Recommended exposure limits for polychlorinated biphenyls in soils and sediments, for the protection of ecosystems

An assessment of a derivation method developed by the
National Institute of Public Health and the Environment (RIVM)

Gezondheidsraad
Health Council of the Netherlands

To the State Secretary for Housing,
Spatial Planning and the Environment

Subject	: Submission of advisory report on recommended exposure limits for PCBs
Your reference	: DGM/SVS/2000024545
Our reference	: -0803/HvD/ts/677-G
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Date	: December 16, 2002

Dear State Secretary,

At the request of the former Minister of Housing, Spatial Planning and the Environment, summarised in letter no. DGM/SVS/2000024545, I hereby submit an advisory report on recommended exposure limits for PCBs. It was drawn up by a Health Council committee, which was appointed by my predecessor, and evaluated by the Standing Committee on Ecotoxicology.

In the advisory report, the Committee sets out its views concerning a new method used by RIVM to derive recommended exposure limits for PCBs in soils and sediments, for the protection of ecosystems. The Committee endorses several of RIVM's major starting points, particularly the aim of getting a better picture of the uncertainties involved and that of setting a standard for a mixture of substances which have a common mechanism of action and which also occur together in the environment. There are, however, a number of points on which the Committee takes issue with the way in which RIVM has calculated the derived values. This relates both to the recommended exposure limits for individual PCBs and to the recommended exposure limit for a mixture of these substances. For this reason, the Committee takes the view that, in its present form, the method is unsuitable for use in the derivation of ecotoxicological recommended exposure limits for PCBs. I trust, however, that the Committee's critical comments, as well as its recommendations, will ultimately contribute to the creation of scientifically well-founded recommended exposure limits for PCBs in soils and sediments.

Yours sincerely,
(signed)
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National Institute of Public Health and the Environment (RIVM)

to:

the State Secretary for Housing, Spatial Planning and the Environment

No. 2002/17E, The Hague, 16 December 2002

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The Health Council receives most requests for advice from the Ministers of Health, Welfare & Sport; Housing, Spatial Planning & the Environment; Social Affairs & Employment; and Agriculture, Nature management & Fisheries. The Council can publish advisory reports on its own initiative. It usually does this in order to ask attention for developments or trends that are thought to be relevant to government policy.

Most Health Council reports are prepared by multidisciplinary committees of Dutch or, sometimes, foreign experts, appointed in a personal capacity. The reports are available to the public.

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Executive summary

Polychlorinated biphenyls (PCBs) in soils or sediments can pose a hazard to biotic communities. For proper management of the risk involved, recommended exposure limits based on ecotoxicological research are required for these organochlorine compounds. Since they form the basis for standard setting, these recommended exposure limits also provide a basis for decisions concerning measures to be taken in cases of soil pollution. The RIVM (National Institute of Public Health and the Environment) has developed a new method for deriving recommended exposure limits for PCBs in soils and sediments. On 15 March 2000, the Minister of Housing, Spatial Planning and the Environment requested the Health Council's opinion regarding this new method. A Health Council committee has reported its findings in the present advisory report.

The Committee endorses the major principles used by the RIVM to derive recommended exposure limits for PCBs in soils and sediments. This is in relation to the attempt to better illustrate the uncertainties involved and to view as mixtures substances with a common mechanism of action which occur together in the environment. However, in terms of its execution, this has proved deficient in a number of areas. For this reason, the Committee feels that the method is not useful for deriving ecotoxicological recommended exposure limits for PCBs in soils and sediments.

With regard to the recommended exposure limits for individual PCB compounds, the major objection is that the species sensitivity distributions (SSDs) are generally based on toxicity data from less than four species of organisms, and sometimes even on data

from a single species. Furthermore, different toxicological endpoints (NOECs, LD_{50}s and EC_xs) are used for different organisms, which tends to distort the differences in sensitivity between species. As a consequence of this, the spread of the probability distributions mentioned above is only marginally based on actual interspecies differences in sensitivity. Accordingly, the probability distributions cannot be regarded as genuine SSDs. The recommended exposure limits based on these distributions cannot, therefore, be considered to provide protection to 95% of all species. It should be pointed out that recommended exposure limits for individual PCBs (inasmuch as these exert their effect via a common mechanism of action) are of secondary importance, because, in soils and sediments, these substances are always present as mixtures.

Nor can the Committee endorse the method used to derive the recommended exposure limit for a mixture of planar PCBs, which exert their effect via an interaction with the Aryl hydrocarbon receptor (Ah receptor). This receptor occurs in the cells of vertebrates. The RIVM erroneously based its recommended exposure limit for the mixture partly on toxicity data for species of organisms which do not possess a classical Ah receptor. Furthermore, the scaling factors which describe the relative toxicity of the various planar PCBs are based on highly incongruous sets of toxicity data. This produces a distorted picture of the relative toxicity in question. In addition, the institute uses a single scaling factor for each planar PCB compound. This approach tends to overlook the fact that the relative toxicity of the various PCBs is specific to certain groups of animals. It is precisely for this reason that the World Health Organization (WHO) has established separate scaling factors (TEF values) for mammals, birds and fish. Finally, the Committee would like to point out that the recommended exposure limit for a mixture of planar PCBs takes no account of dibenzodioxins and dibenzofurans. Yet these substances, like PCBs, exert their effect via the Ah receptor, and they are also present in considerable quantities in Dutch soils and sediments.

The Committee recommends that future recommended exposure limits for PCBs and related substances be based on a few, closely related, sensitive species or on just one such species. It feels that the most eligible candidates would be birds or mammals at the top of the food chain. Since it is not known exactly which species is the most sensitive, the toxicity data for this limited group of species could be used to derive a probability distribution, which in turn could provide the basis for a recommended exposure limit. This would require the availability of toxicity data on at least four different species of animals. In conclusion, the Committee urges that WHO's internationally accepted TEF concept be adopted. This would enable all relevant substances, whose effects are known to be based on their interaction with the Ah receptor, to be taken into consideration.

Chapter 1

Background

1.1 Introduction

Polychlorinated biphenyls, which are usually referred to as PCBs, are chlorinated aromatic hydrocarbons. The general structural formula is $C_{12}H_{10-n}Cl_n$ (figure 1), where the number of chlorine atoms (n) can vary from 1 to 10. This means that there are 209 different possible compounds. These are referred to as congeners. From 1930 until the 1980s, PCB mixtures were produced commercially and sold under various trade names, such as Arochlor. They were used in many products, such as transformers, condensers, paint and coatings. As a result, large quantities of PCBs were released into the environment. In industrialised countries, such as the Netherlands, the production of polychlorinated biphenyls has been banned for many years. Yet the soils and sediments of lakes, rivers and coastal waters still contain relatively high levels of these substances, since they are not readily degradable. Furthermore, new material is being added all the time, some as a result of leakage from discarded equipment and some from abroad, carried along major rivers or through the air. PCBs are toxic and they accumulate in animal species which are at the end of food chains (see, for example, IPCS93). They therefore pose a serious threat to ecosystems. Effective risk management requires recommended exposure limits that are based on ecotoxicological research. These form the basis for standard setting and for decisions concerning the steps to be taken when soils or sediments have been contaminated.

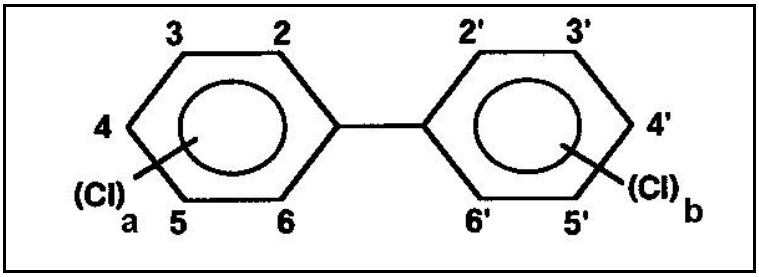

Figure 1 The structure of polychlorinated biphenyls: a and b can both vary from 0 to 5, their sum (n) varies from 1 to 10. The so-called ortho positions are 2, 6, 2' and 6'.

