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Presentation and analysis of a general algorithm for risk-assessment on secondary poisoning.

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Summary

The study in this report was carried out in the frame of the project "Evaluation system for new chemical substances". The aim of the study was to present a general algorithm for risk-assessment on secondary poisoning of birds and mammals. Risk-assessment on secondary poisoning can be an asset to risk-assessment on direct poisoning in setting quality standards for the environment. The water - fish - fish-eating bird or mammal pathway was analyzed as an example of a secondary poisoning pathway.
Parameters used for the algorithm are the bioconcentration factor for fish (BCF) and the no-observed effect concentration for the group of fish-eating birds and mammals ($NOEC_{fish\text{-}eater}$). For the derivation of reliable BCF's preference is given to the use of experimentally derived BCF's over QSAR estimates. NOEC's for fish-eaters are derived by extrapolating toxicity data on single species. Because, data on fish-eating species are seldom available, toxicity data on all bird and mammalian species were used.
The proposed algorithm (MTR = $NOEC_{fish\text{-}eater}$ / BCF) was used to calculate maximum tolerable risk levels (MTR's) for the compounds: lindane, dieldrin, cadmium, mercury, PCB153 and PCB118. It was concluded that for mercury and dieldrin secondary poisoning of fish-eating birds constitutes a critical pathway. For these compounds, effects on populations of fish-eating birds and mammals can occur at levels in surface water below the MTR calculated by risk-assessment for aquatic organisms. Secondary poisoning of fish-eating birds and mammals is not likely to occur for cadmium at levels in water below the MTR calculated for aquatic organisms.

1. INTRODUCTION

At the National Institute of Public Health and Environmental Protection (RIVM) methods are developed to predict and assess risks to the environment posed by the production and use of new chemicals. This is carried out in the frame of the project "Evaluation system for new chemical substances". The policy document "Premises for risk management" (DGM 1990) sets the Dutch approach to environmental risk management for chemicals. In this document the environmental risk is evaluated by comparing the concentration in the environment (EC) to the concentration at which the no-effect concentration (NEC) for no more than 5% of the species will be exceeded (HC5-value).

Risk is considered to be intolerably high if:	$EC/HC5 > 1$
Risk reduction is considered to be desirable if:	$0.01 < EC/HC5 < 1$
Risk is considered to be negligible if:	$EC/HC5 < 0.01$

HC5-values are derived from the results of laboratory toxicity tests by means of extrapolation procedures (Van Straalen & Denneman 1989, Aldenberg & Slob 1991).

The term risk-quotient is used for the ratio of the environmental concentration and the no effect concentration. This risk-quotient is used as a general basis for the evaluation of chemical substances for a number of purposes:

- setting quality standards for the environment. Environmental concentrations beyond the HC5 - value are intolerable, hence the HC5-value can be termed as the "maximum tolerable risk level" (MTR). Environmental concentrations below HC5/100 pose negligible risks and are therefore termed "desirable levels" (DL).
- a priori risk-assessment on new chemicals. The probability that the EC exceeds the no-effect level should be low in any future situation.
- risk-evaluation on current and new pesticides. Risk should be low for defined exposure situations.
- setting priority for current chemicals. The higher the risk-quotient, the higher the priority.

In an earlier study on setting environmental quality standards (Van de Meent et al. 1990) MTR's have been derived for direct exposure to environmental media. Exposure to contaminated food (secondary poisoning) has not been taken into account.

This document reports on a study that has been carried out to develop a methodology for including risk-assessment on secondary poisoning in the derivation of environmental quality standards (MTR's, DL's). The water - fish - fish-eating bird or mammal food chain is selected here as an example of a secondary poisoning pathway. This selection was made because effects on natural populations are well documented for this pathway.

2. DETERMINATION OF THE CRITICAL PARAMETERS FOR THE ALGORITHM.

MTR's for aquatic organisms (Van de Meent et al. 1990) are determined by calculating no-effect concentrations in surface water (NEC), because toxic effects on aquatic organisms are mainly caused by direct uptake of chemicals from the water. In the case of secondary poisoning, the route of uptake is through ingestion with food. So, MTR's for the pathway analyzed in this report should be determined using no-effect concentrations (NOEC[1]) for chemicals in food. For fish-eating birds and mammals NOEC will be expressed as mg/kg fish. To include risk-assessment on secondary poisoning in setting quality standards for surface water, concentrations in fish should be related to concentrations in water.

Chemicals are distributed in surface water over the water/sediment and biota (such as fish). Fish can accumulate chemicals to levels far beyond the concentration in the waterphase. For this phenomenon, the term bioconcentration factor (BCF) was introduced. The BCF is defined as the concentration of a compound in fish (mg/kg) / the concentration of that compound in water (mg/l).

To include risk-assessment on secondary poisoning in setting quality criteria for surface water, data are needed on:

1. No effect concentrations for aquatic organisms
2. No effect concentrations for fish-eating birds and mammals.
3. Bioconcentration factors

2.1 Methodology

The methodology of deriving NOEC's for aquatic organisms is described in Van de Meent et al. (1990). The methods for deriving NOEC's for fish-eating birds and mammals and BCF's are discussed below. Data were collected on a set of selected compounds to analyze and validate these methods. These compounds are: lindane, dieldrin, cadmium, mercury, PCB153 and PCB118.

There are 2 reasons for the choice of these compounds;

1. The compounds are representatives of three groups that are of great environmental concern: organo-chlorines (lindane & dieldrin), heavy metals (cadmium & mercury), PCB's (congeners nr 153 and 118). Compounds in these groups are known to accumulate in fish. In case-studies, observed effects on bird and mammal populations are often suspected to be caused by a representative of one of these groups. So, the selected compounds are examples for which the selected pathway might be a critical exposure route for the environment.
2. One might expect that a large data set will be available on these compounds because they are well-know. This facilitates their use in analyses and validation of the algorithm.

1 = different criteria are used in several types of studies in toxicology and ecotoxicology, e.g. NOEC, NOEL, NEC NOED and NOLC. For reasons of readability, only NOEC will be used as the criterium henceforth. For the same reason "concentration" will be used even if it is sometimes possible, or even better to use "dose" or "level".

2.1.1 **Bioconcentration factors**

BCF values for lipophilic chemicals can be estimated using QSAR's. Mackay (1982) published a simple relation between K_{ow} (octanol/water partition coefficient) and BCF for fish (on wet weight basis):

$$BCF = 0.048\ K_{ow}$$

Many alternative QSAR's relating BCF to K_{ow} or S (solubility) have been reported (Esser 1986). K_{ow} values can be obtained from industrial reports, literature or the MEDCHEM ClogP data base.

Different methods are used to calculate K_{ow}. Often, a large variation is found in the K_{ow} values of a compound by using different methods. So, if the BCF is estimated using K_{ow} values, this will also vary. A brief discussion on the selection of reliable K_{ow} values is given in section 4.1.1. The ClogP recommended value is used to estimate BCF on the lipophilic compounds in this report.

The predictability of the BCF by means of this QSAR is generally considered to be adequate. However, in this report preference is given to the use of experimentally derived BCF's. The reason for this is that other factors than lipophilicity could influence bioconcentration. This especially holds for compounds with a $\log K_{ow}$ value outside the range 2-6, for which this QSAR gives a less reliable estimate of the BCF.

For the selected compounds in this study, literature was screened on BCF values measured either in laboratory or field studies. A quality assessment was carried out on these studies using a number of criteria:

1. The experimental duration had to be sufficiently long in order to establish or approach a steady-state between concentrations in water and fish.
2. No signs of overt toxicity to fish should have been observed.
3. Only studies reporting on BCF's for whole body of fish (wet weight) were selected.

A geometric mean BCF value was calculated from the values selected from literature. If more than one value was determined on a single species, a geometric mean value was first calculated on this species, before an overall mean value was calculated.

2.1.2. **No-effect concentrations for fish-eating birds and mammals.**

NOEC's for the group of fish-eating birds and mammals can be derived using toxicity values on single species. However, toxicological data on fish-eating birds and mammals are seldom available. Therefore, data on other bird and mammalian species were collected. A discussion on the relevance of toxicity data on non-fish-eating birds and mammals in establishing NOEC's on fish-eating birds and mammals is given in section 4.1.2.

Toxicological data on birds and mammals can either be obtained from studies carried out for the registration of the compound or from literature. Review articles and monographs were used to obtain the toxicological data on the compounds in this study. A search profile is given in appendix I.
For all toxicological data obtained from these reviews, original literature was consulted for details on experimental design. For the PCB congeners and lindane an on-line search was carried out, for only a few data could be obtained from reviews. Only studies reporting on dietary and oral exposure have been screened, for the pathway modelled here is referring exclusively to the uptake through the foodchain.

LD50 and LC50 values were selected from reviews as acute toxicity data. If more than one LD50 or LC50 value was obtained for a species, a geometric mean value was recorded.

Since case studies show that effects on bird and mammal populations are seldom caused by mortality after short-term exposure, the use of LD50 and LC50 values in risk-assessment is inadequate. Other parameters were therefore selected:

NOEC(mo) = No Observed Effect Concentration (mortality), as a parameter for mortality at long-term exposure.
NOEC(re) = No Observed Effect Concentration (reproduction) as a parameter for effects on reproduction at long-term exposure.
NOEC(g) = No Observed Effect Concentration (growth) as a parameter for effects on growth reduction at long-term exposure.

The parameters, mortality, reproduction and growth, were selected because of their importance to the population level (Sheenan et al. '84). A discussion on the restriction with respect to these 3 parameters is given in section 4.1.2.

Studies reporting on mortality were used to determine NOEC(mo) values.
. From these studies the highest test dose causing no significant mortality was recorded as a NOEC value.
. If a study reported on a single dose, and <20 % mortality occurred, or if the lowest dose of a tested range caused < 20% mortality, a NOEC value was calculated by applying a safety factor of 2 on the lowest dose tested. A NOEC calculated in this way was only recorded if no measured NOEC value could be obtained from other studies on the same species.
. If the lowest tested dose caused >20% mortality no NOEC value was recorded.
. If no significant mortality was observed in the highest dose tested no NOEC value was recorded.
. To allow for the uncertainty in the derivation of NOEC values (which are values on toxicity at long-term exposure) from studies on short-term exposure (< 1 month), a safety factor of 10 was applied. This will be discussed further in section 4.1.2.
. If more than 1 NOEC value was found for a single species, a geometric mean value was recorded.

For NOEC values on reproduction, studies were selected that reported on effects on spermatogenesis, fertility, pregnancy rate, number of live foetuses, pupal mortality, egg-shell thinning,

egg production, egg fertility, hatchability and chick survival. Selection of NOEC values from these studies proceeded similar to studies on mortality.

Selection of NOEC values from studies on reduction of growth proceeded as with NOEC values on mortality.

Reported toxicity values on heavy metals have been corrected for the relative contribution of the metal group (Cd, Hg or CH_3Hg) to the molecular weight of the compound for which the study was carried out. This enabled a comparison between studies on different cadmium or mercury compounds.

Although quite substantial data sets were obtained on the selected compounds in this study, it is by no means a complete overview of the available literature. Some, maybe very reliable, values may have been missed.

