occur. Because we know relatively little about this compound is was classifies as high exposure concern.

References
Nikunen. Leinonen and Kultamaa (1990). Environmental properties of chemicals, ministry of environment, Helsinki, Finland.

SRC (2002). Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

PENTACHLOROBENZENE (CAS NO 608-93-5)

Pentachlorobenzene, official chemical name 1,2,3,4,5-pentachlorobenzene. Belongs to the group of chlorophenols and –benzenes.

Chemical characteristics

Molecular formula pentachlorobenzene: C6-H1-Cl5

MW = 250.34

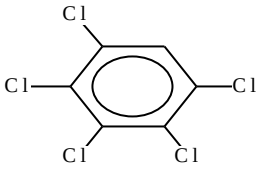


Table 1: Physical/chemical properties of pentachlorobenzene

Parameter	Pentachlorobenzene
Water solubility (ng/L 25°C)	1.33 (Yalkowsky 1992 in HSDB)
Vapour pressure (mm Hg 25°C)	1.01 x 10-3 (SRC) 6.5 x 10-3 (Resendes 1988 in HSDB)
Log Kow	5.17 (Hansch 1985 in HSDB)
Henrys Law constant (atm cu3 m/mole)	7.1 x 10-4 (Oliver1985 in HSDB)
Koh (cm3/molecule sec)	5.9·10-14 (Meylan 1993 in HSDB)
Biodegradation	Very slow
BCF (L/kg)	1909 (SRC) 1100-8600 (CITI 1992 in HSDB)
Koc (L/kg)	2002 (SRC) 3160-126000 L/kg (HSDB)

Abiotic degradation
Pentachlorobenzene does not hydrolyse in the environment (HSDB) but does photolyse in air and water. In the atmosphere, reaction with hydroxyl radicals occurs with half-lives of about 277 days (SRC in HSDB). Pentachlorobenzene will photolyse in surface waters and 41 % reduction in concentration have been measured after 24 hours of irradiation with light of wavelengths longer than 290 nm (Choudry 1984 in HSDB).

Biotic Degradation
Experiments have shown that pentachlorobenzene degrades very slowly in the environment. 0 % BOD degradation was observed in sludge over a four week incubation period (SRC in HSDB), and soil half lives of 194 and 345 days have been measured (Beck 1974in HSDB). There is some indication that dechlorination may take place anaerobically (Beurskens 1995 and Masunga 1996 both in HSDB).

Bioconcentration
An estimated BCF of 1,100-6,800, measured in carp, indicates that bioconcentration in aquatic organisms is very high. (CITI 1992 in HSDB).

Use, exposure and emissions
In the past pentachlorobenzene just like trichlorobenzenes and tetrachlorobenzenes were used togeteher with PCB in dielectric fluids. Furthermore it was used as a fungicide and as an intermediate for the production of pentachloronitrobenzene, better known as quintozene (CEPA, Ullmanns in HSDB; UNECE). However, the use of pentachlorobenzene in dielectric fluids and as a fungicide have ceased. Furthermore, alternative techniques are available to produce quintozene without the use of pentachlorobenzene. Due to these developments, use and production of pentachlorobenzene (in the EU) have completely come to an end.
However, although severely restricted exposure to pentachlorobenzene is still expected because of its persistency in the environment and redistribution via long-range air transport. Moreover, pentachlorobenzene may also arise from photolytic degradation of hexachlorobenzene (HCB) (Clayton 1981 in HSDB). The use of the highly persistent fungicide HCB, however, is also is severely restricted and banned in the EU (UNECE).

Release to the environment
Pentachlorobenzene may be released to the environment via spillage as a result of its former use as a dielectric fluid. Due to the availability of alternative techniques, release as a result from the use of the fungicide quintozene, in which it formerly occured as an impurity, will be minimal. However, pentachlorobenzene may also be released by the incineration of plastics, organic solvents and is

found in effluents from municipal and hazardous waste incinerators (HSDB). Although release to the environment does not arise from current use or production, exposure is still expected due to its former use, its persistent nature and the possibility of redistribution via long-range air transport (CEPA, UNECE).

Summary of environmental fate
After emission to water, pentachlorobenzene is expected to sorb to sediment and suspended particles. It is also expected to volatilise from the water surface. A river and a lake model showed volatilisation half lives of 7 hours and 180 hours respectively, when sorption is disregarded. Sorption may attenuate volatilisation (Lyman 1990 and SRC in HSDB). Pentachlorobenzene is expected to photolyse in water.

After emission to soil, pentachlorobenzene is expected to be immobilised by sorption to soil particles. It is expected to volatilise from moist soil surfaces but it is not expected to volatilise from dry soil surfaces, due to low vapour pressure. Pentachlorobenzene is only expected to be degraded slowly in soil (HSDB).

After emission to air, pentachlorobenzene is expected to exist as a vapour in the atmosphere where it is degraded slowly by photolysis and reaction with hydroxyl radicals (HSDB).

Environmental concentrations
Pentachlorobenzene was detected in the Wall and Ourde maas rivers, Holland, in concentrations of 1-34 ppt, Lek river 0-3 ppt, Meuse river: 2-4 ppt (Duinker 1979 in HSDB). In the Rhine river Germany concentrations were 1-200 ppt (Fisher 1978 in HSDB).

Pentachlorobenzene was detected in the estuary of river Meuse in Holland in concentrations from 0.1-18 ppt (Kuntz 1984 in HSDB) and in the Scheldt estuary, The Netherlands, in concentrations of 1-13 ng/g (Vanzoest 1991 in HSDB).

Pentachlorobenzene has been found in sediments of many polluted water bodies, e.g. in most samples from lake Ontario, Canada. In the sediment of the Norwegian fjord Frierfjord average concentrations of 37 ppm were found (Bjeih 1980 in HSDB). In the Dutch lake Ketelmeer, concentrations of 10 and 15 ng/kg have been observed (Beurskens 1994 in HSDB). Pentachlorobenzene has also been measured in suspended particles in concentrations of 3-500 ppb (Duinker 1979 in HSDB).

In urban/suburban air of Bavaria, pentachlorobenzene was detected in concentrations of 100-190 pg/m^3. Pentachlorobenzene has also been found in the air of remote areas. I the air of Spitzbergen, Norway, concentrations of 5.1-37 pg/m^3 was measured in 1980-1981 (Oehme 1984 in HSDB) and in the air of the Enewtak atoll, concentrations of 27-39 pg/m^3 was found (Giam 1984 in HSDB).

In the European COMMPS program European environmental concentration of pentachlorobenzene was determined in the water compartment (row 1 table 2) and water sediment (row 2 table 2)

Table 2: Occurrence of PCP in the European environment (COMMPS)

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
608-93-5	pentachlorobenzene	0.0014	0.0010	0.0009	0.0002	7	179	83
608-93-5	pentachlorobenzene	48.72	5.12	14.59	13.89	22	459	375

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

Vulnerable use and vulnerable groups
No vulnerable uses or groups have been identified, but Workers involved in production and use of pentachlorobenzene (HSDB) are expected to be exposed more than the general public.

Conclusion
Although no current use of pentachlorobenzene is reported, humans and wildlife may still be exposed to this compound due to its former uses (dielectric fluids, fungicide and intermediate of quintozene), its persistent nature and its possibility to redistribute via long-range air transport. Furthermore, pentachlorobenzene is observed to be present in different environmental compartments and is highly

bioaccumulative. Hence, although pentachlorobenzene is in the phase of phasing out it is considered to be of high exposure concern.

References

CEPA, Canadian Environmental Protection Act: Priority substance list assessment report pentachlorobenzene (http://www.hc-sc.gc.ca/hecs-sesc/exsd/cepa/pentachlorobenzene.pdf)

Howard, P.H. (ed.) (1997) Handbook of environmental fate and exposure data for organic chemicals. Lewis publishers, Boca Raton USA.

HSDB, (2002). Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov)

UNECE, United Nations Economic Commission for Europe: Summary of information related to scheduled reassessment of substance related provisions in the protocol on POPs and associated expert judgement (http://www.unece.org/env/popsxg/executive_summary.pdf)

PENTACHLOROPHENOL (PCP) (CAS NO 87-86-5)

Pentachlorophenol, official chemical name 1-hydroxy-2,3,4,5,6-pentachlorobenzene, belongs to the group of chlorophenoles and –benzenes.
Trade names include, penchlorol, santophen 20, pentacon, penwar, penta, chlorophen, dowicide EC-7 7Pol-NU, Oz-88, Osmoplastic, Forepen; Dura-Treet, cryptogil oil, durotox, EP 30, fungifen, grundier arbezol, lauxtol, liroprem, term-i-trol, thompson's wood fix, penta-kil, peratox, permacide, permagard, permasan, permite, priltox and santobrite.

Chemical characteristics

Molecular formula PCP: C6-H1-O1-Cl5

MW = 266.34

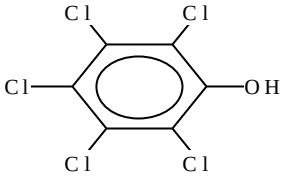


Table 1: Physical/chemical parameters pentachlorophenol

Parameter	PCP
Water solubility (ng/L 25°C)	14 (Yalkowsky 1992 in HSDB)
Vapour pressure (mm Hg 25°C)	1.1x 10-4 (Callahan1979 in HSDB)
Log Kow	5.12 (Hansch 1995 in HSDB)
Henrys Law constant (atm cu3 m/mole)	2.45 x 10-8 (Hellman 1987 in HSDB)
Koh (cm3/molecule sec)	5.5 x 10-13 (Meylan 1993 in HSDB)
Biodegradation	Slow
BCF (L/kg)	100-1000 (HSDB) 695.7 (SRC)
Koc (L/kg)	1250 - 1800 total 25000 undissociated (HSDB) 3380 (DSRC)
pKa	4.7 (Cessna 1978 in HSDB)

Abiotic degradation
The dissociated form of pentachlorophenol is susceptible to photolysis and 90% degradation has been observed in surface water at pH 7.3 in 10 hours. At pH 3, 40% degradation occurred in 90 hours (Weiss 1982 in HSDB). Photolysis may also take place in air. Reaction with ambient concentrations of hydroxyl radicals in air causes half lives of about 29 days (Meylan 1993 in HSDB). Hydrolysis does not seem to occur (HSDB).

Biotic Degradation
The degradation of pentachlorophenol is dependent on the concentration, probably because pentachlorophenol is toxic to degrading organisms. At concentrations of 30 mg/kg soil degradation rates were 0.3-0.5 mg/kg/day with 82% recovered as CO_2 in seven months. At higher concentrations, 100 mg/kg, only 2 % were transformed to CO_2 in seven months (Miethling 1996 in HSDB). Half-life of pentachlorophenol in soil is weeks to months (HSDB).

In sediments, complete degradation occurred after 17 days of which the first 11 days were a lag period (HSDB).

In natural waters, biodegradation rates of less than 5 ng/L·day have been observed Hudak 1988 in HSDB). In studies with artificial streams, pentachlorophenol was shown to degrade both aerobically and anaerobically but removal in six sewage treatment plants was low (Van loin 1984 in HSDB).

In HSDB it was concluded that pentachlorophenol degrades but may require several weeks for acclimatisation.

Bioconcentration
An estimated BCF of 100-1000 L/kg, indicates that bioconcentration in aquatic organisms is high. (Parrish 1978, Lu1975, Devillers 1996 and Bude 1985 all in HSDB).

Use, exposure and emissions
Pentachlorophenol was earlier widely used as a pesticide and as a wood preservative. However, since 1984, the purchase and use of pentachlorophenol in the US has been restricted to certified

applicators. It is no longer available to the general public. It is still used industrially as a wood preservative for utility poles, railroad ties, and wharf pilings (ATSDR 2001). It has also been used in textiles and leathers (HSDB), but this use is expected to have ceased in Europe while not elsewhere.

Release to the environment
Pentachlorophenol may be released to the environment from wood treating facilities, saw mills and from waste deposit sites and waste incineration facilities (HSDB).

Fate summary
After emission to water, pentachlorophenol is expected to sorb to sediment and suspended particles with the highest sorption occurring in acidic waters. Pentachlorophenol is not expected to evaporate from water surfaces (HSDB). In water and sediment pentachlorophenol is only biologically degraded very slowly, but photolysis may be an important degradation process.

It is also expected to volatilise from the water surface. A river and a lake model showed volatilisation half lives of 7 hours and 180 hours respectively, when sorption is disregarded. Sorption may attenuate volatilisation (Lyman 1990 and SRC in HSDB). Pentachlorobenzene will photolyse in surface waters and 41 % reduction in concentration have been measured after 24 hours of irradiation with light of wavelengths longer than 290 nm (Choudry 1984 in HSDB).

After emission to soil, pentachlorophenol is expected to be immobilised by sorption to soil particles. The degree of immobilisation will depend on pH with the highest immobility occurring at low pH. Pentachlorophenol is not expected to evaporate from moist soil surfaces due to low Henry's law constant, but in studies of terrestrial ecosystems where pentachlorophenol was applied as formulated pesticide, significant volatilisation took place with 25-51 % of the pentachlorophenol being detected in air (Gile 1979 and Metcalf 1979 in HSDB). Pentachlorophenol it is not expected to evaporate from dry soil surfaces, due to low vapour pressure (HSDB). At low concentrations biotic degradation in soil is expected to be slow and very slow at high concentrations (HSDB). Photolysis in soil may be significant (Donaldson 1997 in HSDB).

After emission to air, pentachlorophenol is expected to exist both as a vapour and as particulate in the atmosphere. Pentachlorophenol is degraded by reaction with hydroxyl radicals (half-life 29 days) and by direct photolysis. The particulate pentachlorophenol may be removed from the atmosphere by wet and dry deposition (HSDB).

Environmental concentrations
Pentachlorophenol was detected in large European rivers in concentrations up to 9.9 μg/L (HSDB). Waters in the vicinity of a Swedish papermill had concentrations of 43-1080 ng/L with the highest concentration very close to the mill (Soderstrpm 1994 in HSDB). In a Finnish brook close to a saw mill concentrations of 0.040 – 5.26 μg/L were measured (Lampi 1992).

Pentachlorophenol has been measured in the sediments of streams. Near a wood treatment facility in Canada, concentrations of up to 590 μg/kg were measured (IARC 1998 in HSDB).

In seawater of North West Belgium and South East Holland concentrations of 0.02-0.18 ppb has been measured (VanZoest 1994 in HSDB).

The pentachlorophenol concentration in the air of Hamburg was 0.67 ppt (Bruckman 1988 in HSDB).

In the European COMMPS program European environmental concentration of PCP was determined in the water compartment (row 1 table 2) and water sediment (row 2 table 2)

Table 2: Occurrence of PCP in the European environment (COMMPS)

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
87-86-5	pentachlorophenol	0.1351	0.0706	0.4509	3.3787	85	2296	1527
87-86-5	pentachlorophenol	62.30	15.50	25.84	16.44	20	66	61

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

Vulnerable use and vulnerable groups
Workers involved in the use of pentachlorophenol for preserving wood and workers working with wood preserved with pentachlorophenol are expected to see the highest exposure (HSDB).