The National Institute of Public Health and the Environment (RIVM) has derived recommended exposure limits for environmental quality for various groups of substances (such as heavy metals, pesticides, polycyclic aromatic hydrocarbons) that are based on ecotoxicological research. Here, the RIVM has endeavoured to achieve intercompartmental harmonisation. This means that a recommended exposure limit for a substance in a given environmental compartment (soil, sediment, water or air) should also provide protection to organisms in adjoining environmental compartments. The Health Council has published several advisory reports concerning the derivation methods used (GR85, GR88, GR91, GR93, GR94, GR95, GR96). Partly in response to these reports, the RIVM developed a modified method for deriving recommended exposure limits for PCBs in soils and sediments (Wez99, Wez00). This is based on the assumption that PCBs in equilibrium situations are distributed between the various environmental compartments (soil or sediment, water, organisms) in fixed ratios, which is known as equilibrium partitioning (see, for example, Ber95). A novel aspect of RIVM's method is the inclusion, via a so-called probabilistic approach, of the variation (natural and otherwise) in these fixed ratios (the so-called partition coefficients) when deriving the recommended exposure limits. Another novel feature is the use of field measurements for partition coefficients and the calculation of a recommended exposure limit for a mixture of PCBs.

1.2 Request for advice

On 15 March 2000, the Minister of Housing, Spatial Planning and the Environment requested the Health Council's opinion regarding the new method used by RIVM. More particularly, the Minister would like to have the following questions answered:

1 What is the Health Council's assessment of this novel method for deriving standards for PCBs? I would be interested to hear your views on the use of field data, the method for the assessment of sec-

ondary poisoning, probabilistic modelling and the determination of the maximum permissible risk level (MPRL) for the mixture.

2 Through the use of probabilistic modelling, the MPRL was established at the 5th percentile value of the probabilistic distribution. Does the Health Council concur with the reasoning behind the selection of 5% as the level of protection for ecosystems? Does the Health Council take the view that the introduction of probabilistic techniques has produced genuine improvements in the underpinning and transparency of standard setting?

3 How does the Health Council feel about setting standards for the most commonly occurring individual PCBs and for the PCB#118 mixture?

4 Would you recommend that parts of this method (i.e. the use of field data, the method for the assessment of secondary poisoning, and probabilistic modelling) also be used for the derivation of standards for other substances? If so, for which groups of substances could they be used?

The full text of the request for advice is reproduced in Annex A. The Minister has submitted the same questions to the Technical Committee on Soil Protection. This committee issued a report in 2001 (TCB01).

1.3 Committee and procedures

In response to the Minister's questions, the President of the Health Council appointed an expert committee on 21 May 2001. The make-up of the Committee is set out in Annex B. The Committee has examined the assumptions made in the fields of environmental chemistry, toxicology, ecology and statistics, which form the basis of the RIVM's derivation method as described by Van Wezel *et al.* (Wez99, Wez00). It has also examined the available toxicological and environmental chemical data, since these will ultimately determine the method's usefulness. It is also important to determine whether the method is a genuine improvement relative to previous derivation methods, in terms of both the insights and the scientific underpinning provided (does the method make the best use of available expertise). The Committee's brief was simply to test RIVM's method. Accordingly, it has refrained from giving a detailed analysis of how any identified deficiencies might be improved and has instead confined itself to making constructive suggestions. Finally, it should be noted that the Committee has focused on assessing the derivation method in question. It has made no attempt to determine the extent to which the proposed recommended exposure limits actually protect ecosystems against PCBs.

The starting point for the Committee was a verbal presentation by RIVM of its derivation method and two reports from Ecostat consultancy in Leiden, concerning the statistical approach used by RIVM (Hoe01a,b). Both reports, which were drawn up specifically for this purpose, were commissioned by the Council. The Committee has also based its deliberations on the relevant scientific literature, the above-mentioned

report by the Technical Committee on Soil Protection (TCB01) and previous Health Council advisory reports in the field of ecotoxicological standard setting for substances.

It has also consulted a number of foreign experts. Their names and written comments are contained in Annexes C and D. The Committee questioned two Dutch biostatisticians, who attended as guest experts. Their names are also given in Annex C. The draft text of the advisory report was checked by the Standing Committee on Ecotoxicology, after which the definitive version was presented to the President of the Health Council.

1.4 Structure of this advisory report

In Chapter 2 the Committee sets out the main points of RIVM's approach. Chapter 3 contains its comments about each individual part of the method. It presents its general conclusions and recommendations in Chapter 4. The Committee concludes the advisory report with its reply to the Minister's questions (Chapter 5). In addition to the appendices mentioned above, the advisory report also contains a glossary (Annex E) and a scientific publication (Wez00), which contains full details of the RIVM method (Annex F).

Chapter 2

The RIVM method

In this chapter, the Committee briefly describes how RIVM derives recommended exposure limits for a number of PCB congeners, namely PCB #77, #105, #118, #126, #153, #156, #157 and #169. To this end, it divides the derivation method into three separate steps:

1 Converting toxicity data from laboratory tests into concentrations in soil or sediment
2 The derivation of recommended exposure limits for individual PCB congeners from the converted toxicity data
3 The derivation of a recommended exposure limit for a mixture of planar PCBs.

2.1 Converting toxicity data from laboratory tests into concentrations in soil or sediment

In the first step (figure 2, page 19) RIVM collects and selects data from the literature concerning the toxicity of individual PCB congeners for a variety of organisms (invertebrates, fish, birds and mammals). This data was derived from laboratory studies on experimental animals. It shows which concentrations or doses, in the course of an experiment, only just failed to produce an observable effect (NOECs), or produced the smallest observable effect (LOECs) or produced an effect of a given size (EC_x or ED_x, for example an LC_{50}, the exposure concentration at which 50% of the animals die). The only data selected concerns effects that are directly important in terms of the organisms' population size, namely mortality and changes in growth or reproduction.

It is assumed that, at the same level of exposure, effects seen in the laboratory occur to the same extent in the field. An 'effect concentration' in a glass beaker in the laboratory could therefore be directly translated to an 'effect concentration' in the water of a polder ditch, for example. RIVM then calculates the concentrations in the soil or in the sediment of surface waters in the field which would have the same toxic effect as the above-mentioned concentrations or dosages in the laboratory. These concentrations are referred to as EC_{oc} values. The institute has based its calculations on the so-called equilibrium partitioning. It is assumed here that, following their introduction into the environment, PCB congeners become distributed throughout the compartments of soil/sediment, water and living organisms. After a period of time, an equilibrium situation is achieved in which there is no further change in the ratios of the concentrations in these environmental compartments. Since these substances are highly insoluble in water, it is assumed that they will be preferentially taken up by body fat in animals and by the organic carbon fraction (oc fraction) in soil or sediment. The constant ratios between the concentrations in different environmental compartments are referred to as partition coefficients. RIVM uses various coefficients:

- the BCF_L, which represents the ratio between the concentration in the fat of an animal and the concentration in the surrounding water;
- the $BSAF_L$, which represents the ratio between the concentration in the fat of an animal and the concentration in the organic carbon fraction of the soil or sediment;
- the BMF_L, which represents the ratio between the concentration in the fat of a carnivore and the concentration in the fat of its prey;
- the EBR_L, which represents the ratio between the concentration in the fat of an egg and the concentration in the fat of the mother animal;
- the K_{oc}, which represents the ratio of the concentration in the organic carbon fraction of a soil or sediment and the concentration in the pore water or surface water.