Two extrapolation methods were used in this report to extrapolate from toxicity data on single species to NOEC's for the group of fish-eating species, as was done by Van de Meent et al. for aquatic organisms.

1. A preliminary extrapolation can be made by a method originally developed by the EPA (EPA 1984). A modification of this model was developed at the RIVM and presented at the OECD workshop; "Ecotoxicological Effects Assessment", at Arlington USA (1990). In this method toxicity data are subdivided into taxonomic groups. However, this subdivision of data is not feasible here because data sets on bird and mammalian species are too limited. The method used in this report can be depicted as:

Available information	Extrapolation factor
Less than 3 LC50 values and no NOEC's	1000 on the lowest value
A minimum of 3 LC50 values and no NOEC's	100 on the lowest value
Less than 3 NOEC's	10 on the lowest value this value is subsequently compared to the value extrapolated from the LC50 values (as above). The lowest value is selected.
A minimum of 3 NOEC's	10 on the lowest value

2. A more refined extrapolation method can be used if NOEC's are available for a minimum of 4 different species. This method is a modification of the Van Straalen/Denneman method (1989), developed at the RIVM by Aldenberg & Slob (1991). In this report the one-sided 50% confidence limit to the HC5 value was used as a NOEC for the group of fish-eating birds and mammals. A

condition of the application of this method is that the data are logisticly distributed. This was tested using the Kolmogorov-Smirnov method (D'Agostino & Stephens, 1986).

NOEC values on different toxicological endpoints were combined for both methods. If for a single species a NOEC was derived on more than one toxicological endpoint, the lowest value was selected as the real NOEC.

At the time this report was written no decision was made on the question whether birds and mammals should be treated as separate groups, or combined into a single group of fish-eaters. Extrapolation was, therefore, carried out on separate data sets as well as a combined data set. The derived values are NOEC's for the group of fish-eating birds and/or mammals, depending on the set of data on which the extrapolation was carried out.

2.2 Validation

As stated above, the bioconcentration factor (BCF) can be used to relate concentrations of chemicals in water to internal concentrations in fish. The methods used to derive BCF values on the selected compounds are described in section 2.1.1. For these compounds concentrations in Dutch surface waters are continuously monitored. Data are reported in the bulletins "Kwaliteitsonderzoek in Rijkswateren" (VROM/RIVM) and " Metingen van radioactiviteit en xenobiotische stoffen in het biologisch milieu in Nederland" (CCRX/VROM), and in the DBW/RIZA Meuse (Kalkhoven 1990) and Rhine (Heymen 1990) reports. A calculation of the mean concentration of a chemical in fish from Dutch surface waters can be made by applying EC * BCF (geometric mean concentration in water * bioconcentration factor). Data on measured concentrations of the selected compounds in consumption fish from Dutch surface waters are available in the annual report (1989) of the RIVO and in the CCRX publications. On the basis of these measured data, BCF values derived in this report can be validated.

For this validation a test on goodness-of-fit was carried out as described by Parrish & Smith (1990). The 0-hypothesis being: the calculated value on the average concentration in freshwater fish (EC*BCF) lies within a factor of 2 of the mean measured value.
BCF was estimated using:

1. The geometric mean of experimentally derived BCF values from literature.
2. The maximum value of experimentally derived BCF's from literature.
3. a QSAR estimated value for BCF using the ClogP recommended value for K_{ow}

The Parrish & Smith tests were carried out on log-transformed data. C-values for this test were calculated after a retransformation into a linear scale.

Validation of calculated NOEC's for fish-eating birds and mammals can be carried out using case-studies.

3. RESULTS

The applicability of the methods to derive BCF's for fish and NOEC's for the group of fish-eating birds and mammals is analyzed for the set of selected compounds. The results on each compound are given below.

3.1.1 **Lindane** (gamma-HCH)

The $\log K_{ow}$ value of lindane has been determined by several authors and was found to be in the range of 3.2-3.7. The MEDCHEM Clogp recommended value is 3.61. When a QSAR calculation is made for BCF based on this K_{ow} value, a BCF equal to 196 is found. Table 1 lists experimentally derived BCF's on lindane. The geometric mean value equals 499. BCF(max) equals 1613.

Measured concentrations in Dutch surface waters and Dutch surface water fish are used for validation of these BCF values. Data on measured (dissolved) lindane concentration in Dutch surface waters are given in table 2 for 1980 and 1989. Data on measured lindane concentration in Dutch freshwater fish are given in table 3 for the years 1989 and 1978-1981. The data for 1989 are all on eel (Anguilla anguilla). This is a species with a high lipid content (≈20 %) compared to other fish species (≈5%). For lipophilic compounds like lindane, the BCF, and consequently the concentration in fish, will be strongly influenced by the lipid content. To exclude this influence, data from source literature were standardised for fish with a lipid content of 5%. This was carried out by using published data on lipid content whenever possible, or otherwise assuming a 20% lipid content for eel and 5% for all other species.

The results of the Parrish & Smith test are given in table 4. If BCF is estimated by using the geometric mean of BCF values from literature (table 4a) C-values are 1.6 and 1.2 for 1989 and 1980 respectively. Hence the 0-hypothesis that the calculated values are within a factor 2 of the measured value, cannot be rejected. If BCF(max) or ClogP K_{ow} values are used to estimate BCF, the calculated concentrations in fish do not fit the measured data for 1980 and 1989 respectively (tables 4b and c).

Data on acute and chronic toxicity of the selected compounds to birds and mammals are listed in table 5. Data are presented as they were reported in literature, and converted into a mg/kg food value. Data on bodyweight, daily food intake and daily water intake that were used for the transformation are also given in table 5.

For every species a single value per toxicological endpoint was selected from the range found in literature, as described in section 2.1.2. Extrapolation was carried out using data on birds and mammals as separate sets (tables 6a & 6b), as well as combining them into one data set (table 6c). For the combined data set the Aldenberg & Slob extrapolation method could be used, for a sufficiently large data set was available (n = 5), and the condition of a logistic distribution could not be rejected.

For lindane there seems to be a large difference between the susceptibility of birds and mammals. This difference is caused by the extreme low value recorded as a $NOEC_{(mortality)}$ for Gallus

domesticus (table 5). Because the obtained NOEC value for G. domesticus seems to fall outside the range of NOEC values obtained for other bird and mammalian species, an assessment of the reliability of this value was carried out. The study from which this value was obtained was carried out using three different doses: 4, 16 and 64 mg/kg food (Harrison et al 1963). Groups of 75 newly hatched chicks were exposed for 27 days. A 13% increase in mortality was found in the highest dose group, which is significant at t=0.05. Mortality in the 16 mg/kg food group was below control. Roszkowski & Zadura (1970) found no mortality when dosing chicks orally with an equivalent dose of 114 mg/kg food for 48 days. This study was, however, carried out with 7 weeks old chicks. It is a well known phenomenon that newly hatched chicks are very sensitive, therefore these findings do not necessarily show a discrepancy. Smith et al. (1970) and Sauter & Steele (1972) found effects with doses as low as 5 and 1 mg/kg food, respectively, using egg production as a toxicity parameter. Therefore, the observed NOEC value (16 mg/kg food) found by Harrison et al. (1963) does not seem to be outside the range of values found to be toxic to chicks. A safety factor (10) was applied to this value to reach the listed value (1.6 mg/kg food), for the experimental duration was below 1 month. It is unlikely that this extrapolation is why this value falls outside the range of NOEC values obtained in this report for other bird or mammals, for the same factor was applied on 2 of the other 4 NOEC values (Oryctolagus cuniculus and Mus musculus). So, the obtained value for G. domesticus seems to be reliable.

3.1.2 **Dieldrin**

The in the ClogP data-base recommended value for K_{ow} is 4.32. By QSAR calculation, the estimate for BCF equals 1003. A large range of K_{ow} values is found (4.32-6.2) in the literature. Table 1 lists measured BCF's for dieldrin. A range of 2700-13300 is found with a geometric mean value equal to 7389. Values for internal concentrations in fish from Dutch surface waters can be calculated by applying EC*BCF.

Data on concentrations in eel (Anguilla anguilla) from Dutch surface waters in 1989 are given in table 3. These data were standardised to a 5% lipid content similar to the data on lindane. They are then used for validation of the BCF values. The Parrish & Smith test shows the average calculated value for concentrations in fish in 1989 to fit well to the measured data for 1989, if the geometric mean of experimentally derived BCF values is used. A C-value equal to 1 is found (table 4a). If a maximum value for BCF is used (13300) the calculated value for 1989 is still within a factor 2 of the measured values, however, with a larger C-value (1.9). If the ClogP recommended K_{ow} value is used to estimate BCF a C-value equal to 4.0 is found. In this case the 0-hypothesis is rejected.

Toxicological data on dieldrin are presented in table 5. The results of the extrapolation carried out on these data are given in table 6a for birds, 6b for mammals and 6c for a combined data set. The results of the Aldenberg & Slob extrapolation method indicate that birds and mammals are equally sensitive to dieldrin (6a & 6b). However, for data on mammals the condition of a logistic distribution of the data is not met. Therefore, the EPA-extrapolated value is used as a NOEC for fish-eating mammals (6b).

3.1.3 **Cadmium**

Cadmium is usually found as a compound or free ion in water and rarely as a metal. Cadmium-chloride is usually used for the determination of BCF. An extensive research on BCF values for cadmium was carried out by Taylor (1983), who collected data from over 40 labs. He reported a range in BCF values for freshwater fish of <1 to 3200 with a geometric mean value of 18. The average BCF value calculated from studies by other authors (table 1) is slightly higher (39). It could be concluded that the observed range of BCF factors for cadmium is very large, with maximum values under conditions of low salinity and high temperature (Taylor 1983). The value of 39 was selected to calculate concentrations in fish because of the lack of details in Taylor's study. Because the QSAR for estimation of BCF is valid for neutral organic chemicals only, no estimation was made for cadmium.

Data on the (dissolved) concentrations of cadmium in Dutch surface waters for 1980 are given in table 2. By applying EC*BCF a value can be calculated for the internal cadmium concentration in Dutch freshwater fish. Measured concentrations in consumption fish from Dutch surface waters are given in table 3 for the period of 1977-1982. No correction on these data was carried out for differences in lipid content of species, for cadmium does not primarily accumulate in fat.

The Parrish & Smith goodness-of-fit test showed that the calculated average value for concentration in fish in 1980 gives a good fit to the measured values for 1977-1982, if the geometric mean value of experimentally derived BCF's is used (table 4a). The calculated data for 1980 does not fit the measured data if a maximum value for BCF is used (table 4b). A C-value equal to 6.8 is found.

Data on the toxicity of cadmium to birds and mammals are limited (table 5). Extrapolation to NOEC values for fish-eating species was carried out using the modified EPA method for the separate data sets on birds and mammals (tables 6a & 6b). For the combined data set the Aldenberg & Slob method could be used (table 6c).

3.1.4 **Mercury**

While screening literature for BCF values on mercury, a large difference could be observed between studies in which inorganic mercury concentrations in water were used and studies using organic mercury. Therefore, BCF values for inorganic mercury (as $HgCl_2$ or $HgNO_3$) and (organic) methyl-mercury (CH_3HgCl) were recorded separately (table 1). No QSAR-estimation was made either for inorganic or organic-mercury because this QSAR is not valid for metals or organo-metals.