Conclusion
Although PCP is only expected to be used for special purposes such as wood preserving, human and wildlife exposure is expected. Pentachlorophenol is only slowly biodegradable and has the ability to bioaccumulate in living organisms. Due to these properties and its observed presence in different environmental compartments, it is considered to be of high exposure concern.

References
ATSDR, (2001). Agency for toxic substances and disease registry, USA. Homepage www.atsdr.cdc.gov/tfacts51.html

HSDB, (2002). Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov)

PICLORAM (CAS NO. 1918-02-1)

Picloram, chemical name 4-amino-3,5,6-trichloropyridine-2-carboxylic acid; 4-amino-3,5,6-trichloro-2-picolinic acid or 4-Amino-3,5,6-trichloro-2-pyridinecarboxylic acid, belongs to the group of pyrimidinic fungicides
Trade names include ATCP; Grazon; Tordon; Amdon; Access; borolin; K-PIN

Chemical characteristics

Molecular formula picloram:C6-H3-Cl3-N2-O2

MW = 241.46

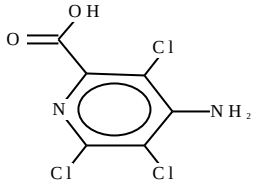


Table 1: Physical/chemical properties of picloram

Parameter	Picloram
Water solubility (ng/L 25°C)	430 (SRC)
Vapour pressure (mm Hg 25°C)	7.21·10-11 (SRC)
Log Kow	0.30 (SRC)
Henrys Law constant (atm cu3 m/mole)	5.33·x 10-14 (SRC)
Koh (cm3/molecule sec)	8.54·10-13 (SRC)
Biodegradation	Slow
BCF (L/kg)	3.2 (SRC) 31 (Garten in HSDB)
Koc (L/kg)	18.1 (SRC) 10-50 (Hamaker, Weidner and Rao in HSDB)

Abiotic degradation
Picloram is stable to hydrolysis (PMEP 2002) but may photodegrade rapidly in water and more slowly on soil surfaces. Photodegradation half-lives of picloram in water range from 2-10 days (Hedlund 1972 in HSDB). The estimated vapour-phase half-life in the atmosphere is 12 days as a result of reaction with photochemically produced hydroxyl radicals (USEPA 1986 in HSDB).

Biotic Degradation
Picloram is moderately to highly persistent in soil but is subject to biodegradation under aerobic conditions. Half-lives in soil ranging from 20-300 days or more have been reported (Wauchope 1991 in ECOTOXNET, PMEP 2002). Other studies report that degradation of 75-100% picloram in soil required 18 months (Kearney 1969 in HSDB) and that no detectable level of degradation in an organic rich soil was seen during 8 weeks following application of picloram (Corbin 1967 in HSDB). Picloram is moderately mobile in soil and due to its high water solubility and poor binding properties, the compound is potentially leached to groundwater. In water, picloram has been reported to decompose to negligible levels within 180 days (HSDB).

Bioconcentration
Based upon the measured BCF of 31 and the low log Kow value, picloram is not expected to bioaccumulate in aquatic organisms. In mammals, orally administrated picloram is rapidly eliminated in an unchanged form (Tomlin 1994).

Use, exposure and emissions
Picloram is used for control of a large number of annual and perennial broadleaf weeds and woody plants on grass-land, in forests and other non-crop areas (Tomlin 1994 and Howley 1981 in HSDB). Picloram acts as a synthetic growth hormone and causes uncontrolled or disorganised growth in susceptible plants. Occupational exposure to picloram may occur though inhalation and dermal contact during manufacturing and handling (incl. use) of the substance (HSDB). The general population may be exposed if they come in contact with spray or sprayed foliage, inhale spray mist, eat plants or animals contaminated with herbicide or via contaminated drinking water (HSDB).

Release to the environment
Release to the environment is an intended result of the use of picloram as a pesticide. Picloram may also be released from the production site.

Summary of environmental fate
Following application to soil, biological degradation is expected to be the major mechanism of removal. Biodegradation in soil is however slow and picloram is moderately to highly persistent. In water and at soil surfaces, picloram may further be removed by photodegradation. Volatilisation from surface soil is not expected (HSDB). Leaching to surface water and ground water may be of concern due to the high water solubility and poor binding properties. In near-surface water, photolysis may be a major removal process.

If released to the atmosphere picloram will be subject to significant deposition and washout due to its low vapour pressure (will adsorb to particulate matter) and significant water solubility. It may also be subject to significant direct photolysis. The estimated vapour phase half-life in the atmosphere is approximately 12 days as a result of reaction with photochemically produced hydroxyl radicals (SRC in HSDB).

Environmental concentrations
In a treated soil, maximal picloram concentrations of 0.96-2.25 mg/kg were measured 225 days after application in the upper soil. This declined to 0.13-0.29 mg/kg one year later (Michael 1989 in HSDB).

In treated fields, average concentrations of 0-238 µg/kg have been measured (Bovey 1975 and1975 in HSDB). In a treated forest soil, the upper soil concentration declined from 12 µg/kg two weeks after spraying to 0.06 µg/kg 7 months after spraying (Neary 1985 in HSDB).

In run off water from treated fields, an average concentration of 464 µg/L was measured 13 days after spraying. This was reduced to 0-3 µg/L at 40-110 days after spraying.

Picloram has been detected in the groundwater of eleven states at concentrations ranging from 0.01 µg/L to 49 µg/L (Howard 1991 in ECOTOXNET).

Vulnerable use and vulnerable groups
Workers involved in manufacturing and handling (incl. use) of the substance are expected to be the most vulnerable groups.

Conclusion
Picloram is a pyrimidine herbicide, mainly used on non-food areas like grasslands, forests and non-crop areas. Human exposure is not expected because picloram is not used on food crops. Wildlife exposure might be expected because of its use as a fungicide. However, picloram is not bioaccumulative and solely moderately persistent and therefore it is categorised as medium exposure concern. However, picloram is observed in ground- and surfacewater, some caution via exposure through contaminated drinking water has to be taken.

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

HSDB (Hazardous Substances Data Bank) (2002). A database of the national library of medicine's TOXNET system, http://toxnet.nlm.nih.gov

PMEP (The Pesticide Management Education Program) Homepage (2002), http://pmep.cce.cornell.edu/

ECOTOXNET, The EXtension TOXicology NETwork (2002). A data base of toxicology and environmental chemistry information about pesticides, http://ace.ace.orst.edu/info/extoxnet/

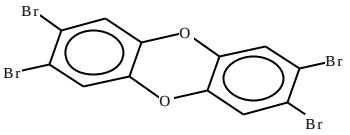
Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

POLYBROMINATED DIBENZO-P-DIOXINS (PBDDS):

2,3,7,8,-tetrabromodibenzo-p-dioxin (TBDD) (Cas no 50585-41-6)

The substance 2,3,7,8- tetrabromodibenzodioxin (2,3,7,8-TBDD or TBDD for short) belongs to the group of polybrominated dibenzo-p-dioxins (PBDD). This group is highly related to the notorious group of polychlorinated dibenzo-p-dioxins (PCDD). PCDD 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD) has been noted as the most toxic of its group. Its PBDD sister TBDD therefore is generally assumed to be the most toxic member of the TBDD group.

Chemical characteristics



Molecular formula TBDD: C12-H4-Br4-O2

MW = 499.78

Table 1: Physical/chemical properties of TBDD

Parameter	**2,3,7,8-TeBDD**
Water solubility (ng/L 25°C)	9.96 - 952 (EHC, SRC)
Vapour pressure (mm Hg 25°C)	4.8 x 10-9 (SRC)
Log Kow	6.50 - 7.90 (EHC, SRC)
Henrys Law constant (atm cu3 m/mole)	3.72 x 10-5 (SRC)
Koh (cm3/molecule sec)	0.6615 x 10-12 (SRC)
Biodegradation	Very recalcitrant
BCF (L/kg)	3757 (SRC)
Koc (L/kg)	1.463 x 10+5 – 3.47 x 10+5 (EHC, SRC)

PBDDs are very poorly soluble in water, have high melting points and low vapour pressures. Due to their lipophilic characteristics they are generally soluble in fats, oils and organic solvents.

Abiotic degradation
PBDDs are sensitive towards photolysis. Sunlight induced-reductive debromination appears to be the major process. However, due to the weaker interaction between carbon and bromine compared to carbon – chlorine interactions, bromine will be replaced by chlorine in the presence of excess chlorine. The latter results in mixed halogenated more stable congeners. Furthermore, when absorbed to particulate matter in either atmosphere or water, photolysis is drastically hampered. Therefore, half-lives for TBDD differ greatly in various environmental conditions. TD50 is 0.8 minutes when dissolved in organic solvents, 32 hours dispersed as solid films and 3-6 months when absorbed in to soil. TBDD are considerably less stable than their chlorinated relatives. For TCDD, TD50 is 300 hours dispersed as a solid film and 10-12 years in soils.
PBDDs are thermostable, depending on residence time, presence/absence of oxygen, polymers and additives as antimoneoxides. PBDDs generally decompose between 600 –900 °C.
TBDD is hardly degraded by hydrolysis due to the lack of hydrolysable groups.

Biotic degradation
TBDD is hardly degraded in living organisms and therefore classified as very recalcitrant. No information about biodegradation was available. However, TBDD probably behaves similar to its chlorinated equivalent TCDD. In an experiment using, [14C] TCDD its half-life time in lakes or ponds in the field was approximately one year (Japan, 1997). Metabolism of PHDDs occurs via the aren oxide formation and hydroxylated metabolites have been determined for tetrachlorinated congeners (Larsen, 1996 in sepa98) In addition cleavage of the ether bridges between the two phenyl rings were shown to occur resulting in catechols (sepa98).
DT50 of TCDD in water and soil is estimated at >1 year (34 riwa, 1998). Expected removal from a sewage treatment plant is >40% by active coal (riwa, 1998).

Bioaccumalation
At present, no BCF values are available on bioaccumulation, bioconcentration or biomagnification. SRC (EPIWINN) based calculations predict a BCF of 3757 L/kg. Based on these calculations, the observed presence of TBDD in animals and humans, their lipophilic properties and the high accumulation potential of their better-studied relatives (PCDDs), TBDD is expected to possess high bioaccumulative properties. Like TCDD, TBDD is expected accumulate primarily in the liver and the fat

of the organisms. Because the degradation/metabolisation in organisms is low, the level of PBDDs in organisms higher in the food chain, will be higher than of organisms lower in the food chain.

Use, Exposure and emissions
PBDDs are not known to occur naturally. They are not intentionally produced (except for scientific purposes) but are generated as undesired by products in various processes. They can be formed by chemical, photochemical or thermal reactions. PBDDs have been found as contaminants in over 40 brominated organic chemicals. Such chemicals include flame-retardants and fire extinguishers, pesticides (e.g. bromophenoles, bromophos and bromoxynil), solvents and chemical intermediates or additives. The highest concentrations of tetrabrominated dibenzo-p-dioxins were found in 1,2bis(tribromophenoxy)ethane (8350 ug/kg), followed by 2,4,6-tribromophenol (84 ug/kg) and 2,4,6 tribromoaniline (5.5 ug/kg).
Other sources include municipal waste incineration, polymer/plastic production, metal production and reclamation, traffic, incineration of electrical equipment as televisions and computers. Furthermore TBDD was present in solvent wastes of chemical laboratories at levels of 10 ng/kg.

PBDD consists of 75 possible congeners. The relative amounts of PBDD congeners vary with production and congener pattern can therefore be used to identify a source. PBDDs are highly hydrophobic and log Kow in the range of 6.5 to 10 for tetra- to octaBDD have been reported. TBDD is the most toxic PBDD congener and therefore is used as a standard of toxicity. The Toxic equivalence factor (TEQ) for other compounds is set as the potency of the compound versus the potency of TBDD. The concentrations of PBDDs and another group the polybrominated dibenzofurans (PBDF) are often presented as the sum of the concentration multiplied with the TEF, yielding toxic equivalents (TEQs) in the sample (sepa98).

Release to the environment
Release of TBDD to the environment is unintended. It is generated as undesired by-product during production of especially flame retardants, fire extinguishers, brominated pesticides and solvents. Furthermore, municipal waste incineration, traffic, plastic production and metal reclamation are important TBDD producing sources.

Summary of environmental fate
When released to air TBDD will exist in both vapour- and particulate phase. Due to its lipophilic characteristics it will mainly be absorbed to particulate matter. Absorbed TBDD and particulate matter will be cleared from the atmosphere through photolysis or wet (or dry) deposition. If released to other environmental compartments. TBDD will accumulate in either sediment or soil. Due to its low water solubility and its strong absorption to particulate matter, mobility of TBDD is low to immobile; no leaching to the groundwater compartment will occur. However, in special cases, such as waste disposal sites where organic solvents are concomitantly present, leaching is observed. Henrys law coefficients for different PBDDs vary from very low to medium volatilisation, depending on the degree of bromination. Despite the fact that TBDD is not volatile, distribution primarily takes place through air. In soil and sediment TBDD is considered to form an immobile sink in the environment. TBDD is a very persistent substance, and although biodegradation is observed it is a very slow fate process.

Vulnerable use and vulnerable groups
TBDD is a bioaccumalative substance that particularly affects fatty tissues, liver and milk. Degradation/metabolisation in organisms is low, therefore the level of PBDDs in organisms higher in the food chain, will be higher than of organisms lower in the food chain.
Vulnerable groups are: breast feeding babies and small children; and in wildlife predators of e.g. fish or mussels contaminated with PBDDs.

Environmental concentrations
Little environmental monitoring data are available on TBDD alone. In the majority of the monitoring programmes all tetrabromodibenzo-p-dioxin congeners (TBDDs) are displayed in solely one value. Despite analysing all TBDDs together, environmental TBDDs concentrations do not often succeed detection limit. Smaller PBDDs (mono- and dibromo compounds) or mixed halogenated dibenzo-p-dioxins and PBDFs, on the other hand, are more frequently observed. TBDD was detected in pine needles near a German highway (Schwind in EHC), and in Dutch shrimps, mussels and fish (De Jong in EHC). The amounts however were not quantified.

Table 2: Occurrence of TBDD (or TBDDs) in the environment

Compound	Compartment	Year	Area	Concentration	Reference
TBDDs	Air	1990	Motorway tunnel Essen, Germany	Max 0.18 pg/m3	Papke (1990) in EHC
TBDDs	Air	1990	Urban area Dusseldorf, Germany	Max 0.04 pg/m3	Papke (1990) in EHC
TBDDs	Air	1992	Urban area Osaka, Japan	Max. 0.3 pg/m3	Watanabe (1992) in EHC
TBDDs	Air	1992	Recycling resource centre, Taiwan	Max. 0.2 pg/m3	Watanabe (1992) in EHC
TBDDs	Air dust	1978	Motorway tunnel, Japan	110 ng/kg	Japanese Institute of Env. Sc. (1978) in EHC
PBDD	sediment	1995	River and marine sediment, Japan	0.03-0.37 ug/kg dry weight	Watanabe (1995) in EHC
TBDDs	soil	1992	Fire warehouse with bromine containing pellets	3.5 ng/kg	Neupert & Pump (1992) in EHC
PBDFs	Sewage sludge	1992	Wastewater treatment plant, Germany	0.29-3.05 ug/kg	Hagenmeijer (1992) in EHC

There is no quantitative information available on exposure of infants or the general population to TBDD. Solely a few studies were performed to analyse PBDD levels in human tissue, blood or milk sample. Again, TBDD levels appeared to below detection limit in all samples.