An item of toxicity data from the laboratory is converted to a concentration in the soil or sediment by means of formulas that have been constructed from these partition coefficients. Furthermore, some formulas contain a factor for the fat content of an animal, in order to convert concentrations in the entire animal into concentrations in the body fat.

In the case of those species of organisms for which RIVM has toxicity data, the values of the partition coefficients in question are not usually available in published literature. The institute therefore estimates the requisite values on the basis of available data from other species. This data is used to derive a probability distribution for each partition coefficient. This shows which values the partition coefficient can have and, for each of these values, it indicates the probability that the value in question will appear. Next, for each partition coefficient, one thousand values are selected at random from the asso-

ciated probability distribution and entered into the above-mentioned conversion formula. This technique, which is a type of Monte Carlo Simulation, results in one thousand estimates of the effect concentration in the soil or sediment (the EC_{oc} value) for each effect concentration found in the laboratory. Together, these thousand values form a probability distribution of effect concentrations in the soil or sediment. Figure 2 on page 19 illustrates the entire process by which an item of toxicity data from the laboratory is converted into an effect concentration in sediment.

2.2 The derivation of recommended exposure limits for individual PCB congeners from the converted toxicity data

In the second step (figure 3, page 19), the toxicity data that had been converted to soil or sediment values by this means is used to derive a safe recommended exposure limit for each PCB congener in soils or sediments. To this end, for each PCB congener, the EC_{oc} values for all the species of organisms which were calculated in the first step are then combined. For the purpose of illustration: for PCB #77 this produces seven times one thousand values.

The aim here is to derive a probability distribution for the sensitivity of all species of organisms to the PCB congener in question. This is the *species sensitivity distribution* (SSD). To this end, a test is conducted to determine whether all those thousands of values could originate from a single so-called log-normal distribution. If the test indicates that this is possible, then an estimate is made of the mean and the standard deviation of this lognormal distribution, which are then used to calculate the 5% percentile. In accordance with previous derivation methods such as Aldenberg & Slob's HC_5 method (Ald93), this is then elevated to the status of recommended exposure limit. The situation is then that, for 95% of all species of organisms, exposure remains below the level that is considered to be safe. The assumption is that this is sufficient to protect the ecosystem. If the test indicates that it is higly improbable that the values originate from a single lognormal distribution, then all values relating to aquatic organisms are omitted and the test is repeated using only those values that relate to birds and mammals. If, after this, the common lognormal distribution is not rejected, then the recommended exposure limit is again calculated from the 5% percentile. If the test still rejects the lognormal distribution, however, then only the thousand values for the most sensitive organism are used to derive the recommended exposure limit.

2.3 The derivation of a recommended exposure limit for a mixture of planar PCBs

PCB congeners without a chlorine atom at any of the *ortho* positions (see figure 1) or with only one, are referred to as non-*ortho* PCBs and mono-*ortho* PCBs respectively. With these congeners, both rings can lie in the same plane, as is the case with dioxins. This is why they are often referred to as planar or dioxin-like PCBs. The toxicity of PCBs of this type is mainly due to a mechanism of action based on interaction with a given receptor in the cells of living organisms, the *Aryl hydrocarbon receptor* (Ah receptor). The Committee notes that a brief explanation of this can be found in the Health Council advisory report on dioxins (GR96). These PCBs all cause the same effects. However, some do so at lower concentrations than others, and are therefore more toxic. Since these planar PCBs almost always occur in the environment as mixtures, for some of them (congeners #77, #105, #118, #126, #156, #157 and #169), RIVM calculates a recommended exposure limit for the mixture in the third and final step of the derivation method. Summing the concentrations of these substances (weighted for their level of toxicity) is part of this process. This is because research has shown that observed effects often correlate well with this 'summed concentration' of dioxin-like compounds (Ber98, Bla02). On the basis of a number of field measurements in the catchment area of the Rhine, RIVM has assumed that the PCB congeners in Dutch sediments are usually present as a mixture of constant composition. In addition, the lognormal distributions for the sensitivity of organisms to the individual congeners, which were derived in step two are, in turn, used to derive the mutual relative toxicity which is expressed as a scaling factor. Using this relative toxicity and constant mixture composition, RIVM calculates PCB #118's share of the total toxicity of the mixture. Multiplication of this share by the individual recommended exposure limit for PCB #118 results in a recommended exposure limit for the mixture on the basis of PCB #118. The assumption is that the ecosystem is protected against the whole mixture of the seven PCBs mentioned, as long as the concentration of PCB #118 remains below the recommended exposure limit for the mixture.

Spatial restrictions prevent PCB congeners with two or more chlorine atoms at the *ortho* position from adopting a planar configuration, which means that they would not fit onto the Ah-receptor. As a consequence, they have a different mechanism of action. RIVM points out that for these non-planar PCBs too, concentration addition and the calculation of a recommended exposure limit for a mixture would be a straightforward matter. Due to a lack of toxicological data, however, a recommended exposure limit will be derived for just one non-planar PCB, namely PCB #153.

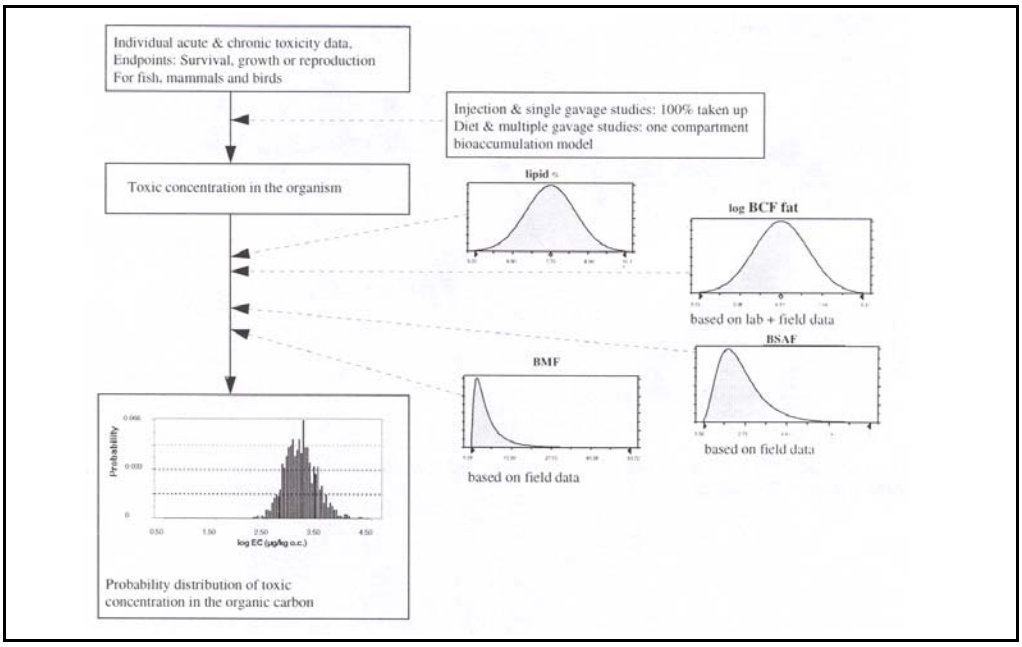

Figure 2 Converting toxicity data from laboratory tests into concentrations in soil or sediment (Wez99).