In natural water systems there is a continuous process of methylation of inorganic mercury. This transformation is carried out by micro-organisms in the water column and sediment (Korthals & Winfrey, 1987). Rudd et al. (1980) found that methylation can also occur in the intestinal and mucous layers of fish. Therefore, calculation of internal concentrations in fish using measured methyl-mercury concentrations in the water column may lead to a severe underestimation of the accumulation potential in the field. From values given by Lee (1987) a concentration factor as high as $4 * 10^6$ can be calculated for the methyl-mercury concentration in the water column and concentrations in pike (Esox lucius). This value is 2 to 3 orders of magnitude higher than the BCF values obtained from

literature (table 1). It, therefore, seems more feasible to use mercury concentrations in the water column regardless of speciation, rather than only methyl-mercury concentrations as EC.
On the other hand, methylation is a rather slow process, and demethylation occurs as well. Moreover, fish can probably take up considerable amounts of methyl-mercury through the foodchain. Verta (1990) concludes, in a study on mercury bioaccumulation in Finnish lakes, that in general concentrations of mercury in water only poorly explain the mercury levels in fish.

Dissolved mercury concentrations in Dutch surface waters in 1989 and 1980 are given in table 2. Measured concentration in fish for the periods 1988-1989 and 1979-1982 are given in table 3. Huckabee et al. (1979) and Luten et al. (1980) report that 80-99% of the mercury in fish is found as methyl-mercury. A validation was carried out on the calculated data for methyl-mercury assuming that all mercury present in fish would be in the methylised form. As for cadmium no correction for the lipid content was carried out, for mercury does not primarily accumulate in fat. The Parrish & Smith test shows that calculated average values for concentrations in fish in 1989 and 1980 are within a factor 2 of the measured values for respectively 1988-1989 and 1979-1982 if a geometric mean BCF value is used. If a maximum value for BCF is used a good fit is found between the calculated value for 1989 and measured values for 1988-1989. The calculated value for 1980, however, does not fit the measured values for 1979-1982 in this case (C = 4.4). The ClogP data base does not give a K_{ow} value for methyl mercury.

An overestimation of internal methyl-mercury concentrations in fish was expected here, for the assumption was made that all mercury in the water column was present as or converted into methyl-mercury, prior to the uptake by fish. The comparison between estimated and measured concentrations using a geometric mean BCF, however, demonstrated that this assumption did not result in a large overestimation.
Hence, an adequate estimation of concentrations in fish was obtained with the simple calculation made here despite the points raised above on the weak relationship between mercury levels in water and fish.

Data on the acute and chronic toxicity of inorganic and organic (methyl-) mercury are presented in table 5. Results of the extrapolation methods are presented in tables 6a, b and c. As for BCF factors, important differences are found between inorganic and organic mercury regarding the toxicity to birds and mammals. For methyl-mercury the Aldenberg & Slob method could be used for both seperate bas well as the combined data sets for birds and mammals. For inorganic mercury the EPA method was used.

NOEC values found for methyl-mercury are lower than for lindane, dieldrin or cadmium. Hence it could be concluded that fish-eating birds and mammals are very susceptible to methyl-mercury. For methyl-mercury a NOEC for fish-eating birds is found to be equal to 0.09 mg/kg. This value can be validated, for case studies on exposure of fish-eating birds to mercury in fish are available in literature. In Finland and Sweden many incidents have been reported on mercury poisoning of the white-tailed eagle (Haliaeetus albicilla) and osprey (Pandion haliaetus) which feed predominantly on fish. Average methyl-mercury concentrations found in the prey of these birds range from 0.2 to 0.7 mg/kg (Koivusaari 1976). Barr (1986) reports on a reduced reproduction success of the common loon (Gavia immer) at methyl-mercury concentrations between 0.3 and 0.4 mg/kg fish. Internal methyl-mercury concentrations in Dutch freshwater fish (table 3) are frequently in excess of these

values. For mammals (NOEC = 0.1 mg/kg) Mason et al. (1986) reports on sublethal effects on and mortality to otters (Lutra Lutra) caused by mercury. Claasen & de Jongh (1988) state that next to PCB's, mercury poses the largest threat to the otter population in The Netherlands.

3.1.5 **PCB153**

Opperhuizen (1985) found BCF values for PCB's to be strongly influenced by steric effects in addition to hydrophobicity. Hawker & Connel (1988) calculated a $\log K_{ow}$ value of 6.92 for PCB153 based on molecular size. Chiou et al. (1977) reported a value 6.72 using a standard shake-flask method. This value is however outside the range for which this method gives a reliable estimate. The Clogp data base gives a considerable higher recommended value (7.75). The QSAR estimate for BCF equals 2699238. No experimentally derived BCF values were found for PCB153. Instead a geometric mean K_{ow} was calculated from the Hawker & Connel and ClogP data. This resulted in a QSAR-estimated BCF value equal to 1010396.

Data on concentrations of PCB153 in Dutch surface waters are limited. This is due to the fact that PCB153 has a strong tendency to bind to particles. Hence concentrations in (filtered) surface water are extremely low (0.2-0.3 ng/l) and difficult to analyze. The Rhine (Heymen 1990) and Meuse (Kalkhoven 1990) reports state that in 1989 concentrations were below 1 ng/l. Assuming the concentration in water to be equal to 0.25 ng/l and using the estimated BCF's mentioned above, internal concentrations in fish were calculated. Large data sets are available on measured concentrations of PCB153 in fish. The data for 1989 are presented in table 3. Because PCB's are highly accumulative in fat, a correction for the lipid content has been applied on these data.

The Parrish & Smith goodness-of-fit test shows the calculated value for concentrations in fish in 1989 to be within a factor 2 of the observed values for 1989 if the geometric mean K_{ow} is used (table 4a). If however, the ClogP recommended K_{ow} value is used (table 4c), the calculated data for the concentration in fish does not fit the measured data (C = 4.6).

The data set on the toxicity of PCB153 to birds and mammals is limited (table 5). An extrapolation to a NOEC value for fish-eating birds and/or mammals was carried out using the modified EPA-method (tables 6a, b and c).

3.1.6 **PCB118**

The $\log K_{ow}$ for PCB118 was calculated by Hawker & Connel (1988) to be 6.74. The recommended value in the Clogp data base is 7.12. A QSAR estimation of BCF for PCB118 can be made equal to 406103 using a geometric mean $\log K_{ow}$ (6.93) and 632763 using the ClogP recommended value. Assuming the concentration in water to be equal to 0.25 ng/l, as was done for PCB153, a calculation of the concentration in fish can be made to equal 0.102 mg/kg and 0.158 mg/kg respectively. For 1989 data on the PCB118 concentrations in fish are given in table 3. A compensation for lipid content has been carried out on these values.

The Parrish & Smith test showed the calculated value for 1989 to be just within a factor 2 of the measured value if a geometric mean K_{ow} value was used to estimate BCF (table 4a). The calculated concentration in fish does not fit the measured data if the Clogp data base recommended value is used to calculate BCF (C = 2.9).

No toxicological data have been found on PCB118. Hence NOEC values for fish-eating birds and mammals can not be calculated.

3.2. Determination of maximum tolerable risk levels regarding secondary poisoning.

The definition of a NOEC implies that when concentrations in fish are smaller than the NOEC value for a sensitive bird or mammalian species (C_i(fish)/$NOEC_{fish\text{-}eater}$ <1), effects on fish-eating birds or mammals are unlikely to occur. When aiming on protection of fish-eating birds and mammals one could argue that if C_i = $NOEC_{fish\text{-}eater}$, a maximum tolerable risk level (MTR) is reached. In the current report it is shown that (for the selected compounds) C_i can quite accurately be determined using EC* BCF. Thus on the basis of the NOEC and BCF a maximum tolerable concentration in water can be calculated. The algorithm in Van de Meent et al. (1990) furthermore, implies that there is a constant factor of 100 between desirable levels (DL) and the MTR.

In this way an algorithm can be derived to obtain standards based on risk-assessment on secondary poisoning:

$$NOEC_{fish\text{-}eater}/BCF = MTR$$
$$NOEC_{fish\text{-}eater}/BCF*0.01 = DL$$

The calculation of MTR values by means of this algorithm can be an asset to MTR values derived with risk-assessments on aquatic ecosystems, as was stated by Van de Meent et al. (1990). For the selected compounds in this report MTR values calculated on both combined and separate data sets for birds and mammals are given in table 7. These are compared to MTR values calculated for aquatic ecosystems as listed in Van de Meent et al. (1990).

For lindane table 7a shows the MTR value obtained for fish-eating birds to be below the MTR value estimated by Van de Meent et al. for aquatic ecosystems. This implies that toxic effects on fish-eating birds could occur at lindane concentrations in water, that are considered to be tolerable if only aquatic organisms are concerned. So with regard to lindane secondary poisoning of fish-eating birds could be a critical pathway and should be taken into account when quality standards for surface water are set.
If MTR values for lindane are calculated based on the data set on mammals or on a combined data set on birds and mammals (tables 7b and c), values will be found beyond the value calculated by Van de Meent et al. In this case it could be concluded that secondary poisoning of fish-eaters is not a critical pathway for lindane. These results stress the caution with which one should proceed when combining toxicity data for birds and mammals.
The MTR values calculated in this report for dieldrin and mercury are equal to or below the values calculated on these compounds for the aquatic ecosystem. So, secondary poisoning of fish-eating birds and mammals could be a critical pathway for dieldrin and mercury. MTR values for mercury are

calculated exclusively on data on methyl-mercury, for the risk-assessment made above (section 3.3.4) showed this to be the mercury form of the highest environmental concern.
With regard to cadmium, MTR values calculated in this report are beyond the value calculated for the aquatic ecosystem, even if a worst-case (BCF max.) approach is taken.
No MTR value was calculated for PCB153 by Van de Meent et al. for the aquatic ecosystem. The values that are derived, in this report, for fish-eating birds and mammals are based on a limited data set and could therefore have large confidence limits. The MTR for this compound should be used as an indicative value. No MTR value could be derived on PCB118 because of the lack of toxicity data.

4. DISCUSSION

4.1 Discussion on the parameters used for the algorithm.

4.1.1 **BCF**

As mentioned in section 2.1.1 BCF's for lipophilic compounds can be estimated using K_{ow} values. K_{ow} values are measured using different methods: shake-flask, RP-HPLC, RP-TLC, or calculated using substituent constants, as described by Hansch & Leo (1979). K_{ow} values that had been obtained from literature for the pesticides and PCB's in this report show a large variation (near 2 orders of magnitude for dieldrin). This is probably due to the use of these different methods. De Bruijn et al. (1989) discuss the restrictions of the above mentioned K_{ow} determination methods in their presentation of the slow-stirring method. They concluded that the reliability of the different methods varies with the properties of the compound tested. Quality criteria should thus be used when selecting a K_{ow} value to calculate the BCF. The MEDCHEM ClogP data base gives a recommended K_{ow} value based on quality criteria, and is thus theoretically suitable to obtain reliable K_{ow} values. If, however, the ClogP recommended value was used to calculate the BCF for compounds in this report, a poor fit was found between calculated and measured concentrations in fish for all compounds.