A set of data regarding TBDD exposure of employees of chemical industries producing flame-retardants or plastics are available. TBDD, however was not detected during moulding of polybromoterphenyls, acrylonitrile-butadiene-styrene, polystyrene or polyamide resins blended with various brominated flame-retardants. PCDFs, however were frequently observed with TBDF concentrations rising up to 6.92 ng/m3 air.

Conclusion

Although environmental TBDD concentrations are below detection limit and occupational exposure to TBDD is just seldomly reported, TBDD composes a high-risk exposure concern to both humans and wildlife. Emission of TBDD can not be prevailed, therefore TBDD (and other PBDDs en PBDFs) will. TBDD is highly bioaccumulative and biodegradation is a ver slow fate process. In the presence of excess chlorine, TBDD can be transformed to mixed-halogenated or chlorinated dibenzo-p-dioxins that are even more persistent. These compounds are just like TBDD associated with endocrine disruptive activity.

Due to accumulation in fat and liver tissue, predators of fish and mussel just as breast feeding babies and small children are likely to be the most vulnerable groups.

References

EHC, (1998). Environmental Health criteria 205; polybrominated dibenzo-p-dioxins and dibenzofurans, WHO, Geneva.

Japan, 1997. A Study on Hormone-Like (Hormone-Mimic) Effects of Exogenous Substances, Shortened English Version. Japan Chemical Industry Association. Japan Chemical Industry Ecology-Toxicology and Information Center.

RIWA (1998). Xeno-oestrogenen en drinkwater(bronnen).

SEPA, (1998). Olsson, P-E, et al, 1998, Endocrine disruption chemicals, Swedish Environment Protection Agency, report no. 4859.

SRC (2002). Syracuse research corporation PhysPop on-line database, http://esc.syrres.com

POLYCHLORINATED BIPHENYLS (PCBS):

Group 1: Trichlorinated Biphenyls (TCB): 2,2'5-TCB (PCB 18); 2,3,4-TCB (PCB 21); 2,4,4'-TCB (PCB 28) 2,4,6-TBP (PCB 30); 3,4',5-TCB (PCB 39)

Group 2: Tetrachlorinated biphenyls (TeCB): 2,2',5,5'-TeCB (PCB 52)

Group 3: Pentachlorinated biphenyls (PeCB):2,2'4,6,6'-PeCB (PCB 104); 2,3,3',4,4'-PeCB (PCB 105); 2,3,4,4',5-PeCB (PCB 114); 2,3,3',4,5-PeCB (PCB 122); 2,3',4,4',5-PeCB (PCB 118); 3,3,',4,4',5-PeCB (PCB 126)

Group 4: Hexachlorinated biphenyls (HCB): 2,2',3,3',4,4'-HCB (PCB 128); 2,2',3,4,4',5'-HCB (PCB 138)

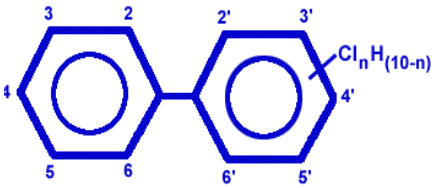
Group 5: Heptachlorinated biphenyls (HeCB); 2,2',3,4,4',5,5'-HeCB (PCB 180)

Group 6: Hydroxylated chlorinated Biphenyls: 4-OH-2,2',5-TCB; 4-OH-2'4'6'-TCB; 4-OH-3,4',5-TCB; 3-OH-2',3',4',5'-TeCB; 4-OH-2',3',4',5'-TeCB; 4-OH-3,3',4',5'-TeCB; 4,4'-diOH-2,3,5,6-TeCB; 4,4'-diOH-3,3',5,5'-TeCB; 4-OH-2,2',4',5,5'-PeCB

Group 7: PCB Mixtures: Aroclor 1016; Clophen A30; Clophen A50 and a mixture of 2,3,4,5-TeCB (PCB 61) + 2,2',4,5,5'-PeCB (PCB 101) + 2,2',3,3',4,4',5,5'-OCB (PCB 194)

Chemical characteristics

PCBs are produced as mixtures. Their nomenclature is presented in two ways: IUPAC nomenclature which gives a number to each of the congeners (e.g. PCB 58). Whereas mixtures of specific congeners often are referred to as Aroclors or Clophen (e.g. Aroclor 1242).



Polychlorinated Biphenyl (PCB)

Table 1 Physical/chemical properties of PCBs (obtained from SRC)

Parameter	4-OH-2,4,6-TCB	PCB 28	PCB 52	PCB 118	PCB 138	PCB 180
Water solubility (mg/l 25°C)	2.355	0.27	0.015-0.05	0.0134	0.0015	0.28 x 10-3
Vapour pressure (mm Hg 25°C)	5.24 x 10-7	4.0 x 10-4	8.5 x 10-6	8.97 x 10-6	3.79 x 10-6	9.77 x 10-7
Log Kow	5.21	5.62	6.09	7.12	7.62	8.27
Henry's coeff. (Atm cu-m3/mole 25°C)	8.0 x 10-8	2.00 x 10-4	2.00 x 10-4	2.88 x 10-4	4.74x 10-4	1.0 x 10-5
Koh (cm3/molecule-sec)	1.03 x 10-11	1.19 x 10-12	0.73 x 10-12	0.33 x 10-12	0.16 x 10-12	0.10 x 10-12
Biodegradation	Moderate	Moderate	Slow	Slow	Very slow	Very slow
Fish BCF (L/kg)	2051	17680	40760	184300	37590	4922
Koc (L/kg)	4.48 x 10+4	2.71 x 10+4	4.48 x 10+4	7.41 x 10+4	1.25 x 10+5	2.07 x 10+5

Because PCBs within one group have similar chemical characteristics, not all 28 PCBs (or PCB-mixtures) are summed up in the table above. We have selected 1 PCB of each group (except for group of mixtures because the individual components of the mixtures belong to either one of group 1 to 6). PCB 28, PCB 52, PCB 118 and PCB 138 were chosen as group references because they are often used for determining PCB amounts in sewage sludge, whereas 4-OH-2,4,6-TCB and PCB 180 were chosen because they have the lowest respectively highest log Kow value of the entire PCB-set.

PCBs are poorly to very poorly soluble in water (0.0001-0.1 mg/l). The log Kow values of PCBs vary from 5.2 to 8.3 which indicates that they are very lipophilic compounds. PCBs accumulate strongly in organisms. Furthermore they are persistent. High log Kow values indicate that PCBs have a medium to high sorption to sediment (fra97). The high Henry's law coefficients indicate a relative high volatility.

Abiotic degradation

In the vapour phase, reactions with photochemically induced hydroxyl radicals are main conversion processes. Half - lives of photodegradation processes vary from 10 days (monochlorobiphenyl) to 1.5 years (heptachlorobiphenyl). Absorption to particulate matter in the atmosphere severely hampers photodegradation, therefore volatile PCB may travel long air distances and deposit in sensitive remote areas far away from the original source.

In water, neither hydrolysis nor oxidation reactions are important fate processes in the degradation of PCBs. Photolysis is presumed to be majorly responsible for degradation, but the actual significance in the environmental degradation is to be studied

Biotic degradation
Environmental degradation of PCBs predominantly depends on degree of chlorination of the biphenyl moiety. In general the more highly chlorinated PCB analogues undergo slower degradation..
Microorganisms moderately degrade Mono-, Di- and Trichloro biphenyls. The rate of degradation of Tetrachlorobiphenyls is slow, and additionally more highly chlorinated biphenyls are not degraded by biodegradation at all.
The analogues, which have two chlorine atoms in *ortho* position of one or both rings, are remarkably slowly degraded, while the analogues in which chlorine atoms are localised concentrate to one ring are easily degraded.
PCB analogues, which have high chlorine content, are metabolised into analogues which have lower chlorine content by reductive dechlorination reactions under anaerobic conditions. Two types of dechlorination reactions are observed. One is related to dechlorination degree occurring at *ortho*, *meta* and *para* positions and reductive potential, the other depends on dechlorination degree occurring at *meta* and *para* position as well as the molecular shape.

Bioaccumulation
Since PCBs are highly lipid-soluble and the rate of metabolism and excretion is slow, they tend to bioaccumulate particularly in adipose tissues of most living animals and plants. The degree of bioconcentration in the adipose tissues depends on various factors such as period and levels of exposure, chemical structure of compound, including position and pattern of substitution. Analogues with higher chlorine content have the larger Kow and are more easily bioaccumulated (Japan, 1997).

Use, Exposure and emissions
PCBs are produced in 1-2 million tonnes/year (gre96). In the past PCBs have been used in electrical equipment, heath-transfer systems, hydraulic systems as well as in plastics, coats, paints, glues, drill- and cutting oil and carbon-free paper (Devoogt en Brinkman 1989 in fra97). PCBs may also be formed as an unwanted by-product during industrial production of other chemicals. Important sources of emission of PCBs are waste incineration processes.

PCBs, which had been previously released to the environment, are widely distributed in the global environment at present. PCB is volatilised into the air from soil and water, transferred into the air and re-distributed in both soil and water by rainfall again. A large quantity of PCBs persists in soil and water sediment, which is considered to have a role as sink. In Japan, PCB manufacturing was prohibited in 1972. During 17 years 50,000 t - 60,000 t PCBs were manufactured , whereas estimated cumulative amounts were 44,800 t (Japan, 1997).

In EC council regulation 2455/92 Annex 1 chemicals are listed that are banned or severely restricted to certain uses. In this regulation it is referred that PCBs except mono- and dichlorinated biphenyl's, or preparations, including waste oils, with a PCB content higher than 0.005% by weight may not be used.
The production and use of PCB-containing products are forbidden in the Netherlands (RIVM, 1994 in fra97).

Summary of environmental fate
After evaporation into the air, PCBs persist in vapour phase at first, thereafter they are immediately adsorbed to present particulate matter. The tendency of adsorption rises with the degree of chlorination. World-wide distribution of PCBs is considered to be a consequence of long range air transport. At present it is demonstrated that the major source of exposure to PCBs is due to such re-distribution of previously released portions.
PCB in water strongly adsorbed to bottom soil and other organic compounds. The experimental data or monitoring data show that PCB levels in bottom soil or in floating materials are higher than that in water. The degree of adsorption is remarkably high with highly chlorinated analogues. From the solubility and octanol/water partition coefficient, PCB analogues that have lower chlorine contents are more weakly adsorbed and more easily degraded.
As the adsorbed PCBs are slowly released to water, PCBs in bottom function as a sink. The loaded amounts of PCB to the environment are assumed to exist in the bottom of water ways.

PCBs have low water solubility. Due to strong adsorption to soil particles they hardly leach to the groundwater compartment.

Vulnerable use and vulnerable groups
PCBs are released in the environment during production, use of PCB containing products, in case of fires/explosions and during incineration of PCB containing waste.

Humans become exposed to PCB's by 3 main routes:
- Uptake from the environment by fish, birds, livestock (via food chains) and crops.
- Migration from packaging materials into food (mainly below 1 mg/kg, but in some cases up to 10 mg/kg.
- Direct contamination of food or animal feed by an industrial accident.

Vulnerable groups like babies may become exposed to PCBs via breast milk.

PCBs may contaminate surface water from atmospheric fallout, from direct emissions from point sources, or from waste disposal.

Vulnerable wildlife groups are predators of e.g. fish or mussels contaminated with PCBs.

Environmental concentrations
PCBs have been measured in several organisms, like flounder, dab and mussels. PCB concentrations in these organisms vary between 0.021 and 2.1 mg/kg. They have also been measured in sediment and suspended matter (fra97).

In the European COMMPS program European environmental concentration of 5 PCBs belonging to the 28 selected PCBs of this report were determined in water sediment:

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
37680-73-2	PCB 101	26.60	8.33	13.66	11.34	77	186	175
35065-27-1	PCB 153	44.69	14.90	23.58	20.54	85	202	191
35065-29-3	PCB 180	35.11	11.88	17.08	18.00	80	190	179
7012-37-5	PCB 28	12.40	2.80	6.64	9.00	49	135	101
35693-99-3	PCB 52	26.29	4.01	14.54	39.84	56	152	134

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements with concentrations higher than the corresponding determination limit

Other detected environmental concentrations include:

Compound	Sample	Year	Location	Concentration	No samples	Reference
PCB 28	Sediment	1996	Rhine, Netherlands	11.14 ug/kg	1	Fra97
PCB 28	Suspended matter	1991-1995	Netherlands	0.9-15 ug/kg	134	Fra97
PCB 28	Mussel	1996	Netherlands	7-29 ug/kg fat	20	Fra97
PCB 28	Fish	1996	Netherlands	2-18 ug/kg fat	71	Fra97
PCB 52	Sediment	1996	Rhine, Netherlands	7-14 ug/kg	2	Fra97
PCB 52	Mussel	1996	Netherlands	29-227 ug/kg fat	20	Fra97
PCB 52	Fish	1996	Netherlands	27-168 ug/kg fat	71	Fra97
PCB 52	Suspended matter	1991-1995	Netherlands	0.9-24 ug/kg	106	Fra97
PCB 118	Sediment	1996	Rhine, Netherlands	7-20 ug/kg		Fra97

Compound	Sample	Year	Location	Concentration	No samples	Reference
PCB 118	Mussel	1996	Netherlands	140-507 ug/kg fat	20	Fra97
PCB 118	Fish	1996	Netherlands	81-507 ug/kg fat	71	Fra97
PCB 118	Suspended matter	1991-1996	Netherlands	1.77-4.27 ug/kg	45	Fra97
PCB 138	Sediment	1996	Rhine, Netherlands	9-30 ug/kg		Fra97
PCB 138	Mussel	1996	Netherlands	4-16 ug/kg product	10	Fra97
PCB 138	Fish	1996	Netherlands	27-104 ug/kg product	31	Fra97
PCB 138	Suspended matter	1991-1996	Netherlands	2.4-25 ug/kg	97	Fra97
PCB 180	Sediment	1996	Rhine, Netherlands	8-12 ug/kg	2	Fra97
PCB 180	Mussel	1996	Netherlands	46-207 ug/kg product	10	Fra97
PCB 180	Fish	1996	Netherlands	80-477 ug/kg product	31	Fra97
PCB 180	Suspended matter	1991-1996	Netherlands	1.3-18 ug/kg	65	Fra97
PCBs	Food	1978	Netherlands	0.13-0.17 mg/kg fat	2 pos	EHC140
PCBs	Drinking water	1978	Netherlands	0.035	1 pos	EHC140
PCB 118	Maternal plasma	1992	Netherlands	0.02-0.60 ng/g plasma	418	Koopman-Esseboom
PCB 138	Maternal plasma	1992	Netherlands	0.13-1.60 ng/g plasma	418	Koopman-Esseboom
PCB 180	Maternal plasma	1992	Netherlands	0.08-3.10 ng/g plasma	418	Koopman-Esseboom
PCB 126	Human milk	1992	Netherlands	39.4-443.9 pg/g fat	194	Koopman-Esseboom
PCBs (analogues analysed)	Fish Shellfish, Birds	1994	Japan	0.01 - 0.33 A 0.01 - 0.02 A -	39/70 16/30 0/5	Japan, 1997
PCB 126	Sediment Fish	1994	Japan	0.000099 - 0.00017 mg/kg 0.000005 - 0.00018 mg/kg	2/3 3/3	Japan, 1997
Total PCBs	Sediment Fish	1994	Japan	0.380 - 1.4 mg/kg 0.750 - 1.5 mg/kg	2/3 2/3	Japan, 1997

PCBs are accumulated in both human adipose tissues and mother's milk. PCB levels in various organs and tissues except in brain depend on the contents of fats. Mean levels of total PCBs in human milk fat vary from houses and lifestyle of donors who offer their samples, and the analytical methods used. Milk of women living in heavy industrialised area or city, or who eat fishes caught in heavily polluted area, has the possibility of containing high levels of PCBs.