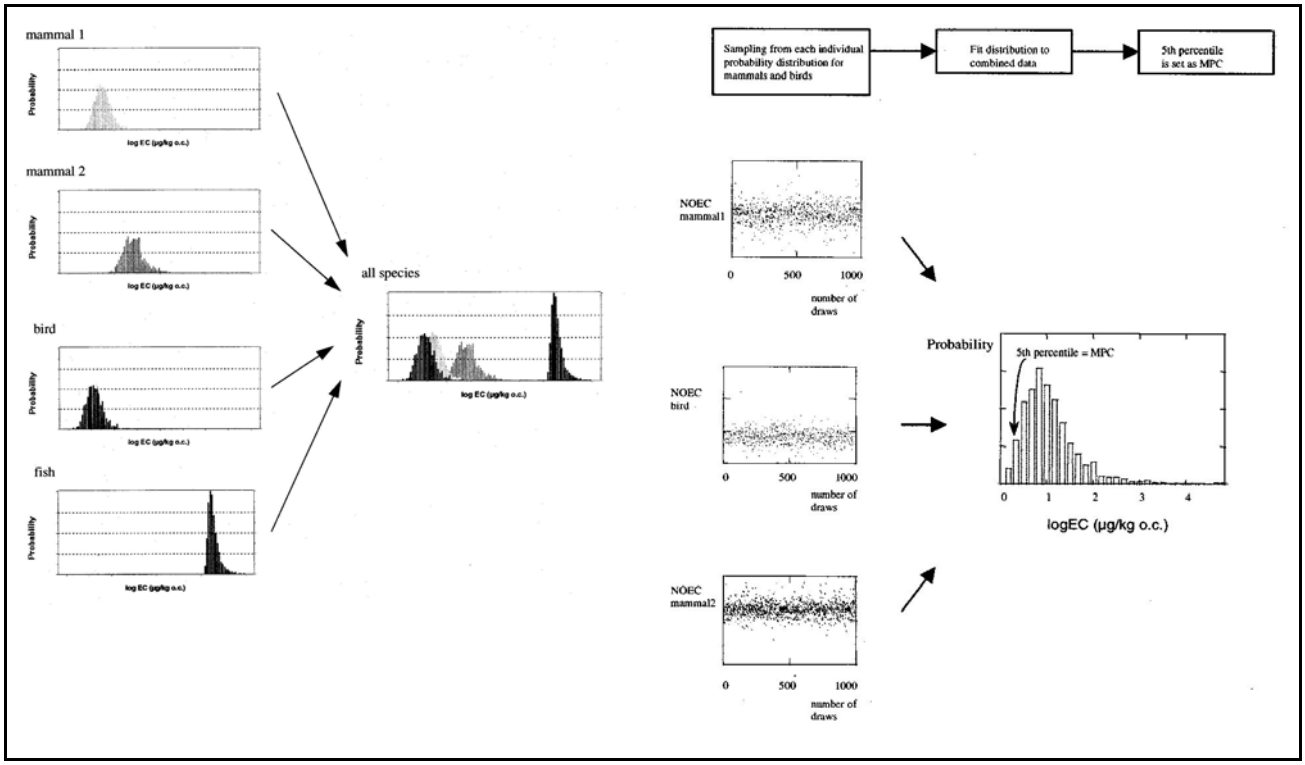

Figure 3 The derivation of recommended exposure limits (or maximum permissible concentrations) for the individual PCB congeners from the converted toxicity data (Wez99).

Chapter 3

The Committee's standpoint

In this chapter, the Committee comments on the RIVM derivation method. It does so on the basis of the three steps that it identified in the previous chapter.

3.1 Conversion to concentrations in soil or sediment

Variation in partition coefficients and fat levels

When converting toxicity data obtained in the laboratory into effect concentrations in the soil or in the sediment of surface water, RIVM makes use of the variation in the partition coefficients and fat levels. In this way, each item of toxicity data obtained in the laboratory generates a probability distribution of effect concentrations in soils or sediments. For example, the laboratory value for the No Observed Effect Concentration in water ($NOEC_w$) of PCB #77 for the water flea, produces a probability distribution of NOECs of PCB #77 in the sediment (especially its organic carbon component) for this organism (probability distribution of $NOEC_{oc}$s). The Committee points out that this probability distribution reflects uncertainty, rather than natural variation in the sensitivity of individual water fleas to concentrations in the sediment. It is not only the usual analytical and methodological variation which gives rise to this uncertainty, it also stems from the lack of measurement values for the water flea's BSAF and BCF. Estimates have to be made for these values on the basis of data from other species of organisms. On the whole, the Committee approves of RIVM's attempt to address this uncertainty.

It would like to point out, however, that the calculated probability distributions for sediment concentrations do not fully reflect the uncertainty involved. In particular, the uncertainty relating to the type of probability distributions associated with the partition coefficients has not been discounted here. However, the type of distribution selected (normal, lognormal, uniform) for the values of partition coefficients and fat concentrations makes only a marginal contribution to the total uncertainty, according to the analyses performed by RIVM. However, the Committee does feel that lognormal distributions should be assumed in the case of variables which cannot have negative values. A still more important question, in the Committee's view, is how representative is the available partition coefficient data and, consequently, the associated probability distributions for the data that one is attempting to estimate. RIVM has estimated the water flea's BSAF for PCB #77 using three BSAF values, those for two species of shellfish and one species of fish. The institute derives the BMF of a mouse relative to its prey from the BMF values of various Mustelids relative to their prey. If the available BSAF and BMF values were for species other than those mentioned above, then the probability distributions of both coefficients would also have been different. This uncertainty, which is not dealt with by RIVM, increases as the amount of data on which the probability distributions of partition coefficients are based decreases and as the differences in the partition coefficients between species of organisms increase. In this connection, the Committee would like to point out that most of the probability distributions of partition coefficients derived by RIVM are based on very little data, in some cases only a single datum.

Variation in other data

In the laboratory, different toxicity tests on the same substance, the same species of animal and the same studied effect can produce very different results. This can result from factors such as differences in experimental design, the duration of exposure and the circumstances under which exposure occurs, as well as genetic differences between the experimental animals used. RIVM has not addressed this 'intraspecific variation' in the toxicity data. The Committee appreciates that this is because it lacks the requisite data. Nevertheless, it feels that, as a result, the overall picture is somewhat unbalanced. Conversely, variation in the partition coefficients has been the focus of considerable attention, even though the requisite data is often lacking here too. There is also an issue with the assimilation efficiency (A) and the elimination rate constant (K), which are used in mammals to convert exposure concentration in the food into an internal concentration within the animal itself. For reasons which are unclear, these factors have not been subjected to a probabilistic approach.

K_{oc}

In order to convert the $NOEC_w$ of PCB #77 for the water flea into a probability distribution of $NOEC_{oc}$ values in the sediment, RIVM prefers to use the quotient of the BCF_L and the $BSAF_L$ rather than the K_{oc}, since the latter is difficult to determine by experimental means. For want of something better, the BCF and BSAF values for different individuals are used and even those of different species of organisms. This means that any differences in biotic processes (such as biotransformation and biomagnification) between these individuals or species will affect the quotient of the BCF and the BSAF. RIVM refers to this as an advantage. The Committee takes the view that this should instead be seen as a drawback, since it results in an incorrect estimate of the sediment/water partition coefficient. This is, after all, independent of processes within organisms.

Equilibrium

Models constructed from partition coefficients contain two major assumptions. Firstly, equilibria develop in the distribution of a substance between the various environmental compartments. Secondly, the values of partition coefficients were measured in equilibrium situations. RIVM prefers to use field data for the BMF and BSAF values, on the assumption that the condition of equilibium is more likely to be satisfied in the field than in the laboratory and because it is difficult to simulate all uptake routes in the laboratory. However, the Committee takes the view that highly persistent compounds such as PCBs often do not reach equilibrium situations in the field either. This is because organisms cannot easily break down or excrete these substances. Other contributory factors which can prevent the concentration of a substance in an organism from reaching equilibrium with its concentration in the immediate surroundings are the flow of water, the mobility of animals and growth dilution. This is why it does not consider field data to be automatically superior to laboratory data.