The only method of determining the BCF that resulted in a good fit of calculated concentrations in fish to measured concentrations in all cases, was the calculation of a geometric mean from experimentally derived BCF values. Therefore, this method should be preferred when risk-assessments on secondary poisoning are made.

The bioconcentration factors used in this report were measured in laboratory. Fish used in these tests were predominantly fed uncontaminated food. For methyl-mercury (Wiener 1987), PCB's and probably dieldrin (RIVO 1989) however, a significant part of the total body burden of fish from natural ecosystems might be accumulated through dietary uptake. It is, therefore, surprising that in this report a good fit was found between the calculated and measured concentrations in fish.
From a 2 year field study carried out by Wiener et al. (1990) a BCF value for 1 year old yellow perch (Perca flavescens) equal to 114000 can be calculated, using total mercury concentration in water, as was done in this report. This value is 8 times higher than the value used in this report (14210). The contribution of dietary uptake could be the reason for the difference in these two values.

4.1.2 **Toxicological data & extrapolation**

For this study, it was decided to select data on mortality, reproduction and growth, but not on other toxicological endpoints. This decision was based on the assumption that only these parameters can cause major effects on the population level. A virus infection recently decimated the seal population in the Dutch Waddensea. One can ask whether immunosuppression, known to occur at exposure to heavy metals and PCB's, played a part in this. So, the question arises whether data on other sub-

lethal endpoints should be included in the risk-assessment. The inclusion of such sublethal parameters could lead to a decreased $NOEC_{fish\text{-}eater}$ value and therefore a lower MTR.

NOEC values selected from literature in this report are based on chronic, sub-chronic as well as on sub-acute exposure. A safety factor (10) was applied to data on sub-acute exposure (< 1 month) in order to allow for the uncertainty caused by the experimental duration. No factor was applied to data from sub-chronic (> 1 month) exposure experiments. This was decided on the basis of selected values for a number of chemicals for which criteria documents were available (data not given in this report). It was found that NOEC values for chronic exposure were on average 9 times as low as NOEC values for sub-acute exposure (range 1-25) and 3 times as low as values for sub-chronic exposure (range 1 to 5). But since the data set only contains data on a few chemicals (8) and two species (rats and mice) the value of these findings is limited, and the choice of safety factors thus arbitrary. Moreover, it could be argued that this factor cannot equally well be applied to studies on reproduction as to studies on growth and mortality. This is because birds and mammals usually have more than one complete reproductive cycle in their lifetime. If a species is exposed to a chemical during 1 month, this period could constitute a considerable part of the time spent for a reproductive cycle, while it could well be insignificant to its entire lifetime. Hence this 1 month period should be regarded as a chronic exposure when reproductive effects are concerned, and as sub-acute for mortality or growth.

The extrapolation method used in this report depended on the availability of data. If a sufficiently large data set (4 NOEC's) was available, preference has been given to the use of the Aldenberg & Slob method. On a limited data set the EPA method was used, leading to a more conservative $NOEC_{fish\text{-}eater}$ value. A further condition to the use of the Aldenberg & Slob method is the log-logistic distribution of the data. The question arises which extrapolation method should be used when a large data set is available, but fails the Kolmogorov-Smirnov log-logistic distribution test. Since the conditions are not met, the Aldenberg & Slob method cannot be used. Application of the EPA method however, could lead to an unrealistically conservative (low) value.

From table 6c it can be concluded that the EPA extrapolation will lead to a more conservative value than the Aldenberg & Slob method. This is convenient, for the EPA method is only used if a limited data set is available, or as a preliminary value. In both cases the reliability is relatively low.

In the EPA extrapolation method (acute) LC50 values can be used to determine a (chronic) NOEC value. However, the acute toxicity of a compound is often not tested with the standard 5-day dietary exposure test from which LC50's can be calculated, but with a single oral dose test. From these oral exposure tests LD50 values are calculated. To test whether these LD50 values can also be used in the EPA method, a study was performed on the relation between LC50 and LD50. A regression analyses was carried out on a set of 120 paired LC50-LD50 values for birds.

This resulted in the relation:

$$LC50 = 10^{1.93 + 0.47 * \log LD50} / 13.9 \qquad (r^2 = 0.32)$$

Thus, if no LC50 values are available for a compound, these can be calculated using LD50 values. The r-square value of this regression, however, was low (0.32), and data were all on pesticides. So,

the application of this relation is limited. Because of these limitations, this method for calculating LC50 values should not be used on a routine basis in risk-assessment. If a risk-assessment has to be carried out on a limited data set, however (e.g in the frame of the "Evaluation system for new chemical substances" project), this relation could be useful.
For separate pesticide groups (organo-chlorines, carbamates and OP-esters), regression lines with higher r-square values were found (appendix II).

The Aldenberg & Slob method was developed to be used on aquatic and terrestrial vertebrates and invertebrates. This method aims at arriving at a "safe" value for 95% of all species. Therefore, this method allows effects on the other 5% of the species. In this report the input in the method consists of data on mortality, reproduction and development of birds and mammals, which would mean that at the calculated value, 5% of all bird and mammalian species could suffer from such severe effects. Moreover, there is an indication that fish-eating species could as a group be more sensitive than all other bird or mammalian species. Ronnis & Walker (1989) and Walker (1990) reported that fish-eating bird species differ in metabolism of lipophilic pollutants from other bird species, and consequently could as a group be more sensitive to such pollutants. Moreover, these fish-eating species could have a higher daily food intake relative to their body weight in comparison to other birds and mammals due to the low energy content of their food. This leads them to be exposed to higher doses. The need for the use of factors to compensate for these differences between fish-eating and non-fish-eating species is at present studied by the Institute for Tidal Waters (DGW) (Lahr & Van der Valk, 1991). These differences could implicate that for the fish-eaters more than 5% of the species are endangered at the calculated "safe" value. One could ask whether this is an acceptable effect. It may be necessary to reconsider the 5% level, which is a chosen parameter in the method.

4.2 MTR's

Derivation of MTR's was carried out in this report using data sets on birds and mammals separately as well as combined into one set. Walker (1983) reported that birds and mammals are not equally sensitive to xenobiotics. This would advocate to carry out risk-assessments on separate data sets. The Aldenberg & Slob extrapolation method, however, allows for differences in sensitivity of taxonomic groups as long as the data follow a log-logistic distribution. Hence data sets can be combined. Nevertheless, it is possible that, when a $NOEC_{fish\text{-}eater}$ is calculated using this method, the 5% of the species which have a NOEC below this level consists entirely of members of the most sensitive group. The percentage of species from this group that will not be protected by the calculated value will then possibly be $>> 5$.
At the time this report was written, no decision was made on whether a separate or combined data set on birds and mammals should be used. The calculated MTR values for lindane show that this decision can have important consequences.

The MTR values proposed by Van de Meent et al., to which MTR values in this report were compared, were derived using a different method (modification 2 to the Van Straalen/Denneman method), which in general results in more conservative values. Because at the moment questions are raised concerning the method followed in modification 2, it could be possible that a recalculation of these MTR's for aquatic ecosystems will be carried out in the future.

4.3 General.

The proposed algorithm in this report is based exclusively on the water-fish-bird/mammal pathway. Fish-eating birds and mammals, however, can also be exposed to chemicals in surface water through different pathways:

1. by drinking water.
2. through dermal contact.
3. through different (larger) foodchains or foodwebs.

Hence, the proposed algorithm could underestimate the risk presented by the presence of a chemical in water.

Fish-eating birds and mammals may be exposed to more than one chemical at the same time. Possible additive effects of chemicals are not included in the methodology presented in this report. Additivity is suspected to occur between the effect of different PCB congeners or between PCB congeners and heavy metals. To compensate for this uncertainty factor the desirable levels (DL) (section 3.2) are introduced.

Furthermore, the risk-assessment made in this report does not include the influence of seasonal changes of the body weight of birds and mammals. Migratorial species are known to lose a considerable proportion of their body weight during the migration. During such a period birds metabolise their fat reserves. Lipophilic chemicals (such as lindane, dieldrin and PCB,s) which were stored in these fat reserves could then be re-introduced into the circulation system, and thus may cause toxic effects.

5. CONCLUSION

The aim of the study in this report was to present a general algorithm for risk-assessment on secondary poisoning. This was approached by analyzing the water - fish - fish-eating bird/mammal pathway. A simple algorithm was proposed using the bioconcentration factor for fish (BCF) and a no- observed-effect concentrations (NOEC) for the group of fish-eating birds and mammals extrapolated from single species data on survival, reproduction and growth. From these parameters maximum tolerable risk levels (MTR) and desirable levels (DL) in water can be derived.

$$MTR = NOEC_{(fish\text{-}eater)} / BCF$$
$$DL = NOEC_{fish\text{-}eater}/BCF * 0.01$$

By calculating MTR values for secondary poisoning, and subsequently comparing these values with MTR values based on risk-assessment on aquatic organisms, it was concluded that for mercury, dieldrin and probably lindane the water - fish - fish-eating bird/mammal could be a critical pathway. Risk-assessment on fish-eating species should therefore be included, if quality standards for surface water are set for these compounds. For cadmium the analyzed pathway is probably of minor importance. For the PCB congeners no conclusion could be drawn on the relevance of secondary poisoning due to the lack of data.

The following conclusions were drawn with regard to the use of the parameters for the algorithm:

1. Preference is given to the use of experimentally derived BCF values over QSAR estimates.
2. A geometric mean value calculated from data presented in literature resulted in the most realistic estimate for the BCF.
3. The choice between the use of a combined or separate data sets for birds and mammals can lead to discrepancies in the conclusion on the relevance of secondary poisoning. This stresses the caution with which one should proceed in combining data sets for different taxonomic groups.

Recommendations for further research:

1. The aim of this study was to present a general algorithm for secondary poisoning. This was achieved by analyzing the water - fish - fish-eating bird/mammal as an example of secondary poisoning. The applicability of the proposed algorithm to other aquatic or terrestrial pathways of secondary poisoning will be the subject for further study. The pathway soil - earthworm - bird/mammal will be analyzed and presented in a follow-up report.

2. Differences in sensitivity to chemicals between fish-eating and non-fish-eating birds are suspected on the grounds of differences in metabolism of xenobiotics. A safety factor should be applied on the MTR values calculated in this report, if fish-eating birds are as a group more sensitive to chemicals. These differences could also be present between fish-eating and non-fish-eating mammals. Hence, there is a need for determining (long-term) toxicity values on chemicals for fish-eating birds and mammals.

3. The Aldenberg & Slob extrapolation method calculates a value at which 95% of the species is protected. Hence 5% of the species might still be at risk at this level. For aquatic organisms this is considered to be a tolerable effect. One can ask, as was mentioned in section 4.1.2, whether this is still considered a tolerable effect, when birds and mammals are considered. A study should be carried out on whether it is necessary to reconsider this 95% level, which is a chosen parameter in the Aldenberg & Slob method.