Main foods that have problems are fishery products, the crustacea, meats, milk and other dairy products. If compared with the previous data, PCB levels in fishes are moderately decreasing (Japan, 1997).

Most of compositions of PCBs extracted in the samples analysed in the environment including human adipose tissues and milk are not similar to those of PCB mixtures on the market.
The patters of gas chromatogram in human adipose tissues and mother's milk show that highly chlorinated PCBs predominantly are detected in higher levels. For example the analogues shown below are typically found (Koopman-Esseboom, 1994):
PCB105: 2,4,5,3',4'-Pentachlorobiphenyl, PCB153 2,4,5,2',4',5 '-Hexachlorobiphenyl,
PCB128 2,3,4,2',4',5'-Hexachlorobiphenyl, PCB180: 2,3,4,5,2',4',5'-Heptachlorobiphenyl,
PCB170: 2,3,4,5,2',3',4'-Heptachlorobiphenyl
Levels of other PCB homologues such as highly toxic coplanar PCB77: 3,4,3',4'-Tetrachloro-biphenyl, PCB126: 3,4,5,3',4 '-Pentachlorobiphenyl and 3,4,5,3',4',5'-Hexachlorobiphenyl, are very low

Conclusion
PCBs are of high concern for human exposure. Vulnerable groups that are exposed are breast-feeding babies.

PCBs are measured at many locations in sediments, suspended solids and biota and are considered as persistent.

In the environment especially predators of fish and mussel are of high concern.

References
EHC140: Environmental Health criteria 140 of polychlorinated biphenyls and terphenyls (second edition. WHO document 1993.

Fra97 Franse & de Voogt, 1997 Oestrogene verbindingen in het Nederlands milieu, MTC report.

Gre96: Greve, (1996). (Dutch Health Council). Hormoon-verstorende stoffen in Nederland. Gebruik, emissie, milieuconcentraties en fysisch/chemische karakteristieken

Japan, 1997. A Study on Hormone-Like (Hormone-Mimic) Effects of Exogenous Substances, Shortened English Version. Japan Chemical Industry Association. Japan Chemical Industry Ecology-Toxicology and Information Center.

Koopman-Esseboom (1994); PCB and dioxin levels in human milk of 418 Dutch women and their infants. Predictive value of PCB congener levels in maternal plams for fetal and infants exposure to PCBs and dioxins

Syracuse 1996. Syracuse calculation programs

UBA98. Gülden, M., et al, (1998), Endocrinically active chemicals and their occurrence in surface waters, UBA-FB 97-068, Research report 102 04 279

POLYCHLORINATED DIBENZOFURANS (PCDFS):

6-Methyl-1,3,8-tri-chlorodibenzofuran (6-M-TCDF) (Cas no 118174-38-2)

The substance 6-methyl-1,3,8-tri-chlorodibenzofuran belongs to the group of polychlorinated dibenzo-p-furans (PCDF). PCDFs have much structure and activity resemblance with the group of polychlorinated dibenzo-p-dioxines (PCDD).

Chemical characteristics

Molecular formula 6-M-TCDF: C13-H7-Cl3-O

MW = 285.557

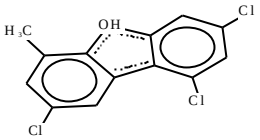


Table 1: Physical/chemical properties of 6-M-TCDF

Parameter	2,3,7,8-TeCDF
Water solubility (mg/L 25°C)	5.91 x 10-3 (SRC)
Vapour pressure (mm Hg 25°C)	2.29 x 10-6 (SRC)
Log Kow	6.20 (SRC)
Henrys Law constant (atm m3/mole)	2.30 x 10-5 (SRC)
Koh (cm3/molecule sec)	1.14 x 10-12 (SRC)
Biodegradation	Very recalcitrant (SRC)
Fish BCF (L/kg)	11760 (SRC)
Koc (L/kg)	8.10 x 10+4 (SRC)

No information was available on this specific PCDF. Therefore a more general profile on PCDFs was drawn up. PCDFs are very poorly soluble in water (1 to 500 ng/l) and have a high lipophilic character (log Kow > 6).

Abiotic degradation
TCDFs are hardly degradable by hydrolysis due to the lack of hydrolysable groups (Lyman et al 1990 in HSDB). Photolysis half-life of 2,3,7,8-TCDF is about 63 days (Meylan and Howard 1993 in HSDB).
However, when absorbed to particulate matter in either atmosphere or water, photolysis is drastically hampered. Therefore, half-lives for PCDFs differ greatly in various environmental conditions.
PCDFs are thermostable, depending on residence time, presence/absence of oxygen, polymers and additives as antimoneoxides. PCDFs generally decompose between 600 –900 °C.

Biotic degradation
TCDFs are hardly degraded in living organisms and therefore classified as very recalcitrant.
Metabolism of PCDFs occurs via the aren oxide formation and hydroxylated metabolites have been determined for at least tetrachlorinated congeners (Larsen, 1996 in sepa98) In addition cleavage of the ether bridges between the two phenyl rings were shown to occur resulting in catechols (sepa98).
In biodegradation tests both the anaerobic as the aerobic degradation was shown to be very low (Eljarrat et al 1997; Toussaint et al 1998 both in HSDB).

Bioaccumalation
At present, no BCF values are available on bioaccumulation, bioconcentration or biomagnification. SRC (EPIWINN) based calculations predict a BCF of 11760 L/kg. Based on these calculations, the observed presence of PCDFs in animals and humans, their lipophilic properties and the high accumulation potential of its better-studied relatives (PCDFs), 6-M-TCDF is expected to possess high bioaccumulative properties. Like other TCDFs, 6-M-TCDF is expected to accumulate primarily in the liver and the fat of the organisms. Because the degradation/metabolisation in organisms is low, the level of PCDFs in organisms higher in the food chain, will be higher than of organisms lower in the food chain.

Use, Exposure and emissions
PCDFs are unintentionally formed during combustion (e.g. municipal waste incineration, traffic, cable roating houses), metal production and reclamation, production of pulp and paper, chlorophenols, and chlorinated phenoxy herbicides, and at chlorine-alkali plants using graphites electrodes (rappe 1994 in sepa98). Incinerators of wastes are the greatest source of PCDFs (80% of the total emission). Another emission route is the volatilisation from with pentachlorophenol preserved wood (RIKZ nota in fra97).

PCDF consists of 135 congeners. The relative amounts of PCDF congeners vary with production and congener pattern can therefore be used to identify a source (rappe 1994 in sepa98). These compounds are highly hydrophobic and log Kow in the range of 6 to 9 have been reported (gotz 1994 in sepa98). The toxicity of these compounds is compared to the most toxic TCDD equivalent, being 2,3,7,8-TCDD. The Toxic equivalence factor (TEQ) for other compounds is set as the potency of the compound/the potency of 2,3,7,8-TCDD. The concentrations of PCDFs are often presented as the sum of the concentration multiplied with the TEF, yielding toxic equivalents (TEQs) in the sample (sepa98).

Release to the environment
Release of PCDFs to the environment is unintended. They are generated as undesired by-product during combustion, metal production and reclamation, production of pulp and paper, chlorinated herbicides herbicides, and at chlorine-alkali plants using graphite electrodes (rappe 1994 in sepa98). Incinerators of wastes are the greatest source of PCDFs (80% of the total emission). Another emission route is the volatilisation from with pentachlorophenol preserved wood (RIKZ nota in fra97).

Summary of environmental fate
When released to air PCDFs will exist in both vapour- and particulate phase. Due to its lipophilic characteristics it will mainly be absorbed to particulate matter. Absorbed PCDFs and particulate matter will be cleared from the atmosphere through photolysis or wet (or dry) deposition. If released to other environmental compartments, PCDFs will accumulate in either sediment or soil. Due to their low water solubility and their strong absorption to particulate matter, mobility of PCDFs are low to immobile; no leaching to the groundwater compartment will occur. However, in special cases, such as waste disposal sites where organic solvents are concomitantly present, leaching is observed. Henrys law coefficients for different PCDFs vary from very low to medium volatilisation, depending on the degree of Chlorination. Despite the fact that PCDFs are not volatile, distribution primarily takes place through air (CCRX, 1991 in fra97). In soil and sediment PCDFs are considered to form an immobile sink in the environment. PCDFs are very persistent substances, and although biodegradation is observed it is a very slow fate process.

Vulnerable use and vulnerable groups
PCDFs are bioaccumulative substances that particularly affect fatty tissues, liver and milk. Degradation/metabolisation in organisms is low, therefore the level of PBDDs in organisms higher in the food chain, will be higher than of organisms lower in the food chain.
Vulnerable groups are: breast feeding babies and small children; and in wildlife predators of e.g. fish or mussels contaminated with PBDDs..

Environmental concentrations
Most monitoring programmes involving PCDFs are not specifically based on one PCDF congener. The sum of total PCDF congeners is generally expressed as pg TEQ/m3. In this value, dioxins from where the TEQ originates, are often included as well. In the river Rhine concentrations have been measured of 0.01 ng TEQ/kg dry sediment upstream to 310 ng TEQ/kg dry sediment downstream. The highest measured concentration in the Rhine sediment is 219 ng TEQ/kg dw. The most important source of dioxines for water organisms will be through suspended matter and water bottom. Dioxin concentrations in eel, fish liver and molluscs have been measured. Through deposition from air, the overflowing of the river forelands, the use of contaminated fertiliser and dumping cq incineration of waste, dioxines may contaminate the soil. In total yearly > 2 kg TEQ falls onto the soil (fra97).
Geographically PHDD/Fs are of approx. the same level in herring at different locations along the Swedish east coast (150 ppt TEQ lw) but are lower in herring from the west coast (24 ppt TEQ lw in 1994). The levels of PHDDs/Fs are very low in terrestrial species (De wit in sepa98). Chemically levels of total PHDD/Fs in herring from the Baltic have been reported to be around 700 ppt lw. The levels in seals are considerably lower, 11 and 50 ppt in ringed seal and grey seal resp. (asplund 1990 in sepa98). The levels in fish-eating birds is much higher, 1,00 and 2,700 ppt in guillemot and sea eagle resp., but the levels have been decreased about five times from 1972 to 1992 (de wit 1994 in sepa98).

Dioxin levels in the air have been monitored as one of the measurement parameters of “The monitoring on non-regulated pollutants in the air” by the Environmental Agency, Japan, every other year from 1986. It is reported that Dioxins levels in the air is highest in the residential areas neighbouring industrial factories and in large areas, followed by medium sized cities and background area (mountain region). Namely, from the average levels from 1991 to 1994 the representative levels are assumed to be 0.6 pgTEQ/m3 in a large city area, 0.5 pgTEQ/m3 in a small-to-medium city area and 0.06 pgTEQ/m3 in a background area.

Compound	Compartment	Year	Area	Concentration	Reference
PCDF	Human milk	1990-1992	Netherlands	50.3 pg/g fat	Koopman-Esseboom 1994
2,3,4,7,8-PCDF	Sediment Fish Shellfish	1994	Japan	0.001 - 0.024 µg/kg (25/36) 0.001 - 0.007 µg/kg (12/34) - (0/1)	Japan, 1997

Recently the US EPA has set a limit value for PHDDs/Fs at 0.3 µg TEQ/kg dry sludge, based a comprehensive human risk assessment for PHDDs/Fs in sludge assuming a standard consumption pattern (Hayward, 2000). In 1990 a tolerable daily intake of 10 pg TEQ/kg bw per day was derived for 2,3,7,8-TCDD. In Europe the estimated intake of PHDDs/Fs is estimated at 1 pg TEQ/kg bw per day (70 pg TEQ/man/day) and for breast-fed infants appr. 150 pg TEQ/kg bw per day (RIVM, 1993).

Conclusion

PCDFs are of high exposure concern for humans and wildlife. Vulnerable groups that are exposed are breast-feeding infants. In the environment especially predators of fish and mussel are of high concern.

PCDFs are measured in air, sediments, suspended solids and biota and are considered as persistent. Decreased breeding success, and developmental aberrations in terns and have been attributed to food contaminated with PCDFs, DDE, PCB's, in the period 60s to 90s. In the last years effects have become more subtle (CSTEE, 1999). The exposure and effects of this specific PCDF is unknown. The group of PCDFs as a whole has a high exposure concern profile.

References

CSTEE, 1999. Opinion on human and wildlife health effects of endocrine disrupting chemicals, with emphasis on wildlife and on ecotoxicology test methods. Report of the working group on endocrine disrupter of the Scientific Committee on Toxicity, Ecotoxicity and the Environment (CSTEE) of DGXXIV, Consumers Policy and Consumer Health Protection.

Fra97 Franse & de Voogt, 1997 Oestrogene verbindingen in het Nederlands milieu, MTC report.

Hayward, (2000). Relying on risk. Water 21, 9.

HSDB, (2002). Hazardous Substances Data Bank, a database of the library of medicine's TOXNET system http://toxnet.nlm.nih.gov

Japan, (1997). A Study on Hormone-Like (Hormone-Mimic) Effects of Exogenous Substances, Shortened English Version. Japan Chemical Industry Association. Japan Chemical Industry Ecology-Toxicology and Information Center.

Koopman-Esseboom, (1994). PCB and dioxin levels in human milk of 418 Dutch women and their infants. Predictive value of PCB congener levels in maternal plasms for fetal and infants exposure to PCBs and dioxins.

RIVM, (1993). Integrated criteria document dioxins. Report no. 710401032.

RIWA (1998). Xeno-oestrogenen en drinkwater(bronnen).

SEPA, (1998). Olsson, P-E, et al, 1998, Endocrine disruption chemicals, Swedish Environment Protection Agency, report no. 4859.