Soils

The Committee regards the models used as being mainly applicable to aquatic ecosystems and less so to terrestrial ecosystems. Terrestrial soils are much more heterogeneous than sediments. Furthermore, our knowledge of the processes taking place in terrestrial ecosystems is much more limited.

3.2 The derivation of recommended exposure limits for individual PCBs

'Interspecies variation'

The Committee does not concur with the way in which the recommended exposure limits for individual PCB congeners are derived. Its main objection is that the SSDs (as depicted in table 5.3 of the RIVM report) for a number of PCBs are based to only a limited extent (or not at all) on differences in sensitivity between different species of organisms. This is partly due to the limited availability, in the international literature, of toxicological data on individual PCB congeners. It is also a result of discarding some of the toxicity data for statistically unsound reasons. This is because the result of the Kolmogorov-Smirnov test (which is used to determine whether all of the EC_{oc} values could be derived from a single lognormal distribution) is highly dependent on the number of EC_{oc} values that are generated per original item of toxicity data, using Monte Carlo simulation. The institute has arbitrarily selected a quantity of one thousand. If one million values had been generated then the normal distribution would have been rejected even more often and the number of items of (original) toxicity data used would have been even fewer1.

Previously, Aldenberg & Slob's HC_5 method for deriving an SSD was only used if toxicity data (NOECs) from at least four different species of organisms was available (Slo92). Furthermore, these species must be as representative as possible of all existing species, in terms of their ecological function, body structure and exposure route (GR88, Slo92). In the current method, proposed by RIVM, these two requirements are by no means always met. In the case of five of the eight PCB congeners for which the institute has derived a recommended exposure limit, the SSD is ultimately based on less than four original items of toxicity data. The value for PCB #105 is actually based on toxicity data for just a single animal species, namely the most sensitive of the three species investigated. The distribution's standard deviation is entirely accounted for by the uncertainty surrounding the partition coefficients for that one species. It does not incorporate any 'interspecific variation' whatsoever. In addition, the Committee feels that this approach to standard setting is not well balanced. The recommended exposure limit for the one PCB congener, especially that for #77, is based on toxicity data for a wide range of species with extremely varied levels of sensitivity.

1 The Committee feels that a better approach would be to take a single value, per congener, from the EC_{oc} probability distribution for each animal species, calculate a normal distribution on the basis of these values and determine the 5% percentile. Repeat this one thousand times. This will give rise to a probability distribution of 5% percentiles. A given percentile from this distribution can then be elevated to the status of a recommended exposure limit.

Conversely, the recommended exposure limit for another congener, PCB #105, was solely derived from its toxicity to the most sensitive species. The RIVM method seems to continually skip from one concept to another, namely standard setting on the basis of all species (HC_5 method) versus standard setting on the basis of the most sensitive species. No clear choice is made, and the price of this is particularly evident when deriving the recommended exposure limit for the mixture (see the following section).

Various measures of toxicity

Previous HC_5 methods (Str89; Ald93) were based purely on NOECs. The present approach differs from these by making combined use of a range of different measures of toxicity (NOEC, LOEC, as well as $L(E)C(D)_x$ where the value of x can vary from 36 to 80). RIVM justifies this by citing the steepness of the dose-response curves, whereby the difference between the NOEC and the LC_{50} within a single animal species is small compared to the differences between the NOECs of different animal species. There is, however, no evidence whatsoever that the dose-response curves of PCBs are any steeper than those of other substances. Furthermore, the use of an LOEC rather than an NOEC (as occurred in the case of PCB #105) leads directly to a less strict recommended exposure limit.

Even more importantly, the Committee feels that the combined use of different measures of toxicity represents an additional source of variation. This clouds the view of the most interesting source of variation, namely interspecific variation. PCB #118 can serve as an example here (see figure 5.5 on page 43 of Wez99). Two items of toxicity data are available for this congener, one for the rat and one for the chicken. The rat appears to be more sensitive than the chicken by a factor of ten, but that is deceptive. The difference can partly be attributed to the fact that the value available for the rat is an $NOEC_{growth}$ while that for the chicken is an LD_{45}. Had an $NOEC_{growth}$ also been available for the chicken, then the difference in sensitivity would probably have been smaller. It is unclear as to how much of the difference can actually be ascribed to a difference between animal species. The standard deviation of the SSD on which RIVM bases the recommended exposure limit for PCB #118 mainly stems from a difference in toxicity measure (NOEC *versus* LD_{45}), from a difference in measured endpoint (growth retardation *versus* mortality) and from the uncertainty regarding the partition coefficients for each of these species. Interspecific variation becomes completely obscured and plays virtually no part at all. The same is true, to a greater or lesser extent, of the remaining PCB congeners. Accordingly, the Committee finds that the frequency distributions derived by RIVM (see table 5.3 on page 48 of Wez99) can hardly be viewed as SSDs and that the recommended exposure limits which are based on them cannot therefore be considered to offer protection to 95% of all species.

The 5% percentile as a recommended exposure limit

RIVM's decision to elevate the 5% percentile of the SSDs to the status of recommended exposure limit is in keeping with the preceding HC_5 methods (Str89, Ald93). This is a policy-based choice inspired by the practical consideration that a line has to be drawn somewhere if a recommended exposure limit is ultimately to be derived. In the case of a few substances, further research is carried out using multispecies test systems or field trials. In these studies, at exposure concentrations equivalent to the level of the HC_5 method, few or no effects were observed in aquatic ecosystems (Ema93, Okk93, Lah98, Wij98, Lee02). This has been less thoroughly investigated in the case of terrestrial systems (Str02). Also, it is unclear just how much protection a recommended exposure limit for PCBs based on the HC_5 method would provide for birds and mammals.

Confidence interval

Previous HC_5 methods took account of the fact that the HC_5 produces different results if different sets of toxicity data are available. They did so by determining a confidence interval of the 5% percentile of the SSD, and then elevating its lower limit to the status of a recommended exposure limit. This approach means that the sparser the toxicity data and the greater the degree of confidence required, the stricter will be the recommended exposure limits obtained. The present method, from RIVM, provides no insight whatsoever into the degree of confidence associated with the 5% percentile of the SSD. The Committee feels that this is regrettable, all the more so because the recommended exposure limits derived by RIVM are based on so little toxicity data. The Committee's proposed method for determining the 5% percentile (see the footnote earlier in this section) makes it possible to calculate the above-mentioned confidence interval.

3.3 The derivation of a recommended exposure limit for the mixture

Scaling factors

Using a concentration addition model, RIVM has calculated a recommended exposure limit for a mixture containing a number of planar PCBs. In doing so, the institute has assumed that these congeners have a constant relative toxicity with regard to each other. The Committee takes issue with the method used by RIVM to calculate this relative toxicity, which is expressed as a scaling factor. RIVM derives a recommended exposure limit for a mixture of some planar PCBs, because they all have the same mechanism of action, which involves interaction with the Ah receptor. This is also why the institute excludes the non-planar congener PCB #153 when deriving a recommended exposure

limit for the mixture. The Committee feels that this approach automatically excludes all toxicity data except that relating to species with an Ah receptor and to effects that are based on interaction with this receptor. Invertebrates in particular are more likely to lack an Ah receptor of the type seen in vertebrates (Hah98, Jam98). The concentration addition model selected by RIVM cannot, therefore, be applied to invertebrates. Accordingly, the Committee takes the view that it is not justifiable to partly base the scaling factor for PCB #77 on toxicity data relating to the water flea.