4. A research on the differences between sensitivity of birds and mammals at chronic exposure to chemicals might help to decide whether MTR's should be calculated using a separate or combined data set for birds and mammals.

5. If a sufficiently large data set is present, the extrapolation method described by Aldenberg & Slob (1991) should be preferred over the EPA method for calculating NOEC's. A problem will arise if a large data set is present, but the condition of a log-logistic distribution of the data is not met. At present a study is being performed at the R.I.V.M. on how, in this case, extrapolation should be carried out (Slooff et al. in prep.).

6. In this report, a conclusion was drawn on the relevance of secondary poisoning, by comparing MTR values calculated based on risk-assessment for fish-eating birds and mammals, to MTR values derived by risk-assessment on aquatic organisms. The MTR values for aquatic organisms (Van de Meent et al. 1990) were however derived by using slightly different extrapolation methods. To make a fully valid comparison MTR's for aquatic organisms should be recalculated with the extrapolation methods used in this report.

7. No conclusion could be drawn on the relevance of secondary poisoning for the individual PCB congeners, because of the lack of MTR's for aquatic organisms (PCB153 & PCB118) and the lack of data on toxicity to birds and mammals (PCB118). To assess the risks posed by these important environmental pollutants, toxicity tests should be carried out.

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Table 1. Experimentally derived bioconcentration factors (BCF) for fish available in literature.

compound	fish-species	experimental duration	C_w(ug/l)	BCF	reference
Lindane					
	Venerupis japonica	10 d	1	121	28
	Lagodon rhomboides	4 d	18-31	218	22
	Cyprinus carpio	20 d	0.0024	273	23
	Pimephales promelas			290	geometric mean
	(,,	32 d	3.4	180	27)
	(,,	304 d		468	& 12)
	Salmo gairdneri	5 w	0.1-0.6	319	18
	Cyprinodon variegatus	4 d	42-109	490	22
	Gambusia affinis	33 d	1.7	560	16
	Salmo trutta fario	20 d	0.0024	658	23
	Leuciscus idus	20 d	0.0024	973	23
	Poecilia reticulata			1017	geometric mean
	(,,	10 d	1	697	28)
	(,,	20 d	0.03	1485	& 23)
	Pseudorasbora parva	14 d	5-20	1246	8
	Laludesthes s. sicculus	7 d	1.8	1613	14
			geometric mean	499	
Dieldrin					
	Gambusia affinis			4010	geometric mean
	(,,	33 d	1.4	2700	16)
	(,,	33 d	4.7	5957	& 16)
	Salmo trutta			4472	geometric mean
	(,,	?	?	3300	1)
	(,,	?	?	6060	& 26)
	Poecilia reticulata	32 d	0.8-4.2	12500	20
	Cottus perplexus	32 d	0.017-8.6	13300	6
			geometric mean	7389	
Cadmium					
	?	?	var	18 (<1-3200)	25
Other authors					
	Anguilla anguilla	60 d	130	4.3	17
	Leopomis macrochirus	6 m	0.5-3	12.2	4
	Fundulus heteroclitus	11 d	400	39.5	7
	Pimephales promelas	9 w	48	48*	24
	Salmo gairdneri			133	geometric mean
	(,,	70 d	10	33	11)
	(,,	140 d	10	540	& 10)
	Poecilia reticulata	180 d	45	280	3
			geometric mean	39	

Inorganic mercury

Anguilla angiulla	32 days	100	153	17
Poecilia reticulata	11 d	1	267	9
Salmo gairdneri			643	geometric mean
(,,	4 d	50	26	13)
(,,	60 d	1	1800	2)
(,,	30 d	0.1	5670	& 21)
			---	
		geometric mean	297	

Methyl-mercury

Lepomis macrochirus	29 d	0.2	>939	5
Salmo gairdneri			13503	geometric mean
(,,	84 d	0.25	6395	19)
(,,	60 d	1	11000	2)
(,,	30 d	0.1	35000	& 21)
Salvelinus fontinalis	39 w	0.03-0.09	14953	15
			---	
		geometric mean	14210	(> value excluded)

PCB153

no data found

PCB118

no data found

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* = estimated from BCF on dry weight using wet weight : dry weight = 1 : 4.

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Table 2. Measured dissolved concentrations in Dutch freshwater (EC) in ug/L. Data for 1989 are obtained from the DBW/RIZA Rhine (Heymen 1990) and Meuse (Kalkhoven 1990) reports, and CCRX publications. Data for 1980 are obtained from the "Kwaliteitsonderzoek in Rijkswateren" bulletin (VROM/RIVM).

compound	year	location	average	range
Lindane				
	1989	Rhine	0.008	0.000 - 0.014
		Meuse	0.013	0.003 - 0.042
			--,----	----------
		geometric mean	0.010	0.000 - 0.042
	1980	Rhine	0.027	0.00 - 0.12
		Meuse	0.030	0.00 - 0.30
		Hollandsch-diep	0.025	0.01 - 0.03
		Scheldt	0.045	0.00 - 0.15
		IJsselmeer	0.008	0.00 - 0.01
			--,----	----------
		geometric mean	0.024	0.00 - 0.30
Dieldrin				
	1989	Rhine	0.001	0.000 - 0.001
		Meuse	0.001	0.000 - 0.001
			--,----	----------
		geometric mean	0.001	0.000 - 0.001
Cadmium				
	1980	Rhine	0.39	0.1 - 1.9
		Meuse	0.36	0.0 - 2.8
		Hollandsch-diep	0.21	0.1 - 0.5
		Scheldt	0.32	0.1 - 1.0
		IJsselmeer	0.13	0.0 - 0.4
		Northsea-channel	0.18	0.0 - 3.0
			--,----	----------
		geometric mean	0.25	0.0 - 3.0

(table 2)

Mercury

1989	Rhine	0.01	0.01 - 0.02
	Meuse	0.01	0.01 - 0.01
		--.----	----------
	geometric mean	0.01	0.01 - 0.02
1980	Rhine	0.06	0.00 - 0.35
	Meuse	0.03	0.00 - 0.30
	Hollandsch-diep	0.07	0.01 - 0.30
	Scheldt	0.04	0.01 - 0.05
	IJsselmeer	0.06	0.01 - 0.45
	Northsea-channel	0.13	0.00 - 0.60
		--.----	----------
	geometric mean	0.06	0.00 - 0.60

PCB153

1989	Rhine	<0.001	0.0002 - 0.0003
	Meuse	<0.001	0.0002 - 0.0003
		--.----	----------
	geometric mean	<0.001	0.0002 - 0.0003

PCB118

1989		?	0.0002 - 0.0003

Table 3. Data on measured internal concentrations (mg/kg) in fish caught in Dutch freshwater systems.
Values for 1989 were obtained from the Netherlands Institute for Fisheries Investigations (RIVO) annual report.
Values for other years are obtained from CCRX publications.

Compound	species	lipid content (%)	year	location	C_i^*	(range)
Lindane						
	Anguilla anguilla	11.2	1989	Rhine	0.009	
	Anguilla anguilla	22.7	1989	Oude Maas	0.012	
	Anguilla anguilla	22.8	1989	Nieuwe Maas	0.009	
	Anguilla anguilla	25.1	1989	Waal	0.011	
	Anguilla anguilla	22.2	1989	Lek	0.009	
	Anguilla anguilla	20.5	1989	Nieuwe Merwede	0.008	
	Anguilla anguilla	18.3	1989	Hollandsch-diep	0.010	
	Anguilla anguilla	21.0	1989	Haringvliet	0.011	
	Anguilla anguilla	22.8	1989	IJssel	0.009	
	Anguilla anguilla	19.5	1989	Ketelmeer	0.006	
	Anguilla anguilla	31.1	1989	IJsselmeer	0.005	
	Anguilla anguilla	14.8	1989	Roer	0.021	
	Anguilla anguilla	15.5	1989	Meuse	0.021	(0.019-0.023)
	Anguilla anguilla	17.5	1989	Twente kanaal	0.026	
	Anguilla anguilla	19.6	1989	Oude Rijn	0.013	
	Anguilla anguilla	20	1981	IJsselmeer	0.013	
	Stizostedion lucioperca	5	1981	IJsselmeer	0.002	
	Anguilla anguilla	20	1980	IJsselmeer	0.003	
	Stizostedion lucioperca	5	1980	IJsselmeer	0.009	
	Anguilla anguilla	20	1978	IJsselmeer	0.004	
	Stizostedion lucioperca	5	1978	IJsselmeer	0.002	
Dieldrin						
	Anguilla anguilla	11.2	1989	Rhine	0.004	
	Anguilla anguilla	22.8	1989	Nieuwe Maas	0.013	
	Anguilla anguilla	25.1	1989	Waal	0.005	
	Anguilla anguilla	22.2	1989	Lek	0.012	
	Anguilla anguilla	22.7	1989	Oude Maas	0.010	
	Anguilla anguilla	20.5	1989	Nieuwe Merwede	0.005	
	Anguilla anguilla	18.3	1989	Hollandsch-diep	0.005	
	Anguilla anguilla	21.0	1989	Haringvliet	0.007	
	Anguilla anguilla	22.8	1989	IJssel	0.004	
	Anguilla anguilla	19.5	1989	Ketelmeer	0.003	
	Anguilla anguilla	31.1	1989	IJsselmeer	0.004	(0.002-0.004)
	Anguilla anguilla	15.5	1989	Meuse	0.010	(0.008-0.012)
	Anguilla anguilla	14.8	1989	Roer	0.004	
	Anguilla anguilla	17.5	1989	Twente kanaal	0.002	
	Anguilla anguilla	19.6	1989	Oude Rijn	0.007	

(table 3)

Cadmium

Stizostedion lucioperca	1980	n.s.	0.003	(0.002-0.025)
Esox lucius	1980	n.s.	0.001	
Perca fluviatilis	1980	n.s.	0.001	(0.001-0.002)
Anguilla anguilla	1980	n.s.	0.009	
Esox lucius	1979	n.s.	0.023	(0.012-0.034)
Abramis brama	1979	n.s.	0.054	(0.008-0.068)
Leuciscus rubilus	1979	n.s.	0.066	(0.029-0.220)
Leusiscus rubilus	1977	n.s.	0.001	
Anguilla anguilla	1977-1982	n.s.	0.014	(0.004-0.050)
Stizostedion lucioperca	1977-1982	n.s.	0.004	(0.001-0.020)