SRC (2002). Syracuse research corporation PhysPop on-line database, http://esc.syrres.com

POLYCHLORINATED TERPHENYLS (PCTS):

Arochlor 5442 (CAS no. 12642-23-8)

Chemical characteristics
Commercial PCTs are (or were) produced as mixtures and no data have been found in the literature specifically for Aroclor 5442 or other terphenyl congeners. However, the physical and chemical properties of PCTs are similar to those of PCB's why the profile of Aroclor 5442 is based primarily on data for PCB's. The chemical characteristics in the table below have been estimated for a polychlorinated terphenyl structure with 5 chlorine atoms.

Molecular formula C18-H9-Cl5

MW = 402.54

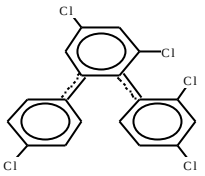


Table 1: Physical/chemical properties of arochlor 5442

Parameter	Arochlor 5442
Water solubility (mg/L 25°C)	1.00 x 10-4 (SRC)
Vapour pressure (mm Hg 25°C)	1.69 x 10-9 (SRC)
Log Kow	8.74 (SRC)
Henrys Law constant (atm cu3 m/mole)	8.8 x 10-6 (SRC)
Koh (cm3/molecule sec)	1.51 x 10-12 (SRC)
Biodegradation	Slow
BCF (L/kg)	1100 (SRC) Bioaccumulate in the food chain (FAO 1992)
Koc (L/kg)	2.79 x 10+6 (SRC)

Abiotic degradation
PCTs are highly resistant against photodegradation (FAO 1992). In aquatic environments, degradation by hydrolysis and oxidation is not believed to be significant (IPCS 1992).

Biotic Degradation
PCTs are highly resistant to microbial degradation in the environment. Persistence is increased with increasing degree of chlorination (FAO 1992, IPCS 1992).

Bioconcentration
Bioconcentration data for PCTs in aquatic species have not been found. However, PCB's have been found to be highly bioaccumulative in the aquatic environment with BCF values ranging from 200-70,000 or higher (IPCS 1992).

Use, exposure and emissions
There is currently no production of PCTs (UNECE 2002). Production of PCTs occurred over the same period as PCB production, but in quantities approximately 15-20 times lower than those of PCB's. Between 1955-1980, the total global production of PCTs is estimated at 60,000 tonnes (UNECE 2002). As for PCB's, PCTs may be found in some countries in old equipment or as components of some products. The main uses of PCTs have been as plasticisers (in synthetic resins, adhesives, lubricants, paper coatings, printing inks, carbonless copying paper, sealants), fire retardants, vapour suppressants (e.g. in insecticides), coatings to render fabric rot-, flame and water proof and in manufacturing of brake linings, abrasives, lacquers, varnishes and paints. PCTs has also had use as asbestos insulation, in electrical wire and cable coatings, as dielectric sealants and in waxes for various purposes. In spite of the fact that PCTs are no longer known to be in production, the presence of PCTs in a wide range of materials along with their persistent properties still leads to human exposure of PCTs previously introduced (HSDB, UNECE 2002). Occupational exposure to PCTs possibly occurs during handling of PCT containing equipment and materials (HSDB). The general population is exposed via contaminated food due to uptake from the environment by fish, livestock, birds and crops, via migration from packaging materials into food and via contaminated drinking water (HSDB).

Release to the environment
Release to the environment may have taken place at production sites where PCTs have been used and produced. PCTs have entered the environment via destruction of PCT containing articles, waste disposal, migration from PCT containing products and through leaching from landfills (HSDB).

Summary of environmental fate
Once entering the environment PCTs are highly resistant to abiotic degradation and microbial attack, the resistance to biodegradation being increased with increasing degree of chlorination. The general fate of PCTs in the environment described in the following section is based on the structural relationship with PCB's.

In soil, the PCTs will be strongly adsorbed to the soil particles due to their low water solubility and high binding affinity. Vapour loss from soil surfaces may be an important fate mechanism with the rate of volatilisation decreasing with increasing chlorination and molecular weight. While the lower chlorinated PCTs will volatilise more readily from soil surfaces, the higher chlorinated species tend to concentrate in soil environments. In spite of a predicted low rate of volatilisation from soils, the total loss by volatilisation over time may be significant because of the persistence and stability of PCTs. If released to water, adsorption to sediment and suspended matter will be an important fate process. As for PCB's, volatilisation from water surfaces may be an important fate process. However, volatilisation from water surfaces will be retarded by adsorption to suspended solids and sediment in the water column (HSDB, IPCS 1992).

If released to the atmosphere, PCTs are likely to exist in both the vapour phase and particulate phase. The vapour pressure of PCTs generally decreases with increasing degree of chlorination; therefore, the higher chlorinated PCTs are more likely to be associated with the particulate-adsorption-phase in air than are the lower chlorinated PCTs. Physical removal of PCTs in the atmosphere is accomplished by wet and dry deposition. Dry deposition occurs only for PCTs associated in the particulate phase. As the degree of chlorination increases, so does the half-life. The ubiquitous presence of PCTs suggests that atmospheric transport play an important role in the environmental distribution (HSDB, IPCS 1992).

Environmental concentrations
No data have been found regarding environmental concentrations of PCTs.

Vulnerable use and vulnerable groups
Workers involved in manufacturing and handling of PCT containing material and equipment are at risk. The general population is regarded as being vulnerable to PCTs due to bioconcentration in food items and release to the environment via waste disposal. An especially vulnerable group may be infants exposed via breast milk (HSDB, IPCS).

Legal status
In the European Union, the use of PCTs is prohibited by directive 85/467/EEC (6^{th} Amendment (PCB's and PCTs) Directive 76/769/EEC) since 1986 (IPCS 1992).

Conclusion
Although the use of PCTs has been prohibited, human exposure still occurs as a consequence of the redistribution of PCTs previously introduced to the environment. As it is the case for PCB's, PCTs are expected to be found in all environmental compartments world-wide due to the persistent properties and due to long range atmospheric transport. PCTs are estimated to be highly bioaccumulative and thus imposes a risk for both animals and humans eating contaminated food sources. The PCTs are thus considered as being of high exposure concern.

References
EPIWIN v.3.10. Environmental property estimation programme package. Office of pollution prevention and toxics, US EPA. 2000.

FAO/UNEP. 1992. Decision Guidance Documents, Crocidolite; Polybrominated Biphenyls, Polychlorinated Biphenyls, Polychlorinated Terphenyls, Tris (2,3-Dibromopropyl) Phosphate. Joint FAO/UNEP programme for the operation of prior informed consent. United Nations Environment Programme. Food and Agriculture Organisation of the United Nations. Rome-Geneva.

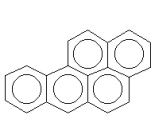
IPCS (International Programme on Chemical Safety) 1992. Health and safety guide no. 68. WHO Geneva.

UNECE (United Nations Economic Commission for Europe) 2002. Convention on Long-Range Transboundary Air Pollution. Compendium of substance-related information. Information dossier on PCTs, http://www.unece.org/env/popsxg/pct.pdf

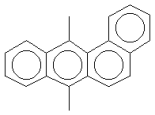
HSDB (Hazardous Substances Data Bank) (2002). A database of the national library of medicine's TOXNET system, http://toxnet.nlm.nih.gov

POLYCYCLIC AROMATIC HYDROCARBONS (PAHS):

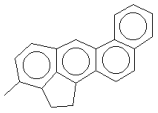
PAHs included in de CAT 1 selection are Benzo(a)pyrene (BAP), 7,12-Dimethyl-1,2-benz(a)anthracene (DMBA), 3-Methylcholanthrene (3-MC), 3,9-dihydroxybenz(a)anthracene (3,9-DBA) and 5,6-cyclopento-1,2-benzanthracene (5,6-CPBA).



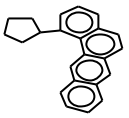
BAP (C20-H12)
MW = 252.32
CAS 56-49-5



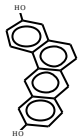
DMBA (C20-H16)
MW = 256.35
CAS 57-97-6



3-MC (C21-H16)
MW = 268.34
CAS 56-49-6



5,6-CPBA (C23-H20)
MW = 296.44
CAS 7099-43-6



3,9-DBA (C18-H12-O2
MW = 260.29
CAS 56614-97-2)

Chemical characteristics

Table 1: Physical/chemical parameters of BAP, DMBA, 3-MC, 3,9-DBA and 5,6-CPBA

	BAP	**DMBA**	**3-MC**	**3,9-DBA**	**5,6-CPBA**
Water solubility (mg/L at T = 25°C)	0.0016 – 0.0038	0.061	0.0029	0.7794	0.000199
Vapour pressure (mm Hg at T = 25°C)	5.5 x 10-9	2.5 x 10-7	2.0 x 10-8	7.1 x 10-11	6.4 x 10-9
log Kow	5.97-6.20	5.80	6.42	4.56	7.85
Henrys law constant (atm cu3 m/mole)	4,57 x 10-7	2.03 x 10-6	2.44 x 10-6	2.68 x 10-4	9.30 x 10-7
Koh ((cm3/molecule-sec)	5.0 x 10-11	1.6 x 10-10	2.0 x 10-10	1.2 x 10-10	2.0 x 10-10
Biodegradation	slow	slow	slow	slow	very slow
fish BCF (L/kg)	8.7-100.000	7100	775-45.000	648	4466
Koc (L/kg)	2.7 x 10+5 – 1.9 x 10+6	2.35 x 10+5	3.6 x 10+5 – 6.3 x 10+6	6.07 x 10+5	4.84 x 10+6

According to the vapour pressures mentioned in the table above, DMBA will be present in both vapour and particulate phases when released to the atmosphere. High Koc values however predict it should be exist mostly absorbed to particulate matter. BAP, 3-MC, 3,9-DBA and 5,6-CPBA should solely exist in a particle phase. Particulate matter will be removed from the atmosphere through wet and dry deposition. When released in water, all PAHs highly absorb to the sediment as expressed by their high Koc values. Due to this high absorbance, and to the estimated Henrys law constants it is suspected that volatilisation from neither surfacewater nor wet (or dry) soils, is an important fate process. High absorbance to soil particles will result in low to no mobility in soil. Therefore, leaching to the groundwater compartment is unexpected.

This PAH profile mainly focuses on BAP. Both DMBA and 3-MC are synthesised PAHs for laboratory use. They could be released to the environment via the atmosphere and various waste streams but concentrations are expected to be low. About 3,9-DBA and 5,6-CPBA little is known. HSDB, Chemfinder, EHC and Internet were advised but little about these compounds could be found. Therefore, BAP was used as a model compound for all 5 PAHs. The fact that all 5 compounds belong to the same class of PAHs with similar chemical en d physical parameters together with the fact that BAP is far out most spread and hence will result in the highest exposure risk, more or less justifies this act.

Abiotic degradation
Most PAHs absorb light above 290 nm and therefore may be susceptible to photolysis. Typical photodegradation reactions mediated by sunlight produced hydroxyl radicals, ozonlysis or nitrogenoxide are reported, half-lives varying from 3 –22 hours. However, photodegradation is drastically impaired by absorbance to particulate matter. The presence of BAP in areas remote from primary sources demonstrates the potential for long transport and its considerable stability in air. Half lives of BAP aerosols were reported to be 8 days, removing BAP from the gasphase however takes a lot longer (TD50 = 1.4 years).

Table 2: Abiotic half-lives of BAP

BAP Abiotic half-life (hrs) (photodegradation)	Comments	reference
1.4-31	Absorbed to air particles	Behymer & Hites in EHC
0.37-1.1	Air	Lyman in EHC
24	Air	Valerio in EHC
77-312	Water-sediment system	Zepp & Schlotzhauer in EHC

Due to the lack of hydrolysable groups, hydrolysis of PAHs is not an important fate process.

Biotic degradation
Biodegradation is the major mechanism for removal of PAHs from soil. The combined action of micro-organisms results in biodegradation of PAHs in soil. Due to the absorption of these highly lipophilic substances to soil particles and their relative stability as a consequence of their conjugated aromatic rings this is a slow fate process. Especially PAHs containing more than four aromatic rings (like BAP) are highly persistent. Volatilisation or photolysis might remove smaller PAHs. Abiotic processes may account for 2-20% of two-and three ring PAHs from soil (Park in EHC). Microbial degradation half-lives are difficult to determine and depend on soil characteristics, microbial populations and characteristics of the PAH itself (number of rings and presence of polar groups). Important soil parameters for example are temperature, pH, oxygen content, soil type, nutrients, and the presence of other substances that can act as co-metabolites. Typical half-lives are reported below.

Table 3: Microbial soil half-lives of BAP

Microbial soil half-life (days)	Comments	reference
120-258	Sandy loams, forest soil and sewage sludge treated roadside soils	Wild and Jones in EHC
218-347	Aerobic degradation in Donneybrook sandy loam, Canada	Bulman in EHC
230	McLaurin sandy loam	Park in EHC
240-2117	Anaerobic	Coover and Sims in EHC
309	Kidman sandy loam	Park in EHC
2993	Rural British soils amended with metal-enriched sewage sludge	Wild in EHC

The extent of mineralisation of BAP from three abandoned coal gasification plants and a coal tar refinery ranged from not detectable to 25% after 180 days (Grosser in HSDB).
If released into a water/sediment system, TD50 values exceed 200 weeks**.**

Bioconcentration
PAHs are highly lipophilic and due to their conjugated aromatic rings highly stable and therefore only slightly biodegradable. PAHs accumulate in the environment as well as in living organisms lacking a fast PAH-metabolising pathway

Table 4: Reported BCF values in different species

Species		BCF (L/kg wet weight)
Algae	*Periphyton*	9.000
Crustaceans	*Daphnia Pulex*	458
	Pontoporeia hoyi	73.000
Molluscs	*Ostrea Edulis*	58
	Physa sp.	2177
Insects	*Culex pipiens*	37
	Hexagenia limbata	5.870
Fish	*Lepomis macrochirus*	12,5
	Lepomis macrochirus	4.900

General biotransformation pathway in higher species is mediated by cytochrome P450 mixed-function oxygenase, for BAP resulting in the highly carcinogenic 7,8-dihydrodiol-9,10-epoxide. Various BCFs are reported for a broad set of organisms. The highest ands lowest per type of species are depicted in table below.

Use, exposure and emissions

PAHs are naturally present in fossil fuels. Processing and use of coal and petroleum products therefore is main source of PAH. Specific emission factor for BAP during coal cooking for example is 0.2 mg/kg coal charged (Ahland in EHC). Whereas the stack of gases of petroleum refinery plants in France and the USA contain 0.4 and 0.261-3.17 ug/m3 BAP respectively (Masclet in EHC). However PAHs not only pre-exist in fossil fuels but more are formed during incomplete combustion processes by a radical mechanism. These sources can be either natural or anthropogenic.

Natural sources for PAHs include volcanic activity and forest fires. In Canada, about 2000 tonnes of airborne PAH per year are attributed to natural forest fires (environment Canada in EHC), whereas the estimated world-wide release of BAP through volcanic action is estimated to be 1.2-14 tonnes a year.

Anthropogenic activities that result in PAH release are vehicle traffic, tobacco smoking, broiling and smoking of food, refuse burning, and industrial processes including aluminium, iron and steel production, foundries, tire production, power plants, incinerators and stubble burning (Anderson in EHC).