Their lack of a 'classical' Ah receptor makes invertebrates less sensitive than vertebrates to planar dioxins (Hah98). Even within the latter group, however, there are considerable differences. Fish, for example, are substantially less sensitive to mono-*ortho* PCBs than birds and mammals (Ber98). RIVM derives the scaling factor for one PCB congener (PCB #77) from toxicity data for a wide range of species (mammals, birds, fish, invertebrates) with widely varying degrees of sensitivity. In the case of another congener (PCB #105), however, the institute bases the same factor solely on an item of toxicity data from the most sensitive species investigated, a bird. This produces a distorted image of the relative toxicity of the congeners with regard to each other. The Committee feels that the scaling factors for the various congeners should be based on comparable sets of toxicity data.

Finally, the Committee points out that the relative toxicity of the PCB congeners is dependent on the species of organism under consideration. For this reason, WHO has derived separate TEF values (which are also a measure of the relative toxicity of PCBs; see below) for mammals, birds and fish (Ber98). This is in agreement with the advisory report produced by the Committee on Risk Assessment of Substances/Dioxins (GR96). This means that separate models of concentration addition, with their own individual scaling factors, should be used for each group of related organisms.

Fixed pattern

RIVM also assumes that there are fixed relationships between the concentrations of PCB congeners in soils and sediments. The Committee endorses RIVM's comment that this presumably fixed pattern should be checked at catchment areas other than that of the Rhine, namely those of the rivers Meuse, Schelde and Eems. In addition, these relationships do not apply near point sources, such as disposal sites for chemical waste. This fixed pattern of congeners is equally inapplicable to terrestrial soils, i.e. soils that are situated permanently above water level. These are particularly affected by PCBs that are carried in via the air, while sediments and flood plain soils are particularly affected by silt-bound PCBs that are carried in via water (Bri01). The congener pattern in each of these sites must be checked first, before a recommended exposure limit can be derived for the mixture in such locations. Finally, the Committee points out that the pattern can

also change over the course of time, partly due to differences between the congeners in terms of evaporation and microbial conversion. For this reason, the pattern should be checked every five or ten years.

Dibenzodioxins and dibenzofurans

Since PCBs are always present in soils and sediments as mixtures, the Committee considers the recommended exposure limits derived by RIVM for the individual congeners as being of lesser importance. In everyday ecological risk assessment, the starting point should almost always be the recommended exposure limit for the mixture. However, this RIVM recommended exposure limit for the mixture includes only some non-*ortho* PCBs and mono-*ortho* PCBs, and does not include polychlorinated dibenzodioxines (PCDDs) and polychlorinated dibenzofurans (PCDFs). These compounds also exert their toxic effect by binding to the Ah receptor. Although the exact figures vary, PCDDs and PCDFs always make a major contribution to the total toxicity of substances with this mechanism of action in the Netherlands. In agreement with a previous advisory report issued by the Health Council (GR96) and with the views expressed by WHO (Ber98), the Committee therefore concludes that a coherent risk assessment of exposure to PCDDs, PCDFs and dioxin-like PCBs is called for. It urges adoption of the internationally accepted TEF concept, which does take into account all of the major groups of substances that bind to the Ah receptor (Ber98, Saf90, Saf94). In this concept, the toxicity of each substance is related to that of the reference substance 2,3,7,8-tetrachlorodibenzo-p-dioxin (2,3,7,8-TCDD). This toxicity relationship is referred to as the Toxic Equivalency Factor or TEF, of the substance in question. Assuming that a given substance is fully biologically available, then it is possible to calculate the number of toxic equivalents (TEQs) for that substance by multiplying the substance's concentration in an environmental compartment by its TEF. This can be done for all substances that exert their effect by binding to the Ah receptor, after which the number of TEQs is added up. These summed TEQs can then form the basis for standard setting or risk assessment.

Bottlenecks and possible solutions when using the TEF concept

There are at least two difficulties associated with the derivation of TEF-based and TEQ-based recommended exposure limits for Ah reactive substances in soils and sediments. As pointed out by a previous Health Council committee, a TEF-based and TEQ-based approach is not particularly suitable for the protection of ecosystems (GR95). The TEFs differ from one species (or group of species) to another. Many species, especially invertebrates, are more likely to lack a functional Ah receptor of the type seen in vertebrates. Since entirely different mechanisms of action could be involved in these organisms,

concentration addition with TEFs is probably not applicable here. Furthermore, within the vertebrate group, TEF values differ between mammals, birds and fish (Ber98). As a result, the concentrations of the various Ah reactive substances for each of these groups of animals must be summed in a different way. The Committee feels that this difficulty can only be resolved by basing the recommended exposure limit on a single species, or a few closely related species, for which binding to the Ah receptor is known to be the major mechanism of action and which are also known to be particularly vulnerable due to their extreme sensitivity and their position at the end of a food chain. The best candidates for this purpose, according to the Committee, are birds or mammals. Since it is not known exactly which species is the most sensitive, the traditional HC_p method can be used, provided that chronic toxicity data is available for at least four species of birds or four species of mammals. If there are fewer than four items of toxicity data, then an extra safety factor can be applied to the data from the most sensitive species investigated (compare Slo92).

The second difficulty is that the toxic effect of PCBs, dibenzodioxins and dibenzofurans in the soil or sediment is partly dependent on the substances' physicochemical properties. Factors such as molecular size and ability to be metabolised determine the amounts that are ultimately found in organisms. These differ from one substance to another. As a result of this, the pattern of substances in an organism will differ from the associated pattern seen in the soil or sediment. Together, the above factors make it impossible to establish a recommended exposure limit for the mixture in soils and sediments on the basis of TEQs. The Committee believes that the only solution is to base the recommended exposure limit for the mixture on the maximum number of TEQs that the body (or body fat) of the most sensitive organism is permitted to contain. If both the identities of the Ah reactive substances in a given soil or sediment and their concentration in its organic carbon component (C_{oc}) are known, then a simple food-chain model incorporating substance-specific $BSAF_L$s and BMF_Ls can be used to calculate the concentrations reached by each of these substances in the organism. TEFs can then be used to convert these concentrations to TEQs. This is shown in the following formula:

$$\sum TEQ = \sum_{i=1}^{n} C_{oc,i} \times BSAF_{L,i} \times BMF_{L,i} \times TEF_i$$

Here, n is the number of Ah reactive substances and i is the i^{th} Ah reactive substance.

The sum of the TEQs can then be compared to the recommended exposure limit. By this means it is possible to determine whether a soil complies with the recommended exposure limit for the mixture. It should be noted here that a previous Health Council com-

mittee decided not to pursue attempts to derive an ecotoxicological recommended exposure limit for a mixture of dioxin-like substances. This was due to excessive variation in the published TEF values for different groups of animals and to the fact that vital data on congener-specific partition coefficients was lacking (GR96). Since then, international consensus has been achieved with regard to TEF values for mammals, birds and fish (Ber98). In addition, RIVM has derived congener-specific $BSAF_L$ and BMF_L values for a number of planar PCBs. The Committee feels that this is a significant step towards the derivation of a mixture-specific recommended exposure limit for ecosystems that is based on TEQs.

Practical objections

Two practical objections could be lodged against the approach proposed by the Committee. However, it considers that neither of these are insurmountable. Firstly, simply knowing the number of TEQs in a soil or sediment is not enough. Accurate information is required concerning the identities and concentrations of any substances in the soil or sediment that are capable of reacting with the Ah receptor. Here there is the option of excluding from consideration those substances that are reliably known

- to be almost completely absent from Dutch soils and sediments ($C_{oc,i}$ practically 0);
- to be released from the sediment (or taken up by organisms) in only negligible amounts ($BSAF_{L,i}$ practically 0);
- to scarcely infiltrate higher trophic levels at all ($BMF_{L,i}$ practically 0);
- to be only very marginally toxic (TEF_i practically 0).