Mercury**

Anguilla anguilla	1989	Rhine	0.234	(0.190-0.260)
Anguilla anguilla	1989	Waal	0.270	(0.230-0.320)
Anguilla anguilla	1989	Lek	0.356	(0.290-0.560)
Anguilla anguilla	1989	Nieuwe Merwede	0.417	(0.300-0.580)
Anguilla anguilla	1989	Hollandsch-diep	0.311	(0.250-0.430)
Anguilla anguilla	1989	Haringvliet	0.696	(0.420-0.980)
Anguilla anguilla	1989	IJssel	0.320	(0.240-0.470)
Anguilla anguilla	1989	Meuse	0.136	(0.120-0.150)
Anguilla anguilla	1989	Dortse Kil	0.417	(0.300-0.620)
Anguilla anguilla	1989	Oude Maas	0.432	(0.320-0.680)
Anguilla anguilla	1989	Ketelmeer	0.118	(0.100-0.140)
Anguilla anguilla	1989	IJsselmeer	0.190	(0.180-0.200)
Perca fluviatilis	1988	Rhine	0.220	
Perca fluviatilis	1988	Nieuwe Merwede	0.240	
Perca fluviatilis	1988	Hollandsch-diep	0.420	
Perca fluviatilis	1988	Haringvliet	0.410	
Perca fluviatilis	1988	IJssel	0.260	
Perca fluviatilis	1988	Ketelmeer	0.380	
Stizostedion lucioperca	1980-1982	variable	0.510	(0.040-1.660)
Anguilla anguilla	1980-1982	n.s	0.270	(0.170-0.480)
Stizostedion lucioperca	1980-1982	n.s	0.300	(0.110-0.740)
Stizostedion lucioperca	1980-1982	Friesland	0.210	(0.025-0.830)
Perca fluviatilis	1980-1982	n.s.	0.510	(0.180-0.820)
Perca fluviatilis	1980-1982	Friesland	0.624	(0.056-1.450)
Esox lucius	1980-1982	n.s.	0.530	(0.270-1.030)
Esox lucius	1980-1982	Friesland	0.082	(0.023-0.160)
Anguilla anguilla	1980	variable	0.300	(0.170-0.480)
Anguilla anguilla	1979	variable	0.219	(0.040-0.740)

(table 3)

PCB153

Anguilla anguilla	11.2	1989	Rhine	0.098	
Anguilla anguilla	22.2	1989	Lek	0.149	
Anguilla anguilla	22.8	1989	Nieuwe Maas	0.110	
Anguilla anguilla	25.1	1989	Waal	0.094	
Anguilla anguilla	22.7	1989	Oude Maas	0.154	
Anguilla anguilla	20.5	1989	Nieuwe Merwede	0.171	
Anguilla anguilla	18.3	1989	Hollands diep	0.131	
Anguilla anguilla	21.0	1989	Haringvliet	0.429	
Anguilla anguilla	22.8	1989	IJssel	0.094	
Anguilla anguilla	19.5	1989	Ketelmeer	0.038	
Anguilla anguilla	31.1	1989	IJsselmeer	0.040	(0.025-0.064)
Anguilla anguilla	15.5	1989	Meuse	0.191	(0.132-0.278)
Anguilla anguilla	14.8	1989	Roer	0.098	
Anguilla anguilla	17.5	1989	Twente kanaal	0.025	
Anguilla anguilla	19.6	1989	Oude Rijn	0.048	

PCB118

Anguilla anguilla	11.2	1989	Rhine	0.038	
Anguilla anguilla	22.2	1989	Lek	0.056	
Anguilla anguilla	22.8	1989	Nieuwe Maas	0.048	
Anguilla anguilla	25.1	1989	Waal	0.040	
Anguilla anguilla	22.7	1989	Oude Maas	0.053	
Anguilla anguilla	20.5	1989	Nieuwe Merwede	0.056	
Anguilla anguilla	18.3	1989	Hollandsch diep	0.046	
Anguilla anguilla	21.0	1989	Haringvliet	0.124	
Anguilla anguilla	22.8	1989	IJssel	0.031	
Anguilla anguilla	19.5	1989	Ketelmeer	0.015	
Anguilla anguilla	31.1	1989	IJsselmeer	0.016	(0.010-0.027)
Anguilla anguilla	15.5	1989	Meuse	0.047	(0.037-0.063)
Anguilla anguilla	14.8	1989	Roer	0.095	
Anguilla anguilla	17.5	1989	Twente kanaal	0.010	
Anguilla anguilla	19.6	1989	Oude Rijn	0.018	

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* = Concentrations in fish standardised for a 5% lipid content, for data on lindane, dieldrin, PCB153 and PCB118.

** = Internal mercury concentrations in fish are for 80-99% in the form of methyl-mercury.

n.s. = not specified.

Table 4. Results of the Parrish & Smith goodness-of-fit test, comparing calculated data on internal concentrations in fish to measured concentrations (at $p < 0.05$). C- values for which the 0-hypothesis (calculated value is within a factor 2 of the measured value) is rejected are given in bold printing.

4a. Using a geometric mean from experimentaly derived BCF values.

Compound	Year	calculated value	lower-limit to the average measured value	average measured value	upper-limit to the average measured value	C-value
Lindane	1989	0.005	0.008	0.011	0.014	1.6
	1980	0.012	0.002	0.004	0.010	1.2
Dieldrin	1989	0.007	0.004	0.006	0.007	1.0
Cadmium	1980	0.010	0.002	0.006	0.020	1.0
Methyl-Mercury	1989	0.142	0.210	0.290	0.401	1.5
	1980	0.853	0.200	0.309	0.477	1.8
PCB153	1989	0.253*	0.065	0.098	0.147	1.7
PCB118	1989	0.102*	0.026	0.038	0.055	1.9

* = Value derived by QSAR estimation on a geometric mean K_{ow}.

4b. Using a maximum value from experimentally derived BCF's.

Compound	Year	calculated value	lower-limit to the average measured value	average measured value	upper-limit to the average measured value	C-value
Lindane	1989	0.016	0.008	0.011	0.014	1.1
	1980	0.039	0.002	0.004	0.010	**3.9**
Dieldrin	1989	0.013	0.004	0.006	0.007	1.9
Cadmium	1980	0.135	0.002	0.006	0.020	**6.8**
Methyl-Mercury	1989	0.350	0.210	0.290	0.401	1.0
	1980	2.100	0.200	0.309	0.477	**4.4**
PCB153	1989	?	0.065	0.098	0.147	?
PCB118	1989	?	0.026	0.038	0.055	?

4c. Using a QSAR estimated value for BCF, with K_{ow} values from the MEDCHEM CLogP data-base.

Compound	Year	calculated value	lower-limit to the average measured value	average measured value	upper-limit to the average measured value	C-value
Lindane	1989	0.002	0.008	0.011	0.014	**4.0**
	1980	0.005	0.002	0.004	0.010	1.0
Dieldrin	1989	0.001	0.004	0.006	0.007	**4.0**
Cadmium	1980	n.d.	0.002	0.006	0.020	n.d.
Methyl-Mercury	1989	n.d.	0.210	0.290	0.401	n.d.
	1980	n.d.	0.200	0.309	0.477	n.d.
PCB153	1989	0.675	0.065	0.098	0.147	**4.6**
PCB118	1989	0.158	0.026	0.038	0.055	**2.9**

n.d. = not determined. The QSAR estimate for BCF using K_{ow} values only holds for neutral organic chemicals, not for metals or organo-metals. Hence no QSAR estimate was made for cadmium or methyl mercury. Moreover, no K_{ow} value is given in the ClogP database for either cadmium or methyl-mercury.

Table 5. Oral and dietary toxicity data on birds and mammals. Values are listed as reported in the literature, and converted into a mg/kg food value (except for LD50's). LD50 = acute mortality (mg/kg bodyweight), LC50= (sub-)acute mortality, NOEC= No Observed Effect Concentration (effect recorded is specified).

parameter effect	species[7]	exposure period	reported value	converted value	reference
Compound: Lindane					
LD50					
	Birds				
	Alectoris rufa		35-85	55	33
	Passer domesticus		56.2	56	71
	Agelaius phoenicea		75	75	71
	Phasianus colchicus		75-100	87	33
	Perdix perdix		65-125	90	33
	Sturnus vulgaris		100	100	71
	Corvus brachyrhynchos		>100	>100	71
	Quiscalus quiscula		>100	>100	71
	Colinus virginianus		120-130	125	14
	Coturnix c. japonica		205	205	13
	Zenaidura macroura		350-400	374	14
	Columba livia		400	400	4
	Anas platyrhynchos		>2000	>2000	56
	Mammals				
	Felis domesticus		25	25	5
	Oryctolagus cuniculus		50-200	88	geometric mean value 9,15,36,63
	Mus musculus		56-246	111	geometric mean value 28,31,63,66,91,92
	Cavia aperea		100-127	113	geometric mean value 9,36
	Rattus norvegicus		88-270	167	geometric mean value 1,11,17,19,27,36,49,59, 60,61,62,70,71,92,93
LC50					
	Birds				
	Coturnix c. japonica	5 days	425	425	39
	Phasianus colchicus	5 days	561	561	39
	Colinus virginianus	5 days	882	882	39
	Anas platyrhynchos	5 days	>5000	>5000	39
	mammals				
	no data found				
NOEC					
	Birds				
Mortality	Gallus domesticus	27 days	16	1.6[2]	35
Eggshell-thinning	Anas platyrhynchos	8 weeks	200	100[1]	10
	Mammals				
No life fetuses & fetal weight	Mus musculus	9 days	30[3]	25[2]	26
Pregnancy rate	Oryctolagus cuniculus	12 days	10[3]	33[2]	64
Fertility rate	Rattus norvegicus	90 days	5[3]	100	79
Mortality	Rattus norvegicus		50-400	141	geometric mean value 23,82

(table 5)

Compound: Dieldrin

LD50

Birds			
Pediocetes phasianellus	6.9	6.9	56
Calipepla california	8.8	8.8	42
Perdix perdix	8.8	8.8	80
Agelaius phoenicea	17.8	18	72
Alectoris graeca	23.4	23	80
Passer domesticus	13-48	25	geometric mean value 72,80
Columba livia	24-67	35	geometric mean value 72,80,81
Quiscalus quiscalus	42	42	72
Gallus domesticus	43	43	74
Coturnix c. japonica	50-75	58	geometric mean value 72,76,80
Phasianus colchicus	79	79	80
Branta canadensis	100	100	80
Dendrocygna bicolor	150	150	80
Sturnus vulgaris	237	237	72
Anas platyrhynchos	381	381	80
Mammals			
Eptericus fuscus	28	28	53
Cavia aperea	10-49	28	geometric mean value 7,44
Mus musculus	30-75	44	geometric mean value 7,18,44
Rattus norvegicus	37-64	44	geometric mean value 7,32,37,52,78
Oryctolagus cuniculus	45-50	47	7
Canis domesticus	65-80	72	7
Microtus canicaudus	100	100	12
Odocoileus h. hemionus	75-150	106	42
Capra hircus	100-200	141	42
Microtus pennsylvanicus	175	175	12
Microtus montanus	205	205	12
Microtus orchrogaster	210	210	12

LC50

Birds				
Numida meleagris	5 days	107	107	87
Colinus virginianus	5 days	166	166	39
Coturnix c. japonica	5 days	278	278	39
Phasianus colchicus	5 days	570	570	39
Anas platyrhynchos	5 days	1500	1500	39
Mammals				
Microtus canicaudus	30 days	40^3	333	12
Microtus orchrogaster	30 days	105^3	872	12

(table 5)