Typical occupational exposures to BAP during different production processes. High exposure occurs during processing and use of coal and mineral oils, such as coal coking, petroleum refining, road paving, asphalt roofing and impregnation of wood with creosols, aluminium production plants and steel and iron foundries.

Table 5: Occupational exposure to BAP

Production process	**Occupational BAP exposure (ug/m3)**	**Reference**
Coke plant	8.02 0.1-6.8 0.01-161	Petry (1994) in HSDB Levin (1995) in HSDB Wallingford (1985) in HSDB
Carbon anode	1.155	Petry (1994) in HSDB
Graphite plant	0.085	Petry (1994) in HSDB
Silicone carbide plant	0.036	Petry (1994) in HSDB
Metal recycling	0.014	Petry (1994) in HSDB
Bitumen pavement plant	0.010	Petry (1994) in HSDB
Chimney sweeping	0.36-0.82	Knecht (1989) in HSDB
Gas workers	6.0-10.3	Yrjanheikki (1995) in HSDB
Tire manufacturing	1.6-2.9	Wallingford (1985) in HSDB
Hot forging	1.4-4.8	Wallingford (1985) in HSDB
Asphalt roofing	0.01-27	Wallingford (1985) in HSDB
Carbon impregnation	0.8-84	Wallingford (1985) in HSDB
Steel mill	0.002-0.032	Wallingford (1985) in HSDB
Petroleum refineries	0.01-9.3	Wallingford (1985) in HSDB
Aluminium plant	0.01-975	Wallingford (1985) in HSDB
Foundries	0.049-0.47	Knecht (1986) in EHC

Occupational situations involving heating organic material may potentially result in exposure to these compounds through inhalation of air particulate matter and dermal contact with combustion products. The general population will be also exposed to PAHs through the smoking (or sidestream smoking) of tobacco, inhalation of polluted air, ingestion of contaminated water and consumption of charcoal-broiled food, roasted coffee and tea, various foods, oils, butter, fats, fruits, vegetables and cereals. The estimated intake of individual PAHs in diet is 0.1-8 ug/day.

Estimated intake of BAP by the general population is depicted in the table below (EHC)

Table 6:Estimated BAP intake by the general population

Source	**BAP intake (ng/m3)**
Indoor air (main source residential heating)	
Wood burning in open stove (Netherlands)	13-370
Smokey coal (China)	14700
Smokeless coal (China)	600
Gas heating (USA)	0.24-2.8
Environmental tobacco smoke	0.04-22
Cigarette smoke	0.5-7.8
Sidestream cigarette smoke	2.5-19.9

The above is true for BAP and 3,9-DBA, DMBA and 3-MC however, are synthesised model PAHs for laboratory use that are not spontaneously formed during combustion. Therefore, exposure to DMBA and 3-MC may occur as a result of its use in biochemical research. NIOSH (NOES Survey 1981-1983) estimated 448 workers are potentially exposed to DMBA through dermal contact or contact via inhalation at workplaces where DMBA is produced or used. About the origin and/or use of 5,6-CPBA no information could be found.

Vulnerable use and vulnerable groups
PAHs are present in fossil fuels and are formed during incomplete production processes. Others however have no natural origin and are solely designed for use in biochemical research. Occupational situations in which coal and petroleum products are used or processed as well as situations involving heating/combustion of organic material (and metals) may potentially result in exposure to these compounds through inhalation of air particulate matter and dermal contact with combustion products. PAH exposure during biochemical research may also occur (NIOSH estimated 448 workers were exposed to DMBA in the USA alone).
Due to the production of PAHs as a result of anthropogenic and natural processes, PAHs are frequently observed in the environment. Therefore, besides occupational hazards the general population may also be at risk. Smoking (or sidestream smoking) of tobacco, inhalation of polluted air, ingestion of contaminated water and consumption of charcoal-broiled food, roasted coffee and tea, various foods, oils, butter, fats, fruits, vegetables and cereals are the main routes of PAH-exposure for the general population. The estimated intake of individual PAHs in diet is 0.1-8 ug/day (especially through cereals and cereal products due to the large intake). In ambient air, residential heating and environmental tobacco smoke are the major sources of intake; exposure to PAHs from environmental tobacco smoke in indoor air 6.4 ug/day (EHC)
PAHs bioaccumulate in the environment. The lack of hydrolysable groups, stability due to conjugated aromatic rings and high absorbance to sediment and particulate matter makes biodegradation very difficult. Uptake of PAHs, especially in organisms lacking PAH metabolising enzymes like the cytochrome P450 mixed-function oxygenase, will result in accumulation of PAHs in fatty tissues. Especially, animals at the top of the food chain, especially larger fish and mammals like the sea lion, whale, otter and seals are at risk. However, animals including humans which do have an PAH-metabolising apparatus, are not free of risk at al. PAH-metabolism leads to the production of carcinogenic reactive intermediates.

Release to the environment
Release of PAHs to the environment is an unintended consequence of processing and use of coals and petroleum in which they naturally occur, or through incomplete combustion processes which can either be natural or anthropogenic (BAP and 3,9-DBA). Some PAHs, like DMBA and 3-MC, are solely released in the environment due to their use in biochemical research. About the origin op 5,6-CPBA no information could be found.

Summary of environmental fate
PAHs emitted in the atmosphere are subject to photolysis. However, strong adsorption to particulate matter drastically hampers photodegradation. This gives atmospheric PAHs the opportunity to travel long distances ton remote areas without primary sources of PAHs, atmospheric half-lives of over a year are reported. Particulate PAHs can be cleared by wet or dry deposition. If released to soil, PAHs will strongly absorb to soil particles and will be considered as immobile. No leaching to the groundwater compartment will occur. When emitted in water, PAHs will strongly adsorb to the sediment. Although volatilisation of PAHs from dry or wet surfaces might occur, it is supposed not be an important fate process due to high absorbance to soil or sediment. Biodegradation in soil and sediment occurs but is a slow fate process. PAHs are reported to accumulate in the environment and in organisms lacking PAH-metabolising enzymes.

Environmental concentrations
PAHs occur in all environmental compartment.

Main sources of PAH contamination in the atmosphere are ambient air, residential heating and vehicle traffic.

Table 7: BAP concentrations in air

Atmosphere	**BAP concentration (ng/m3)**	**Reference**
Rural Background levels		
Mallorca, Spain	0.005	Simo, 1991
Latrobe Valley, Australia	0.002-0.12	Lyall, 1988
Sidsjon, Sweden	0.8-2.5	Thrane & Wickstrom, 1984

Atmosphere	BAP concentration (ng/m3)	Reference
Industrial processes		
Coke plant, Germany	6.3-6.7	Buck, 1991
Aluminium smelters, Canada	2.1-36	Environment Canada, 1994
Incineration plant, Sweden	0.11-0.14	Colmsjo, 1986
Refinery, USA	0.11-0.20	Karlesky, 1987
Urban areas		
Manchester, United Kingdom	0.01-7.02	Clayton, 1992
Los Angeles, USA	0.6-1.6	Arey, 1987
Calcutta, India	30-120	Chakraborti, 1988
Vehicle exhaust		
Soderleds Tunnel, Sweden	12	Ostman, 1991
Chicago tunnel, USA	62.6	Khalili, 1995
Craeybeckx Tunnel, Belgium	9600	De Frey, 1994

PAHs found in the hydrosphere are mostly a result from urban run off, atmospheric deposition or asphalt abrasion (EHC).

Table 8: BAP concentrations in water compartments

Hydrosphere	BAP concentration (ng/m3)	Reference
Surface water		
Surface water, Canada	0.2-1.0	Environment Canada, 1994
Sea water, Germany	0.03-8.8	GFO Sea Navigation & Hydrography, 1993
Emscher, Germany	59-280	Regional Office for water and waste disposal, 1990
Rain water		
Hannover, Germany	1.1-187	Levsen, 1991
Portland, USA	0-0.18	Ligocki, 1984
Netherlands	7-26	Den Hollander, 1986

PAHS are also frequently found in soils and sediments

Table 9: BAP concentrations reported in soils and sediments

Soil and sediment	BAP concentration (ug/kg)	Reference
sediments		
Rhine, Germany	400-1250	Regional office for water and waste disposal, 1989
Various rivers, Japan	5-3700	Environment agency, 1993
Lake superior, USA	45	Hamburg, 1993
Ketelmeer, Netherlands	1100	Netherlands delegation, 1991
North Sea, Netherlands	14-265	Compaan & Laane, 1992
Humber Estuary/The Wash, United Kingdom	33-313	Compaan & Laane, 1992
Pudget Sound, USA	2300	Varanasi, 1992
Various Rhine harbours, Germany	300-19000	Hamburg, 1993
Various harbours near steel mills, Canada	8900-109000	Environment Canada, 1994
Soils		
Near coal gasification plant, Netherlands	38.000	De Leeuw, `1986
Abandoned coal gasification plant, USA	100	Dong & Greenberg, 1988
Brisbane, Australia	24	Pathirana, 1994
Forest brown soil, Germany	143	Bachmann, 1994

Table 10: BAP concentration reported in the European environment (COMMPS program); row 1 represents the aquatic environment, row 2 the sediment

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
50-32-8	benzo(a)pyrene	0.0272	0.0070	0.0123	0.0094	38	579	388
50-32-8	benzo-a-pyrene	976.00	310.00	516.63	655.24	215	1825	1718

90-perctle . - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

The general population is also at risk of exposure to PAHs as a consequence of contamination in their diet. The estimated intake of individual PAHs in the diet is 0.1-8 ug/day. The main contribution appears to be that of cereals or cereal products due to the large amounts consumed. PAHs have been detected in vegetables but are mainly formed during food processing, roasting, frying, or baking. The highest levels were observed in smoked fish and meat, at up to 200 ug/kg food for individual PAHs.

Highest observed amount found of BAP per type of food are depicted in the following table

Table 11: BAP concentrations reported in food

Food	BAP concentration (ug/kg)	Reference
Meat, grilled sausage	1-212	Larsson, 1983
Smoked fish	1-18	McGill, 1982
Vegetables (Lettuce)	2.6	German Ministry of Environment, 1994
Fruits (nuts)	0.4	De Vos, 1990
Puddings, biscuits and cakes	0.04-2.20	Dennis, 1991
Cereals (smoked oats, barley and beans)	0.6-160	Tuominen, 1988
Vegetable oils (corn oil)	0.02-24	Lawrence & Weber, 1984
TOTAL	0.14-1.0	German State Community for Pollution Control (1992)

PAHs have the ability to bioaccumulate in living organisms. Significant amounts of BAP have been detected in a broad set of aquatic species. In algae, waterplants, bivalves, sponges, gastropods, fish and especially lobsters BAP was detected. In Canadian lobsters values up to 1430 ug/kg wet weight were detected near a coking plant, BAP levels in English sole rose up to 570 ug/ kg dry weight near petroleum tanks and up 451 ug BAP/kg dry weight was detected in mussels from the Wadden Sea (Netherlands).

Conclusion

Release of PAHs to the environment is an unintended consequence of processing and use of coals and petroleum in which they naturally occur, or they are released through incomplete combustion processes which can either be natural or anthropogenic. Some PAHs, like DMBA and 3-MC, are solely released in the environment due to their use in biochemical research. Due to their persistent nature PAHs bioaccumulate in the environment. Biodegradation does occur but is a slow fate process, especially in soils and sediments where PAHs are strongly absorbed to particulate matter. Substantial amounts of the PAH BAP have been detected in air, surfacewater, soil and sediment as well as in living organisms including plants as well as animals. Especially aquatic organisms (e.g. crustaceans, bivalves, fish) and mammals and bigger fish at the end of the food chain bear considerable risk.
Humans are also exposed to considerable amounts of BAP. The general population is exposed to PAHs mainly through smoking (or sidestream smoking) of tobacco, ingestion of contaminated water and consumption of contaminated or charbroiled/roasted food. On top of that exposure as a consequence of occupational processes might occur. The latter include the processing and use of coal and petroleum products, industrial processes involving heating and/or combustion of organic material and/or metals and biochemical research.

It can be concluded that PAHs generally (especially BAP) are of high exposure concern. Both human and wildlife exposure is expected. This includes BAP and its slightly less persistent relative 3,9-DBA.

However, DMBA and 3-MC are solely used in biochemical laboratories, which we assume are closed systems. Exposure and disposal into the environment is not expected. Therefore these two PAHs are categorised having a low exposure concern.
Due to lack of information about the origin of 5,6-CPBA categorisation of this PAH is difficult. However, when released to the environment 5,6-CPBA is expected to be the most persistent of all 5 PAHs investigated. Because 5,6-CPBA might be formed during combustion processes it is categorised having a high-exposure concern.

References

EHC Environmental Health Criteria 202, selected non-heterocyclic Polycyclic Aromatic Hydrocarbons, World Health Organisation Geneva 1998.

HSDB Hazardous substances Data Bank, a database of the library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

PROCYMIDONE (CAS NO 32809-16-8)

Procymidone, chemical name 3-(3,5-dichlorophenyl)-1,5-dimethyl-3-azabicyclo[3.1.0]hexane-2,4-dione or N-(3,5-dichlorophenyl)-1,2-dimethylcyclopropane-1,2-dicarboximide, belongs to the group of dicarboximide fungicides.
Trade names include sumilex, sumisclex and S-7131.

Chemical characteristics

Molecular formula procymidone: C13-H11-Cl2-N1-O2

MW = 284.14

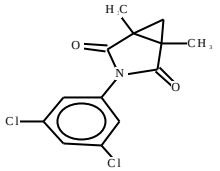


Table 1: Physical/chemical parameters procymidone

Parameter	Procymidone
Water solubility (mg/L 25°C)	2.46 (SANCO) 4.50 (SRC)
Vapour pressure (mm Hg 25°C)	1.40 x 10-4 (SRC) 2.3 x 10-5 Pa (SANCO)
Log Kow	3.08
Henrys Law constant (atm cu3 m/mole)	1.16 x 10-5 (SRC) 2.65 x 10-4 $Pa.m^3$.mol at 20-25°C (SANCO)
Koh (cm3/molecule sec)	7.49 x 10-12 (SRC)
Biodegradation	Slow
BCF (L/kg)	46.95 (SRC)
Koc (L/kg)	430.3 (SRC)

Procymidone is a white granular powder with a musty odour. Its melting point is 163-164.5 °C. The relative density was 1.43 at 22°C. Solubility in organic solvents ranged from 5 g/l (isopropanol) to 216 g/l (chloroform).

Abiotic degradation
Procymidone has a low hydrolytic half-life (more rapid hydrolysis occurs under alkaline pH). It rapidly hydrolyses too its acid derivative PCM-NH-COOH (Max 66.2% in water after 1 day). Procymidone does not dissociate (no pKa found at pH from 2 to 12). Photochemical degradation is from 0.6 days to 10 days. Half-life in air is 9.2 hours.