Such substances will, after all, make virtually no contribution to the sum of TEQs in the fat of the animal species on which the recommended exposure limit is based. The Committee does not believe that it is feasible to base an ecotoxicological risk assessment of dibenzodioxins and dibenzofurans on fixed patterns of substances in sediments and terrestrial soils. These differ from PCBs in that the mutual relationships between the quantities of these compounds vary from place to place.

A second objection might be that the results obtained from an analysis of soil and sediment samples can no longer be directly compared to a recommended exposure limit, instead they must first be converted.

The Committee's proposed method for deriving a recommended exposure limit for ecosystems, in relation to Ah reactive substances, is in keeping with the recommendations of the foreign experts that it consulted, especially those of Dr G Suter II, Dr JP Giesy and Dr AL Blankenship (see annex C).

Chapter 4

Conclusions and recommendations

The Committee endorses several principles used by the RIVM to derive recommended exposure limits for PCBs in soils and sediments. This relates to the aim of getting a better picture of the uncertainties involved and the attempt to derive a recommended exposure limit for a mixture of substances with a common mechanism of action. However, in terms of its execution, this has proved deficient in a number of major areas. The Committee therefore considers the proposed method to be unsuitable for deriving ecotoxicological recommended exposure limits for PCBs.
With regard to the recommended exposure limits for individual congeners, the Committee has the following comments:

1 The method proposed by RIVM seems to skip continually from one concept to another. With one PCB congener, the institute derives a recommended exposure limit on the basis of toxicity data for all species, in accordance with Aldenberg & Slob's (Ald93) HC_5 method, for example. With other congeners, the institute's approach is solely based on data from one (or a few) sensitive species. This produces an unbalanced situation with regard to the recommended exposure limits for the individual PCB congeners.
2 For reasons that are not statistically justified, part of the available toxicity data is excluded from consideration.
3 Because the method provides no confidence intervals for the 5% percentile of the SSDs, it provides no insight into the degree of uncertainty in the recommended

exposure limit. Previous derivation methods, such as Aldenberg & Slob's HC_5 method do provide such insight.

4 Use of Aldenberg & Slob's HC_5 method required NOECs for at least four species of organisms. RIVM has now lost sight of this requirement. In most cases, the species sensitivity distributions (SSDs) derived by the institute (see table 5.3 on page 48 of Wez99) are based on less than four toxicity values, sometimes as few as one. Furthermore, the combined use of different toxicological endpoints (NOECs, LD_{50}s and EC_xs) tends to distort the differences in sensitivity between species. The standard deviation of the SSDs on which RIVM bases its recommended exposure limits is primarily based on uncertainty regarding the partition coefficients and differences in endpoints, and hardly at all on real differences in sensitivity between species. The SSDs derived by RIVM cannot, therefore, be regarded as SSDs. Accordingly, the Committee takes the view that recommended exposure limits based on the above cannot be considered to offer protection to 95% of all species.

5 Since PCBs are always present in soils and sediments as mixtures, the Committee considers the recommended exposure limits derived by RIVM for the individual congeners as being of lesser importance. In everyday ecological risk assessment, the starting point should almost always be the recommended exposure limit for the mixture.

With regard to the recommended exposure limit for the mixture based on PCB #118, the Committee has determined that:

6 When calculating the mixture-specific recommended exposure limit (based on PCB #118) for planar PCBs, RIVM wrongly makes use of toxicity data on species of organisms which almost certainly lack a functional Ah receptor as found in mammals, birds and fishes.

7 The scaling factors for the various planar PCBs are based on extremely unequal sets of toxicity data, which produces a distorted picture of the relative toxicity of the congeners.

8 RIVM uses a single, constant scaling factor for each planar PCB congener. This overlooks the fact that the relative toxicity of the congeners is animal-species specific. It was not without reason that WHO established separate TEF values for mammals, birds and fish.

9 The mixture-specific recommended exposure limit for planar PCBs, which is based on PCB #118, does not include any dibenzodioxins and dibenzofurans. It should do so, however, since these substances (like planar PCBs) exert their effect via the Ah receptor and are present in considerable quantities in Dutch soils and sediments.

The committee recommends the following:

1 Make optimum use of existing knowledge about the effect of PCBs on organisms. It is generally known that the most vulnerable animals are mammals and birds at the end of food chains. It is recommended that standard setting be directed at one, or a few, of these species. The advantages are that less data on toxicity and partition coefficients is required, while the derivation method becomes simpler and, accordingly, more transparent.
   Since it is not known which species is the most sensitive, a HC_5 approach could be employed within the limited group of those organisms that are considered to be most sensitive, provided that toxicity data is available for at least four species of organisms. If the toxicity data is limited to fewer than four species, then an extra safety factor can be applied to the value from the most sensitive species investigated.
2 Follow the TEF concept. This becomes simpler if the risk assessment is based on a few, closely related species of organisms or on just one species. The advantage is that all relevant substances, whose effects are based on their interaction with the Ah receptor, are taken into consideration. Since the TEF concept is widely accepted in international circles (by organizations such as WHO), this will generate more support for the method. The starting point for a recommended exposure limit should be the number of TEQs in the fat of one (or a few) sensitive species. The matter of whether a given soil or sediment satisfies this recommended exposure limit can then be tested using the pattern of Ah reactive substances in that particular soil or sediment, and a simple food-chain model for the organism in question. To this end, the measured concentrations of the individual substances in the soil or sediment should each be multiplied by their own congener-specific BSAF-, BMF- and TEF-values. The sum for all such substances results in an estimate of the total number of TEQs that one can expect to find in the fat of the organism in question, on the basis of the measured concentrations in the soil or sediment. This can then be compared to the recommended exposure limit. Given the international consensus regarding TEF values for mammals, birds and fish, together with the increasing availability of congener-specific partition coefficients, the Committee feels that this approach will soon be within reach.

Aside from its methodological objections to the way in which RIVM derived the recommended exposure limits, the Committee feels that data availability is a make-or-break issue when it comes to the usefulness of any method for deriving recommended exposure limits for substances. This seems to be limited, even in the case of such a relatively well investigated group of compounds as the PCBs. The Committee therefore urges that more energy be devoted to the focused generation of research data that can be used to derive recommended exposure limits for substances, in order to protect ecosystems.

Chapter 5

Answering the Minister's questions

Question 1:

What is the Council’s assessment of this novel method for deriving standards for PCBs? I would be interested to hear your views on the use of field data, the method for the assessment of secondary poisoning, probabilistic modelling and the determination of the maximum permissible risk level (MPRL) for the mixture.

Answer:

The Committee endorses several of the principles on which the derivation method is based, particularly the aim of getting a better picture of the uncertainties involved and the attempt to derive a recommended exposure limit for a mixture of substances with a common mechanism of action. However, in terms of its execution, the Committee feels that this has proved deficient in a number of areas.

The Committee takes the view that while field data can represent a valuable addition to data derived from laboratory research, it is not automatically superior.

The partition-coefficient-based method used by RIVM to assess secondary poisoning is widely accepted in scientific circles. This does not detract from the fact that the most important condition (that a substance’s distribution between the various environmental compartments should be in equilibrium) is often not met in the field. Accordingly, organisms from different trophic levels are often not in equilibrium with one another.

While it appreciates the fact that RIVM has used probabilistic modelling in an attempt to incorporate uncertainties pertaining to the values of partition coefficients into the derivation of recommended exposure limits, the Committee feels that the institute's statistical approach is incorrect.