NOEC

	Birds				
Mortality	Quail[6]	162 days	0.5	0.5	16
Eggshell thinning	Anas platyrhynchos	>1 year	1.6	0.8[1]	50
Mortality	Numida meleagris	21 months	1.5	1.5	89
Fertility & hatchability	Phasianus colchicus	breeding period	2.0	2.0	16
Mortality	Colinus virginianus	34 weeks	2.5	2.5	20
Egg fertility & hatchability	Numida meleagris	21 months	5.0	5.0	89
Chick survival	Gallus domesticus	13 months	10	10	8
Mortality & egg production	Coturnix c. japonica	18 weeks	10	10	84
Egg production	Colinus virginianus	34 weeks	10	10	20
	Mammals				
Mortality	Mus musculus	2 years	1	1.0	43
Mortality	Macaca mulatta	6 years	1	1.0	94
Pup mortality	Rattus norvegicus	life time	1.25	1.25	34
Pup mortality	Mus musculus	6 generations	3	3.0	46
Mortality	Blerina brevicauda	14 days	50	5.0[2]	6
Growth reduction	Canis domesticus	25 months	0.2[3]	8.0	24
Mortality	Canis domesticus		0.2[3]-10	8.9	geometric mean value 24,78
Mortality	Rattus norvegicus	2 years	10	10	24
Mortality	Damaliscus dorcas p.	90 days	15	15	88

Compound: Cadmium

LD50

	Birds				
	no data found				
	Mammals				
	Mus musculus		57	57	86
	Rattus norvegicus		25-250	68	geometric mean value 21,47

LC50

	Birds				
	Gallus domesticus	20 days	562	562	68
	Phasianus colchicus	5 days	767	767	39
	Coturnix c. japonica	5 days	1584	1584	39
	Anas platyrhynchos	5 days	>3065	>3065	39
	Mammals				
	no data found				

NOEC

	Birds				
Aspermatogenesis	Anas platyrhynchos	90 days	1.6	1.6	85
Egg production & mortality	Gallus domesticus	48 weeks	12	12	48
Growth reduction	Coturnix c. japonica	6 weeks	75	38[1]	69
	Mammals				
Growth reduction	Macaca mulatta	3 years	3	3	55
Growth reduction	Rattus norvegicus		10-42	20	geometric mean value 51,67
Mortality	Rattus norvegicus		10-45	21	geometric mean value 25,77

(table 5)

Compound: Inorganic-mercury					
LD50					
	Birds				
	Coturnix c. japonica		31	31	41
	Mammals				
	Rattus norvegicus		26	26	47
LC50					
	Birds				
	Phasianus colchicus	5 days	2805	2805	39
	Anas platyrhynchos	5 days	>3700	>3700	41
	Coturnix c. japonica	5 days	3764-4385	4063	geometric mean value 39,41
	Mammals				
	no data found				
NOEC					
	Birds				
Egg fertility	Coturnix c. japonica	1 year	4	4	40
Hatchability	Gallus domesticus	3 weeks	100	10[2]	73
Mortality & growth reduction	Gallus domesticus	16 weeks	125[4]	250	65
	Mammals				
Weight reduction	Mus musculus	560 days	20	20	30
Compound: Methyl-mercury					
LD50					
	Birds				
	Coturnix c. japonica		15.5	16	41
	Mammals				
	Rattus norvegicus		12	12	54
LC50					
	Birds				
	Coturnix c. japonica	5 days	40.2	40	41
	Mammals				
	no data found				
NOEC					
	Birds				
Egg production	Anas platyrhynchos	3 generations	0.5	0.25[1]	38
Mortality & growth reduction	Anas platyrhynchos	20 days	3.3	0.36[2,5]	29
Mortality & growth reduction	Phasianus colchicus	20 days	3.3	0.36[2,5]	29
Mortality	Gallus domesticus		3.3-12	0.56	geometric mean value 22,29
Mortality	Coturnix c. japonica	9 weeks	2.0	1.70[5]	41
Mortality	Colinus virginianus	6 weeks	4.3	4.30	75
	Mammals				
Growth reduction	Macaca spec.	52 weeks	0.01[3]	0.22[5]	45
Growth reduction & viability index	Rattus norvegicus	3 generations	0.5	0.43[5]	83
Mortality	Mustela vison	93 days	1.1	1.20[5]	90
Growth reduction	Mus musculus	60 days	0.25[3]	2.25[5]	2

(table 5)

Compound: PCB153

LD50

	Birds				
	no data found				
	Mammals				
	Cavia aperea		>10	>10	58
	Mus musculus	28 days	>64.3	>64	3

LC50

	Birds				
	no data found				
	Mammals				
	Mus musculus	28 days	>300	>300	3

NOEC

	Birds				
Growth reduction	Gallus domesticus	3 weeks	400	20[1,2]	57
	Mammals				
Weight gain	Mus musculus	28 days	100	10[2]	3

Compound: PCB118

LD50

Birds	
no data found	
Mammals	
no data found	

LC50

Birds	
no data found	
Mammals	
no data found	

NOEC

Birds	
no data found	
Mammals	
no data found	

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[1] = NOEC value derived by applying a factor 2 on the lowest observed level, which caused less than 20% effect relative to the control group.

[2] = NOEC value derived by applying a factor of 10 on the value obtained from literature to compensate for the uncertainty in establishing a (chronic) NOEC from short-time (< 1 month) studies.

[3] = Value in literature reported in mg/kg bodyweight, these values were converted to a mg/kg food value with the bodyweight/daily food intake factor.

	BW (g)	DFI (g)	BW/DFI
Canis domesticus	10000	250	40
Macaca spec.	5000	250	20
Microtus spec.	25	3	8.3
Mus m.	25	3	8.3
Oryctolagus c.	2000	60	33.3
Rattus n.	200	10	20

[4] = Value reported in literature in mg/l drinking water, converted to mg/kg food with:

	DWI	DFI	DWI/DFI
Gallus domesticus	128.5	64.3	2

[5] = Reported value was not compensated for the relative contribution of the CH_3Hg group to the molecular weight of the compound for which the study was carried out.

[6] = Species name not further specified, hence treated as a species of quail different from Coturnix coturnix japonica or Colinus virginianus.

[7] = List of common species names is given below.

common species names:

Agelaius phoenicea	= redwinged blackbird
Alectoris graeca	= chukar partridge
Alectoris rufa	= red-legged partridge
Anas platyrhynchos	= malard duck
Blerina brevicauda	= short-tailed shrew
Branta canadensis	= Canada goose
Callipepla california	= California quail
Colinus virginianus	= bobwhite-quail
Canis domesticus	= domestic dog
Capra hircus	= domestic goat
Cavia aperea	= guinea pig
Columba livia	= Rock dove
Corvus brachyrhynchos	= american crow
Coturnix coturnix japonica	= Japanese quail
Damaliscus dorcas phillipsi	= blesbuck
Dendrocygna bicolor	= fulvous whistling duck
Eptericus fuscus	= big brown bat
Felis domesticis	= domestic cat
Gallus domesticus	= domestic fowl
Macaca mulatta	= rhesus monkey
Microtus canicaudus	= gray tailed vole
Microtus montanus	= vole
Microtus orchrogaster	= prairie vole
Microtus pennsylvanicus	= eastern meadow vole
Mus musculus	= domestic mouse
Mustela vison	= mink
Numida meleagris	= crowned guinea fowl
Odocoileus hemionus hemionus	= mule deer
Oryctolagus cuniculus	= rabbit
Passer domesticus	= house sparrow
Pedioecetes phasianellus	= sharp-tailed grouse
Perdix perdix	= gray partridge
Phasianus colchicus	= ring-necked pheasant
Quiscalus quiscula	= common grackle
Rattus norvegicus	= laboratory rat
Sturnus vulgaris	= starling
Zenaidura macroura	= mourning dove

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Table 6. Extrapolation of toxicity data on single species to NOEC's for species groups. Data sets on birds (6a), mammals (6b) and combined (6c).

6a. Extrapolation from (single species) toxicity data on birds to a NOEC value for the group of fish-eating birds.

Compound	EPA-method NOEC mg/kg food	Aldenberg/Slob ($\delta 1 = 0.05$, $\delta 2 = 0.5$) NOEC mg/kg food	Value used as NOEC for fish-eating species mg/kg food
Lindane	0.16	-	0.16
Dieldrin	0.05	0.34	0.34
Cadmium	0.16	-	0.16
Inorganic-mercury	0.4	-	0.4
Methyl-mercury	0.025	0.09	0.09
PCB153	2.0	-	2.0
PCB118	-	-	-

6b. Extrapolation from (single species) toxicity data on mammals to NOEC values for the group of fish-eating mammals.

Compound	EPA-method NOEC mg/kg food	Aldenberg/Slob ($\delta = 0.05$, $\delta 2 = 0.5$) NOEC mg/kg food	Value used as NOEC for fish-eating species mg/kg food
Lindane	2.5	-	2.5
Dieldrin	0.1	0.35*	0.1
Cadmium	0.3	-	0.3
Inorganic-mercury	2.0	-	2.0
Methyl-mercury	0.022	0.10	0.10
PCB153	1.0	-	1.0
PCB118	-	-	-

6c. Extrapolation on a combined set of data on birds and mammals to a NOEC value for fish-eaters.

compound	EPA-method NOEC mg/kg food	Aldenberg/Slob ($\delta 1 = 0.05$, $\delta 2 = 0.5$) NOEC mg/kg food	Value used as NOEC for fish-eating species mg/kg/food
Lindane	0.16	1.16	1.16
Dieldrin	0.05	0.41	0.41
Cadmium	0.16	0.74	0.74
Inorganic-mercury	0.40	-	0.40
Methyl-mercury	0.022	0.12	0.12
PCB153	1.0	-	1.0
PCB118	-	-	-

* = The Kolmogorov-Smirnov test rejected the hypotheses of a logistic distribution of the data, hence this value was not used as a NOEC for fish-eating species.

Table 7. Calculated MTR (maximum tolerable riks level) values in surface water for the selected compounds. Comparison to MTR values obtained by risk-assessment for aquatic ecosystems. NOEC are obtained from table 6. BCF's are obtained from table 1. MTR for aquatic ecosystems are obtained from the "streven naar waarden" report (Van de Meent et al. 1990).

7a. MTR-values (ug/l) based on data for birds.

Compound	NOEC mg/kg food	BCF (mean)	BCF (max.)	MTR using mean BCF	MTR using max. BCF	MTR aquatic-ecosystem
Lindane[2]	0.16	499	1613	0.32	0.10	0.55
Dieldrin	0.34	7389	13300	0.046	0.026	0.045
Cadmium[2]	0.16	39	540	4.10	0.30	0.16
Mercury[1]	0.09	14210	35000	0.0063	0.0026	0.01
PCB153[2]	2.00	1010396	?	0.002	?	?
PCB118	?	406103	?	?	?	?

7b. MTR-values (ug/l) based on data for mammals.

Compound	NOEC mg/kg food	BCF (mean)	BCF (max.)	MTR using mean BCF	MTR using max. BCF	MTR aquatic-ecosystem
Lindane[2]	2.50	499	1613	5.01	1.55	0.55
Dieldrin	0.10	7389	13300	0.014	0.008	0.045
Cadmium [2]	0.30	39	540	7.69	0.56	0.16
Mercury[1]	0.10	14210	35000	0.007	0.0029	0.01
PCB153[2]	1.00	1010396	?	0.001	?	?
PCB118	?	406103	?	?	?	?

7c. MTR-values (ug/l) based on a combined data set for birds and mammals.