Hydrolysis rate

Half lives of procymidone	
pH	**15°C**
2	619 d
7	31.5 d
9	13 h

DT_{50} = 8 days under sunlight (distilled water), 10 days in the dark (distilled water), 0.6 days in slightly alkaline river. Degradation of procymidone is mainly hydrolysed especially under basic conditions. The major degradation products were found to be: Procymidone-NH-COOH and Cyclopropane-$(COOH)_2$.

Biotic degradation
In surface waters, high levels of Procymidone – NH-COOH are rapidly formed as a result of imide opening through chemical hydrolysis and biological degradation. This metabolite which can appear in large amounts, is slowly degraded in biologically active water sediment systems. PCM-NH-COOH appears to be slowly degraded in water sediment systems. DT50 would be in the range 48d - 520d (biphasic kinetic) when released to water-sediment. Biodegradation in mineral medium inoculated with extracts from natural sediments is notably faster. Cleavage of molecules is confirmed by formation of major CCA which is shown to be slowly mineralised. In natural water PCM-NH-COOH could be in equilibrium with small amounts of procymidone. The behaviour of the cyclopropyl moiety in water sediment systems has not been described

Under aerobic and anaerobic soil conditions, the major soil residue is procymidone, which is persistent. DT50 would be in the range 48d - 189d. The major metabolites result from , hydroxylation of phenyl and methyl moieties dechlorination , and cleavage of cyclic imide and amide linkages.

Degradation products are not persistent, ultimately degrading to CO_2. Due to possible mobility metabolites might leach to the groundwater compartment

Bioconcentration
Based upon estimated BCF values and slightly high partition coefficient, bio-accumulation of procymidone might be expected.

Use, exposure and emission
Procymidone is a 3',5'-dichloroanilide fungicide on food crops including a wide range of fruits, vegetables, oils seeds, nuts, tobacco and ornamentals. It does not depend on a metabolite or degradation product to exert its intended effect. In principle Procymidone inhibits spore germination, mycelial growth and triglyceride synthesis in funghi. It is applied to spraying or bulb dipping.

Summary of environmental fate
Regarding Koc of 199-513 L/kg and half-life of 48d-520d procymidone is classified as persistent and moderately mobile. As expected the amount of organic matter is an important parameter in the control of the mobility of procymidone. Field studies performed on bare soil reveals that as expected the major part of the residues remain in the upper 10 cm of soil. However, when soils get more alkaline leaching to the groundwater compartment might occur. If released in surfacewater procymidone undergoes hydrolysis. Strong absorption to especially the organic fraction of sediment takes place.
Procymidone has a low vapour pressure(2.3 10-5 Pa. at 25°C) and a rather low Henry's law constant is 2.65*10-3 Pa.m3.mole at 20-25°C. In consequence predicted environmental concentration in air is expected to be negligible.

Environmental concentrations
Procymidone has frequently been observed in different types of food. Wine, grapes and raisins are the main contributors for the chronic risk for the consumers as a result of the treatment against mould on grapes.

Table 2: Calculation of theoretical maximum daily intake according to BBA guidelines in a 4-6 year old child

Commodity	MRL (mg/kg)	97.5 percentile food consumption (g/Person/day)	Intake		% of the ADI[c]
			TMDI 1[a] (mg/Person/day)	TMDI 2[b] (mg/kg bw/day)	
Pears	1.00	6.4	0.00640	0.000474	0.36
Plums (inc. Prunes)	2.00	1.7	0.00340	0.000252	0.19
Peaches and Nectarines	2.00	7.9	0.01580	0.001170	0.90
Apricots	2.00	4.5	0.00900	0.000667	0.51
Cherries (inc. sour)	0.02	5.0	0.000100	0.0000741	0.00
Grapes and raisins	10.00	8.7	0.08700	0.006444	4.96
Strawberries	5.00	4.8	0.02400	0.001778	1.37
Raspberries	0.02*	0.6	0.00001	0.0000008	0.00
Currants	0,02*	2.3	0.00005	0.000004	0.00
Aubergines	2.00	0.7	0.00140	0.000104	0.08
Tomatoes	2.00	15.1	0.03020	0.002237	1.72
Peppers and Chillies - Green	2.00	2.0	0.00400	0.000296	0.23
Cucumber and Gherkins	1.00	11.5	0.01150	0.000852	0.66
Melons, except Water melons	1.00	0.5	0.00050	0.000037	0.03
Head brassicas	2.00	13.2	0.02640	0.001956	1.50
Flowering brassicas	1.00	7.5	0.0075	0.00058	0.42
Lettuce	5.00	1.5	0.00750	0.000556	0.43
Witloof chicory (Sprouts)	2.00	0.3	0.00060	0.000044	0.03
Beans	2.00	3.8	0.00760	0.000563	0.43
Peas	1.00	4.1	0.00410	0.000307	0.23
Beans - Dry	0.20	0.7	0.00014	0.000013	0.01
Peas – Dry	1.00	0.5	0.00050	0.000037	0.03
Oil of Rape seeds	0.20	1.7	0.0003	0.000026	0.02
Oil of Sunflower seeds	1.00	1.8	0.00180	0.000133	0.10
Garlic	0.00	0.4	0.00000	0.000000	0.00
Onions and shallots	0.20	8.3	0.00166	0.000123	0.09

Commodity	MRL (mg/kg)	97.5 percentile food consumption (g/Person/day)	Intake		% of the ADI[c]
			TMDI 1[a] (mg/Person/day)	TMDI 2[b] (mg/kg bw/day)	
Chicken eggs	0.05	37.5	0.00188	0.000139	0.11
Milk	0.05	337.8	0.01689	0.001251	0.96
Meat and Offal	0.05	221.0	0.01105	0.000819	0.63
Animal oils and fats	0.05	10.0	0.00050	0.000037	0.03
TOTAL		**722.0**	**0.38268**	**0.021657**	**16.02**

Table 3: Calculation of theoretical maximum daily intake according to BBA guidelines in a 35-40 year old woman

Commodity	MRL (mg/kg)	97.5 percentile food consumption (g/Person/day)	Intake		% of the ADI[c]
			TMDI 1[a] (mg/Person/day)	TMDI 2[b] (mg/kg bw/day)	
Pears	1.00	6.4	0.00640	0.000107	0.08
Plums (inc. Prunes)	2.00	1.7	0.00340	0.000057	0.04
Peaches and Nectarines	2.00	7.9	0.01580	0.000263	0.20
Apricots	2.00	4.5	0.00900	0.000150	0.12
Cherries (inc. sour)	0.02*	5.0	0.0001000	0.00000167	0.00
Grapes and raisins	10.00	8.7	0.0870	0.00145	1.12
Strawberries	5.00	4.8	0.02400	0.000400	0.31
Raspberries	0.02*	0.6	0.00001	0.000000	0.00
Currants	0.02*	2.3	0.00004	0.000000	0.00
Aubergines	2.00	0.7	0.00140	0.000023	0.02
Tomatoes	2.00	15.1	0.03020	0.000503	0.39
Peppers and Chillies - Green	2.00	2.0	0.00400	0.000067	0.05
Cucumber and Gherkins	1.00	11.5	0.01150	0.000192	0.15
Melons, except Water melons	1.00	0.5	0.00050	0.000008	0.01
Head brassicas	2.00	13.2	0.02640	0.000440	0.34
Flowering brassicas	1.00	7.5	0.0075	0.00012	0.10
Lettuce	5.00	1.5	0.00750	0.000125	0.10
Witloof chicory (Sprouts)	2.00	0.3	0.00060	0.000010	0.01
Beans	2.00	3.8	0.00760	0.000127	0.10
Peas	1.00	4.1	0.0041	0.00006	0.05
Beans - Dry	0.20	0.7	0.00014	0.000024	0.02
Peas – Dry	1.00	0.5	0.00050	0.000008	0.01
Oil of Rape seeds	0.20	1.7	0.00034	0.000005	0.004
Oil of Sunflower seeds	1.00	1.8	0.00180	0.000030	0.02
Garlic	0.00	0.4	0.00000	0.000000	0.00
Onions and shallots	0.20	8.3	0.00166	0.000028	0.02
Wine grape	5.00	97.6	0.48800	0.008133	6.26
Hops	0.00	4.9	0.00000	0.000000	0.00
Chicken eggs	0.05	37.5	0.00188	0.000031	0.02
Milk	0.05	337.8	0.01689	0.000282	0.22
Meat and Offal	0.05	221.0	0.01105	0.000184	0.14
Animal oils and fats	0.05	10.0	0.00050	0.000008	0.01
TOTAL		**824.3**	**0.76981**	**0.01283667**	**9.91**

Metabolites of procymidone including phenyl- and/or methyl hydroxylated PCM, dechlorinated PCM, ring-opened PCM-NH-COOH and PCM carboxylic cyclopropane CCA were not observed in food. Solely a glucoside of methyl hydroxylated PCM was detected in grape juice. The parent compound procymidone is the major reason for general concern.

Procymidone and its metabolites will not likely contaminate the drinking water so that 0.1 ?g/l will not be exceeded. For a consumption of 2 l water/day, the maximum daily intake of procymidone would be 0.2 µg/person per day, corresponding to 0.003 µg/kg bw. Comparing this value with the ADI, there will be no risk to the consumer because of the intake of procymidone through drinking water.

Based on the low vapour pressure of procymidone it is not believed that procymidone will have the tendency to volatilise under practical use conditions. Accumulation of procymidone in the air is therefore not considered likely

Conclusion

Procymidone is a fungicide used on food crops. It is persistent, highly bioaccumulative and residues are frequently observed on food. Especially consumption of wine, grapes, raisins, tomatoes, strawberries, head brassicas, peaches, nectarines, apricots, cucumber, gherkins but also milk and meat might pose a risk. Human exposure is evident and hence procymidone is categorised as high exposure concern.

References

SANCO (2000). SANCO documents on procymidone

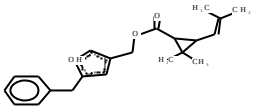
SRC (2002). Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

RESMETHRIN (CAS NO 10453-86-8)

Resmethrin, chemical name 2,2-dimethyl-3-(2-methyl-1-propenyl)cyclopropanecarboxylic acid [5-(phenylmethyl)-3-furanyl]methyl ester, belonging to the group of pyrethroid insecticides
Trade names include crossfire, chryson, pynosect, synthrin, benzofuroline; NIA-17370; pyretherm and premgard,

Chemical characteristics

Molecular formula resmethrin: C22-H26-O3



MW = 338.45

Table 1: Physical/chemical properties of resmethrin

parameter	Resmethrin
Water solubility (mg/L 25°C)	0.0379 (SRC)
Vapour pressure (mm Hg 25°C)	1.13 x 10-8 (SRC)
Log Kow	5.43 (SRC)
Henrys Law constant (atm cu3 m/mole)	1.33 x 10-7 (SRC)
Koh (cm3/molecule sec)	2.9 x 10-10 (SRC)
Biodegradation	Moderate
BCF (L/kg)	68 (HSDB)
Koc (L/kg)	21,400 (SRC in HSDB)

Abiotic degradation
Photolysis seems to be an important process in the degradation of resmethrin in water and air. Photo degradation of 25 % has been observed for resmethrin in water after 60 minutes exposure to a sun lamp (Ueda 1974 in HSDB). A near surface photosensitised oxidation half life of 0.2 hour has been reported for resmethrin in natural water (Zepp 1978 in HSDB).

A second order hydrolysis rate constant of 0.1705 L/mole·sec at 25°C has been estimated. This corresponds to hydrolysis half-lives of 1.3 years, 47 days and 4.7 days at pH 7, 8 and 9 respectively (SRC in HSDB).

Biotic Degradation
There is no data on the biodegradability of resmethrin, but according to HSDB, resmethrin is expected to be readily biodegradable because other pyrethroids are readily biodegradable (HSDB).

Bioconcentration
An estimated BCF of 68 was calculated for resmethrin from a log Kow of 5.43 (HSDB). Thus the potential for bioconcentration is expected to be moderate (Tomlin 1997 in HSDB).

Use, exposure and emissions
Resmethrin is a potent non-systemic insecticide, effective against a wide range of insects. It is used to control agricultural, horticultural, household and public health insect pests often in combination with more persistent pesticides (Tomlin 1994). It is used for houseflies, cockroaches, household insects, pet sprays, pet shampoos, for application on horses and in mosquito control by aerial application (HSDB).

Release to the environment
Release to the environment is an intended result of the use of resmethrin as a pesticide. Resmethrin may also be released from the production site.

Summary of environmental fate
After emission to water, resmethrin is expected to sorb strongly to suspended particles and sediments. Volatilisation from the water surface is not expected to be important. In the aqueous system, it is expected that resmethrin will be removed by hydrolysis, biodegradation and direct and indirect photolysis near the surface (HSDB).

After application to soil, resmethrin is expected mainly to be immobilised at the surface due to relatively strong sorption. Here it will be degraded by microorganisms, sunlight and hydrolysis. Evaporation of deltamethrin from dry and wet soil surfaces is expected to be low (HSDB).

If released to air, resmethrin is expected to be found solely in the particulate phase which will be removed from the atmosphere by dry and wet deposition (HSDB). There is also evidence that resmethrin, present as aerosols, will undergo rapid hydrolysis in sunlight (Samsonov 1996 in HSDB).

Environmental concentrations
No data on environmental concentrations have been found.

Vulnerable use and vulnerable groups
People with chronic respiratory disease, especially asthma, may experience exacerbation of symptoms when exposed to resmethrin (HSDB).

Conclusion
Resmethrin is used as a pesticide to control agricultural-, horicultural-, household- and public health related pests. It is applied in pet shampoos and insect sprays for in-door use. Resmethrin is expected to be readily degradable and moderately bioaccumulative. Although it is hardly detected in the environment, human exposure is expected through consumption of treated crops and in-door use. Resmethrin is categorised as a compound of high exposure concern.

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

HSDB Hazardous Substances Data Bank, a database of the national library of medicine's TOXNET system (http://toxnet.nlm.nih.gov October 2002)

EPIWIN v.3.10. Environmental property estimation programme package. Office of pollution prevention and toxics, US EPA. 2000.

TERBUTRYN (CAS NO. 886-50-0)

Terbutryn, chemical name Butylamino-4-ethylamino-6-methylthio-1,3,5-triazine; Methylthio-4-ethylamino-6-tert-butylamino-1,3,5-triazine; 2-tert-butylamino-4-ethylamino-6-methylthio-1,3,5-triazine or N-(1,1-dimethylethyl)-N'-ethyl-6-(methylthio)-1,3,5-Triazine-2,4-diamine; belongs to the family of triazine herbicides
Trade names include A1866, Clarosan, GS14260, HS14260, Igran, Prebane, Shortstop and Terbutrex

Chemical characteristics

Molecular Formula terbutryn: C10-H19-N5-S1

MW = 241.36

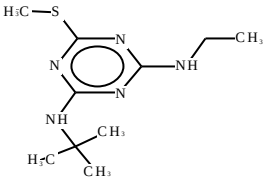


Table 1: Physical/chemical properties terbutryn

Parameter	Terbutryn
Water solubility (ng/L 25°C)	16.9 (SRC)
Vapour pressure (mm Hg 25°C)	2.1·x 10-6 (SRC)
Log Kow	3.74 (SRC)
Henrys Law constant (atm cu3 m/mole)	1.15·x 10-8 (SRC)
Koh (cm3/molecule sec)	1.07. x 10-11 cm^3 (SRC)
Biodegradation	Fast/Moderate
BCF (L/kg)	72.4 (SRC) 100 (Kenega in HSDB)
Koc (L/kg)	635.3 (SRC) 2000 L/kg (Tomlin 1994))

Abiotic degradation
Terbutryn may be subject to slow hydrolysis in water or soil. This prediction is based on a hydrolysis time of 500 years for the similar compound prometryne (Kaufman in HSDB). Terbutryn in the vapour phase may be subject to reaction with photochemically-produced hydroxyl radicals, and an atmospheric half-life of approximately 3.1 hours has been estimated (HSDB). Photodegradation is not regarded as an important mechanism of terbutryn removal from soil (HSDB).