Compound	NOEC mg/kg food	BCF (mean)	BCF (max.)	MTR using mean BCF	MTR using max. BCF	MTR aquatic-ecosystem
Lindane	1.16	499	1613	2.32	0.72	0.55
Dieldrin	0.41	7389	13300	0.055	0.031	0.045
Cadmium	0.74	39	540	18.97	1.37	0.16
Mercury[1]	0.12	14210	35000	0.0084	0.0034	0.010
PCB153[2]	1.00	1010396	?	0.001	?	?
PCB118	?	406103	?	?	?	?

[1]= based on BCF and NOEC's for methyl-mercury
[2]= Value obtained by the EPA extrapolation method.

Appendix I

Literature search profile for toxicological data

1. Reviews & Monographs

Lindane:

- Blaquiere, C., Bodenstein, G., Demozay, D., Herbst, M., Marechal, G & Sieper, H. (1972) Lindane, Monograph of an Insecticide. Ulmann, E. (Ed.) Verlag K. Schillinger, Freiburg in Breisgau.
- Clayton, G.D. & Clayton, F.E. (Ed.) (1981) Patty's Industrial Hygene and Toxicology. Third revised edition, John Wiley & Sons, New York, Chicester, Brisbane, Toronto, Singapore.
- EPA (1989) ATSDR/TP-89/14 Alpha-, Beta-, Gamma and Delta-Hexachlorocyclohexane.
- Janssen, P.J.C.M., Koten-Vermeulen, J.E.M., Krajnc, E.I., Canton, J.H., Van Gestel, C.A.M., Van der Heijden, C.A. & Heijna-Merkus, E. (1988) Appendix to Integrated Criteria Document Hexachlorocyclohexane (RIVM report no 758473 011).
- Schafer, E.W. (1972) The Acute oral toxicity of 369 pesticidal pharmaceuticals and other chemicals to wild birds. Toxicol. Appl. Pharmacol. 21: 315-330.
- De Snoo, G.R. & Canters, K.J. (1987) Neveneffecten van Bestrijdingsmiddelen op terrestrische vertebraten (CML mededelingen 35b)
- Verschuuren, K. (1983) Handbook of Environmental data on organic chemicals. Second edition, Van Nostrand Reinhold company, New York, Cincinnati, Toronto, London, Melbourne.
- Ware, G. (1988) Rev. of Environ. Contam. Toxicol. 104: 147-160. Springer Verlag, New York, Berlin, Heidelberg, London, Paris, Tokyo.
- WHO (1989) IPCS/Environmental Health Criteria draft for Lindane.

Dieldrin:

- EPA (1988) ATSDR/TP-88/01 Toxicological profile for Aldrin/Dieldrin.
- Schafer, E.W. (1972) The acute oral toxicity of 369 pesticidal pharmaceuticals and other chemicals to wild birds. Toxicol. Appl. Pharmacol. 21: 315-330.
- WHO (1989) IPCS/Environmental Health Criteria 91, Aldrin/Dieldrin.

Cadmium:

- EPA (1981) Health Assessment Document for Cadmium EPA 600/8-81-023.
- WHO (1990) IPCS/Environmental Health Criteria draft for Cadmium
- WHO/FAO (1988) Toxicological evaluation of certain food additives (WHO-Food Additive Series no 24). Cadmium pp 163-220.
- Ware, G. (1989) Rev. Environ. Contam. Toxicol. 107: 25-38. Springer verlag, New York, Berlin, Heidelberg, London, Paris, Tokyo.

Mercury:

- EPA (1989) ATSDR/TP-89/16 Toxicological Profile for Mercury.
- Friberg, L & Vostal, J (1972) Mercury in the Environment. CRC-press Cleveland Ohio.
- WHO (1989) IPCS/Environmental Health Criteria 86, Mercury-Environmental Aspects.
- WHO (1990) IPCS/Environmental Health Criteria 101, Methylmercury.
- WHO/FAO (1988) Toxicological evaluation of certain food additives (WHO-Food Additive Series 24) Methylmercury pp 293-328.

PCB's:

- Nicholson, W.J. & Moore, J.A. (1979) Health effects of Halogenated Aromatic Hydrocarbon. Ann. N.Y. Acad. Sci 320.
- WHO (1989) IPCS/Environmental Health Criteria draft for Polychlorinated Biphenyls (PCBs) and Polychlorinated Terphenyls (PCTs).

2. Original Literature

Original literature was collected from references on (sub-) chronic exposure studies in reviews mentioned above.

3. On-Line search

. For PCB's

BIOSIS --,--.70 - --,--.90

- Birds & Mammals
- Toxicity

. For Lindane

BIOSIS --,--.70 - --,--.90

- Birds
- Toxicity

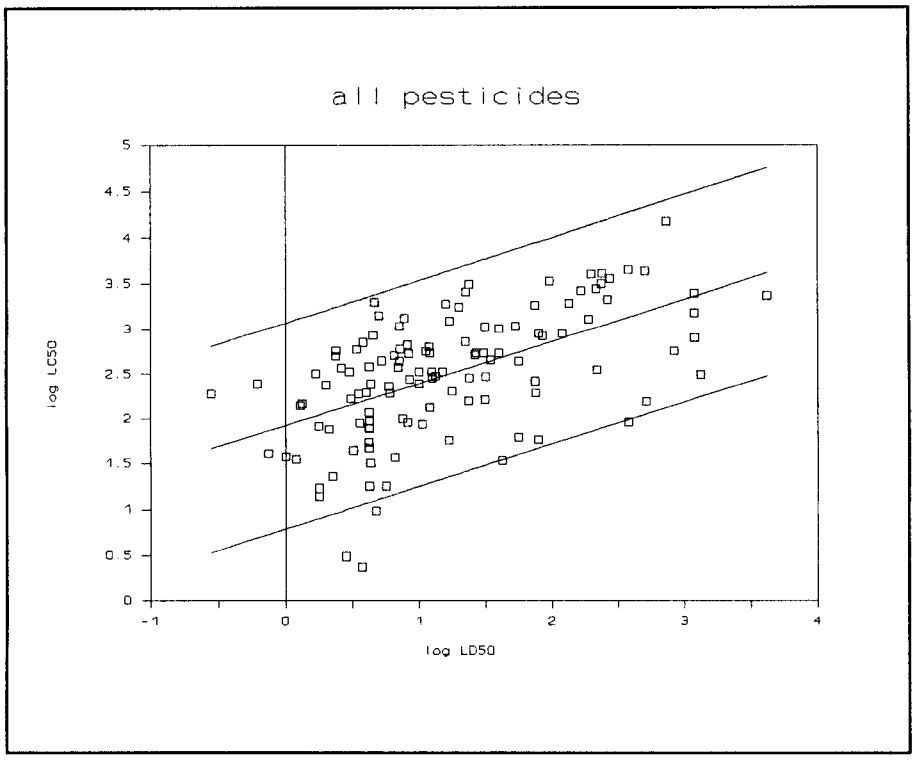
Estimation of LC50 values from LD50 values.

The EPA extrapolation method is used for preliminary risk-assessments on secondary poisoning of birds and mammals. By means of this method, (chronic) NOEC's can be estimated using (acute) LC50 values. However, the acute toxicity of compounds is often not tested with the standard 5-days dietary exposure experiment from which LC50 values can be determined, but by means of single oral dose tests. From these tests LD50 values are determined.
A study was carried out to test whether an LD50 value derived for a compound and for a certain species can be used to estimate the LC50 value for the same species and compound. A regression analyses was carried out on a set of 120 paired LC50 -LD50 values for birds as described by Slooff et al. (1986) (fig. 1). This resulted in the relation:

$$LC50 = 10^{1.93 + 0.47 * \log LD50} / 13.9$$

Thus, LC50 values can be estimated using LD50 values. However, the r-square value of this regression was rather low (0.32), and the data used were all on pesticides. The application of this relation is therefore limited, and should not be used on a routine basis in risk-assessment. When however a risk-assessment has to be carried out on a limited data-set (e.g. in the frame of the "Evaluation system for new chemical substances" project) this relation could be applied.

Figure 1. LD50 versus LC50 for all pesticides



For separate pesticide groups (organo-chlorines, carbamates and OP-esters) regression analyses resulted in relations with higher r-square values:

carbamates:	$LC50 = 10^{2.37+0.73*logLD50} / 2.53$	($r^2 = 0.81$)	(fig.2)
organo-chlorines:	$LC50 = 10^{1.15+0.65*logLD50} / 18.6$	($r^2 = 0.46$)	(fig.3)
OP-esters:	$LC50 = 10^{1.74+0.62*logLD50} / 10.6$	($r^2 = 0.42$)	(fig.4)

Figure 2. LD50 versus LC50 for carbamates.

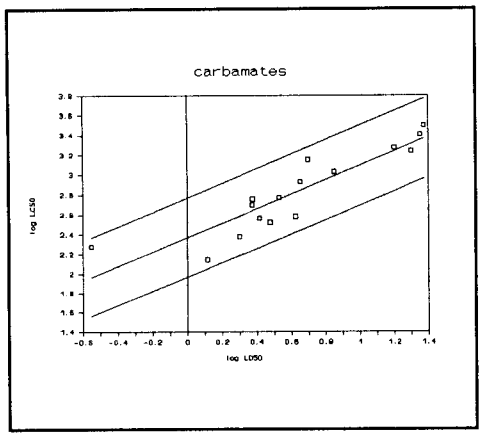


Figure 3. LD50 versus LC50 for OP-esters.

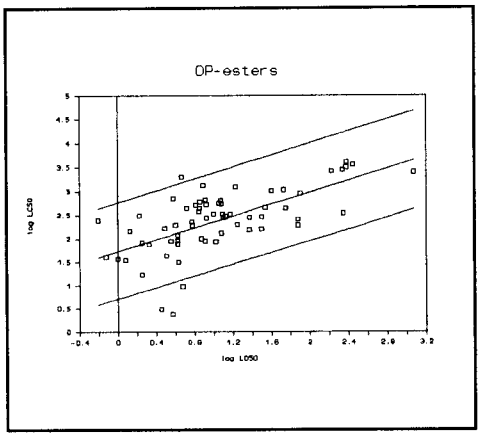
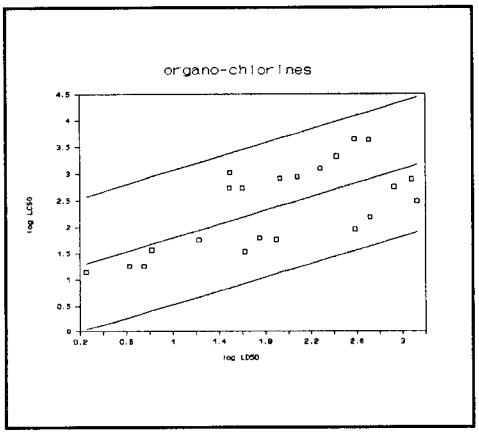


Figure 4. LD50 versus LC50 for organo-chlorines.



Reference

Slooff, W., Oers, J.A.M. & de Zwart D. (1986) Margins of Uncertainty in Ecotoxicological Hazard Assessment. Environ. Toxicol. Chem. 5: 841-852.