Biotic Degradation
Biodegradation is expected to be the most important removal mechanism of terbutryn in soil. The half-live in soil is 14-28 days (Tomlin 1994). In both sandy and clay soil, no residual terbutryn was detected one year after application (Stecko 1972 in HSDB). Depending on rate of application, soil type and climatic conditions, residual terbutryn activity in soil 3-10 weeks after application has been reported (HSDB). A rather low mobility in soil is expected due to the low water solubility and relatively high Koc value, and leaching to surface and ground water is estimated to be of minor importance. If released to water, terbutryn is expected to sorb to sediment and particulate matter. Half-lives of 240 and 180 days have been reported in pond and river sediment, respectively (Muir 1982 in HSDB). Half-lives ranging from approximately 3-4 weeks have been measured in pond water (Muir 1981 in HSDB).

Bioconcentration
Based upon the estimated BCF of 100, terbutryn is not expected to bioaccumulate in aquatic organisms. Due to its low mobility in soil and strong sorption to particulate matter, terbutryn concentrations in water are expected to be very low. Only a low potential for bioaccumulation was observed in a sediment dwelling annelid exposed to contaminated sediment (Muir 1983 in HSDB). In mammals, 73-85% of orally administrated terbutryn is eliminated within 24 hours.

Use, exposure and emissions
Terbutryn is used for control of a large number of grass and broadleaf weeds in agricultural crops. Uptake of terbutryn in plants primarily takes place via the roots and to a lesser extent via the leaves. Terbutryn inhibits photosynthesis in susceptible plants. Terbutryn is also used as an aquatic herbicide for control of algae and macrophytes in water courses, reservoirs and fish ponds (Tomlin 1994) Occupational exposure to terbutryn may occur though inhalation and dermal contact during manufacturing and handling (incl. use) of the substance (HSDB).

Release to the environment
Release to the environment is an intended result of the use of terbutryn as a pesticide. Terbutryn may also be released from the production site.

Summary of environmental fate
Following application to soil, biological degradation is expected to be the major mechanism of removal, however, more specific information about soil degradation half-lives is lacking. Volatilisation from surface soil and photodegradation is not expected to be of significance (HSDB). Leaching to surface water and ground water is not considered to be of major concern. However, hydroxy terbutryn, which is a major degradation product of terbutryn, is more mobile and persistent and may be leached to surface and ground water.
If released to water, terbutryn is expected to sorb to sediment and particulate matter due to its binding properties. Terbutryn is regarded as persistent in sediments. In the water column, rapid degradation of terbutryn is expected.

If released to air, terbutryn is expected to exist predominantly in the particulate phase (Eisenreich 1981 in HSDB) where it may be subject to reaction with hydroxyl radicals.

Environmental concentrations
In the European COMMPS program European environmental concentration of terbutryn was determined in water sediment:

Table 2: Occurrence of terbutryn in the environment

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
886-50-0	terbutryn	0.2785	0.0369	0.0704	0.0840	15	81	19

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

Vulnerable use and vulnerable groups
Workers involved in manufacturing and handling (incl. use) of the substance are expected to be the most vulnerable groups.

Conclusion
Terbutryn belongs to the group of triazol/triazine herbicides against broad-leaved weeds. It is used on food crops. Human exposure might be expected through consumption of treated crops, however no data indicate terbutryn is actually present. Due to its biodegradability and because it is not bioaccumulative, human exposure is less likely. Wildlife exposure can not be excluded because of its use as a herbicide. Terbutryn is categorised as medium exposure concern. Terbutryn metabolites might be more persistent and more mobile, hence some caution in categorisation has to be taken.

References
SRC (2002), Syracuse research corporation PhysProp on-line database, http://esc.syrres.com

HSDB (Hazardous Substances Data Bank) (2002). A database of the national library of medicine's TOXNET system, http://toxnet.nlm.nih.gov

Tomlin, C. (1994). The pesticide manual, 10th ed. British crop protection council, Surrey, UK and the Royal society of chemistry, Cambridge, UK.

TRICHLOROBENZENE (CAS NO 12002-48-1)

Three isomers of trichlorobenzene exist: 1,2,3-trichlorobenzene (Cas no 87-61-6), 1,2,4-trichlorobenzene (Cas no 120-82-1) and 1,3,5-trichlorobenzene (108-70-3). It is usually available as a mixture. Synonyms for trichlorobenzene are: AI3-08095, Invalon TC, Pyranol 1478, TCB, TCBA.

Chemical characteristics

Molecular formula: C6-H3-Cl3

MW = 181.45

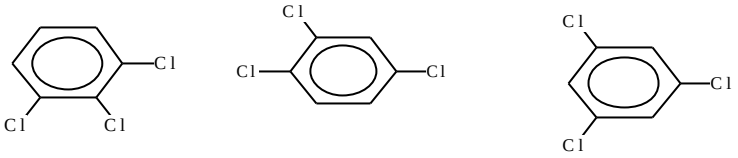


Table 1: physical/chemical parameters of trichlorobenzene

Parameter	1,2,3-Trichlorobenzene	1,2,4 Trichlorobenzene	1,3,5 Trichlorobenzene
Water solubility (mg/L 25°C)	18 (SRC)	49 (SRC)	6.01 – 30 (HSDB; SRC)
Vapour pressure (mm Hg 25°C)	0.21(SRC)	0.46 (SRC)	0.49 (SRC)
Log Kow	4.05 (SRC)	4.02 (SRC)	4.19 (HSDB; SRC)
Henrys Law constant (atm cu3 m/mole)	1.25 x 10-3 (SRC)	1.42 x 10-3 (SRC)	1.89 x 10-3 (SRC)
Koh (cm3/molecule sec)	0.28 x 10-12 (SRC)	0.28 x 10-12 (SRC)	0.68 x 10-12 (SRC)
Biodegradation	Slow	Slow	Slow
BCF (L/kg)	262.1 (SRC) 120-2400 (HSDB)	248.5 (SRC 120-2400 (HSDB)	336 (SRC) 120-2400 (HSDB)
Koc (L/kg)	732.5 (SRC) 630-100000 (HSDB)	717.6 (SRC) 630-100000 (HSDB)	703 (SRC) 630-100000 (HSDB)

At room temperature trichlorobenzene is a colourless liquid (HSDB).

Abiotic degradation

Due to their vapour pressure, trichlorobenzene is expected to be present as a vapour in the atmosphere. There is can be degraded by hydroxyl radicals with an estimated half-life of 24-57 days (Meylan and Howard 1993 in HSDB). Photodegradation and hydrolysis are not expected to be significant degradation processes (SRC in HSDB).

Biotic degradation

In soil trichlorobenzene is expected to degrade slowly. Expected half-lives range from several weeks to a few months. Transfer from soil is slowly; adsorption is high and volatilisation from soil is low (CITI 1992; Masunga et al 1996; both in HSDB).

Biodegradation in water is slowly: the aerobic and anaerobic half-lives for 1,2,4-trichlorobenzene are 28 and 110 days, respectively. Trichlorobenzene will bind to organic matter, and volatilisation from water is an important removal process.

Biodegradation was observed in anaerobic sediment, with half-lives of 23-41 days. Comparable degradation rates have been observed in sewage sludge amended soil. Degradation occurred also in sediment from freshwater streams, with reported half-lives of 50-323 days (Wang and Jones 1994; Peijnenburg et al 1992; both in HSDB).

Bioconcentration

The BCF for trichlorobenzene in fish is calculated to be 336, based on the octanol-water partition. Experimental data show bioconcentration factors, ranging from 120 to 2,400 for carp. Therefore, the bioconcentration potential is considered to be high (CITI 1992; Franke et al 1994; both in HSDB).

Use, exposure and emissions

The major uses of trichlorobenzene are as a chemical intermediate, solvent for dyes, degreasing solvent, dielectric fluid, lubricating oil additive and as heat transfer medium. It has formerly been used as insecticide. Trichlorobenzene is also formed as an impurity by the production of monochlorobenzene (SRI; NRC 1977; Bryant 1993; both in HSDB).

In the 1970s trichlorobenzene was used in the United States in quantities of several thousands of tonnes. No other used data are available (SRI in HSDB).

Occupational exposure to trichlorobenzene is possible via inhalation and dermal contact in workplaces where this chemical is produced or used. The general public may be exposed via ingestion of contaminated food and drinking water or the inhalation of ambient air. Furthermore, contact with wastewater might be a route of exposure (SRC in HSDB).
No emissions have been quantified.

Vulnerable use and vulnerable groups
Trichlorobenzene could form a potential risk to occupational exposed workers. The highest concentration observed in 8 solid waste composting facilities in the USA was 9 µg/m^3 (Eitzer 1995 in HSDB). The compound is irritating to the respiratory tract (Sittig 1985 in HSDB).
The former use as insecticide was more vulnerable, due to the intended diffuse release of the chemical.

Release to the environment
Due to the use in various applications, trichlorobenzene can be released to the environment via various waste streams (Lewis 1993; Bryant 1993; both in HSDB).

Summary of environmental fate
Trichlorobenzene exists in the atmosphere as vapour. There it can be degraded by hydroxyl radicals with a half-life of 24-57 days. Adsorption coefficient predict a low mobility in soils and sediments. Volatilisation from dry soils is unlikely to take place; from moist soils this distribution process is considered to be more important, based on the Henry's law constant. Trichlorobenzene that stay in soils is expected to degrade slowly.
Also in water, adsorption is an important process, as well as volatilisation. Furthermore, aerobic nor anaerobic biodegradation are important removal processes.
Therefore, soil is the most important environmental compartment (SRC in HSDB; Fugicaty calculations in EPIWIN).

Environmental concentrations
Several environmental concentrations of trichlorobenzene are known. It has been detected in Northern American waters up to 8 µg/L (USEPA 1985 in HSDB). More common detected concentrations around the world are in the order of < 10 ng/L (Botta et al 1996; Piet et al 1980; Grob and Grob 1974; Chan 1993; all in HSDB). It has also been detected in the effluent of municipal waste water treatment plants, at an average concentration of 0.13 µg/L. Influent concentrations ranged from 1-60 µg/L (USEPA 1984 in HSDB).
Trichlorobenzene concentrations in fly ash from municipal waste incinerators in the USA were found to be 27-250 µg/kg. In the effluent of a German incinerator concentrations varied from 0.07-0.55 µg/m^3 (Shane et al 1990; Jay and Stieglitz 1995).
Trichlorobenzene has been detected in soil samples from the USA, Russia, China, Japan and the Netherlands. The range of concentrations was very large: 0 - 6800 µg/kg, with the highest concentrations reported in samples from Russia (Staples et al 1985;Hauser and Bomberger 1982; Elder et al 1981; Beurskens et al 1994; Ristola et al 1996; Kawata et al 1997; Van Zoest and Van Eck 1991; Ten Hulscher et al 1997; Lee and Fang 1997; all in HSDB).

Trichlorobenzene has also been detected in different studies in the atmosphere from urban-suburban areas and areas surrounding production sites at concentrations of approximately 130 and 180 ng/m^3, respectively. It was not detected at a remote rural site (USEPA 1982; USEPA 1985; Brodzinski and Singh 1982; all in HSDB).
Trichlorobenzene has also been detected in various species of fish. Concentrations ranged from ND to 2.7 mg/kg (USEPA 1985; Staples et al 1985; Kuehl et al 1983; Oliver and Nicol 1982; Young et al 1980; Jan and Malnersic 1980; Kuehl et al 1994; all in HSDB).

In the European COMMPS program European environmental concentration of trichlorobenzene were determined in water and sediment:

Table 2: Occurrence of trichlorobenzene in the European environment (COMMPS)

CAS	Compound	90-perctle. [µg/l]	Median [µg/l]	ar. Mean [µg/l]	sdev [µg/l]	Sampl. St.	entries used	entries >DL
Water								
87-61-6	1,2,3-trichlorobenzene	0.0309	0.0084	0.0142	0.0207	44	1296	1165
120-82-1	1,2,4-trichlorobenzene	0.1573	0.0117	0.0529	0.0568	63	1605	1308
108-70-3	1,3,5-trichlorobenzene	0.0344	0.0084	0.0247	0.0672	43	1188	1093
Sediment								
87-61-6	1,2,3-trichlorobenzene	23.23	5.56	9.70	9.15	32	761	527
120-82-1	1,2,4-trichlorobenzene	76.72	8.86	25.12	23.42	55	790	658
108-70-3	1,3,5-trichlorobenzene	32.14	6.26	11.25	7.23	28	727	526

90-perctle. - EU-level 90-percentile of substance concentration (used for exposure scoring)
Median - EU-level median
ar. Mean - EU-level arithmetic mean
sdev - standard deviation of arith. mean
Sampl. St. - number of sampling stations from which data were used to calculate the exposure concentrations
entries used - number of measurements used to calculate the exposure concentrations
entries >DL - number of used measurements whith concentrations higher than the corresponding determination limit

Toxicity

Several studies on the toxic effects of trichlorobenzene are available. Decline of hatching success has been reported at 2.32 ppm exposure (Murphy et al 1979 in HSDB). Acute toxicity to mice is low: the retrieved LD50 was 300 mg/kg (Yamamoto et al 1979). A more recent study by Black et al (1988 in HSDB) concluded that there was no evidence of teratogenic or fetotoxic effects of any of the isomers. Greatest toxicity was observed for the 1,2,4-isomer. This is supported by the results from Cote et al (1988 in HSDB).

In the human body trichlorobenzene is detected in highest concentrations in the adipose tissue, which is in accordance with the high K_{ow}. Concentrations are 16.1 ppb for current workers, 16.4 ppb for former workers and 14.5 ppb for the control group (Fait et al 1987 in HSDB).

Conclusion

Trichlorobenzene is a persistent chemical that can bioaccumulate in the environment. Exposure is possible for occupational workers and the general public. It has been detected in the environment in various compartment. Its persistent and bioaccumulative characteristics together with its observed presence in the environment, make trichlorobenzene a substance of high exposure concern.

References

HSDB Hazardous Substance Data Bank, a database of the library of medicine's TOXNET system (http://toxnet.nlm.nih.gov), visited in November 2002

EPIWIN, AopWin and BIOWIN are part of the EPIWIN software, designed by the USEPA