The Committee approves of the derivation of a mixture-specific recommended exposure limit. However, it feels that the mixture-specific recommended exposure limit, which is calculated on the basis of PCB #118, is rather pointless since it does not include any dibenzodioxins and dibenzofurans. These are substances which, like planar PCBs, exert their effect via the Ah receptor and which are present in considerable quantities in Dutch soils and sediments.

Question 2:

Through the use of probabilistic modelling, the MPRL was established at the 5th percentile value of the probabilistic distribution. Does the Health Council concur with the reasoning behind the selection of 5% as the level of protection for ecosystems? Does the Health Council take the view that the introduction of probabilistic techniques has produced genuine improvements in the underpinning and transparency of standard setting?

Answers:

During its examination of the RIVM report (Wez99), the Committee was unable to find any arguments to support the choice of the 5% percentile as the level of protection. It can only note that this choice is in keeping with previous derivation methods, particularly Aldenberg and Slob's HC_5 method (Ald93). This is a policy-based choice inspired by the practical consideration that a line has to be drawn somewhere when a probabilistic approach is used. In the case of a few substances, further research is carried out using multispecies test systems or field trials. In these studies, at exposure concentrations equivalent to the level of the HC_5 method, few or no effects were observed in aquatic ecosystems. This has been less thoroughly investigated in the case of terrestrial systems. Also, it is unclear just how much protection a recommended exposure limit for PCBs based on the HC_5 method would provide for birds and mammals.

The Committee supports the use of probabilistic techniques, but takes the view that these have been incorrectly applied in the derivation method in question. As a result, neither the underpinning nor the transparency of the method of standard setting have been improved.

Question 3:

How does the Health Council feel about setting standards for the most commonly occurring individual PCBs and for the PCB#18 mixture?

Answers:

The Committee feels that it makes little sense to set standards for individual PCB congeners which act via the Ah receptor since, in ecosystems, these substances almost always occur as mixtures. Thus, in practice, policy decisions or measures will almost always have to be taken on the basis of a mixture-specific recommended exposure limit.

The Committee feels that the mixture-specific recommended exposure limit based on PCB #118 is rather pointless, since it disregards dibenzodioxins and dibenzofurans. The Committee advocates adoption of the internationally supported TEF concept and the derivation of a mixture-specific recommended exposure limit on the basis of the number of TEQs in the fat of one (or a few) highly sensitive species.

Question 4:

Would you recommend that parts of this method (i.e. the use of field data, the method for the assessment of secondary poisoning, and probabilistic modelling) also be used for the derivation of recommended exposure limits for other substances? If so, for which groups of substances could they be used?

Answers:

In general, when deriving recommended exposure limits for substances, it is advisable to include both field data and laboratory data, and to make use of secondary poisoning assessment methods and probabilistic modelling. However, the Committee objects to the way in which probabilistic modelling has been used in the derivation method in question. It therefore considers that, in its present form, the method cannot be used to derive ecotoxicological recommended exposure limits for PCBs or other substances (or groups of substances).

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Wij98 Wijngaarden RPA, Van Geest GJ, Brock TCM. Ecologische risico's van bestrijdingsmiddelen in zoetwater ecosystemen. Deel 2: Insecticiden. Utrecht: STOWA, 1998; publicatie nr 98.31.

A The request for advice

B The Committee

C Experts consulted

D Written replies from foreign experts

E Glossary

F Scientific publication by Van Wezel *et al*., 2000

Annexes

Annex **A**

The request for advice

The President of the Health Council received the following letter, dated 15 March 2000, no. DGM/SVS/2000024545, from the Minister of Housing, Spatial Planning and the Environment:

I hereby request that the Health Council advise me concerning the standards for PCBs, for the protection of ecosystems, which have been derived using a new method as part of the Setting Integrated Environmental Quality Objectives project, as described in the appended report entitled Maximum Permissible Concentrations for Polychlorinated Biphenyls (RIVM number 601501006).

The objective of the Setting Integrated Environmental Quality Objectives project is to derive and establish general, non-statutory environmental quality standards (maximum permissible risk levels, MPRLs, and target values, TV) for the compartments of soil, water, sediment, groundwater and air. When drawing up standards, the aim is that the standard for a given compartment should also provide protection to organisms in the other compartments (intercompartmental harmonisation).

The Health Council has, on several occasions, issued advisory reports on ecotoxicological standard setting (Publications 'Advisory report on starting points for standard setting' GR 1985/31, 'Assessing the risk of toxic chemicals for ecosystems' GR 1988/28, 'Ecotoxicological extrapolation methods' GR 1991/11, 'Secondary poisoning. Toxic substances in food chains' GR 1993/04 and 'Ecotoxicology on course' GR 1994/13). In 1995, the Health Council issued an extensive advisory report on the INS project dealing with the INS standards (and the associated methodology) for three groups of substances, namely trace metals, volatile compounds and substances with the potential for secondary poisoning ('The Project: Setting Integrated

Environmental Quality Objectives' GR 1995/07). Finally, the Health Council has issued an advisory report on topics such as standard setting for zinc (Zinc GR 1997/34).

One of the comments made by the Health Council regarding the method used for deriving standards was that for highly hydrophobic compounds, most experimental bioconcentration factors (the ratio between the concentration of a substance in an organism and in an environmental compartment) are unreliable (1995/07). In a number of advisory reports, the Council also points to the uncertainties in the methods used for standard setting (Aldenberg and Slob) and to the underlying assumptions involved. As regards secondary poisoning, the accumulation of toxic substances in the food chain, the Health Council has indicated that the INS method used is a practical one. While it is certainly capable of giving an initial indication of whether secondary poisoning is occurring, this method provides no guarantees regarding the protection of higher organisms (1993/04, 1995/07). Another recurring concern expressed by the Council relates to the differences between laboratory and field data, and the fact that this was not taken into consideration when the INS standards were being derived (1995/07).

On the basis of these advisory reports, RIVM has developed a new method for deriving standards for PCBs which meets some of these criticisms. This new method was developed (and the appended report drawn up) in cooperation with a supervisory committee of national experts in the field of environmental chemistry and toxicology of PCBs and dioxins, as shown on page 5 of the report.

Some of the ways in which the new method, which is used for PCBs, differs from the classical INS method are:

- different dosing methods have been incorporated;
- a different method was used to estimate secondary poisoning, which made it possible to avoid using a possibly uncertain BCF factor;
- field data are also used in support of the MPRLs;
- a probabilistic model is used when calculating the MPRLs, instead of the methods normally used in INS. The advantage of this is that it pinpoints the uncertainties much more clearly.

The selection of PCB, for which individual standards have been set, is based on toxicity, occurrence in the environment and the monitoring programs that have been carried out by the Public Works and Water Management Department for many years. Since the non-ortho PCBs and mono-ortho PCBs have a comparable mechanism of action, and usually occur in comparable patterns in the environment, a mixture-specific MPRL has also been derived, on the basis of the occurrence of PCB #118. Instructions for the use of this MPRL are provided on pages 51-52.

I would be grateful if the Health Council could answer the following questions:

1 What is the Council's assessment of this novel method for deriving standards for PCBs? I would be interested to hear your views on the use of field data, the method for the assessment of secondary poi-

soning, probabilistic modelling and the determination of the maximim permissible risk level (MPRL) for the mixture.

2 Through the use of probabilistic modelling, the MPRL was established at the 5th percentile value of the probabilistic distribution. Does the Health Council concur with the reasoning behind the selection of 5% as the level of protection for ecosystems? Does the Health Council take the view that the introduction of probabilistic techiques has produced genuine improvements in the underpinning and transparency of standard setting?

3 How does the Health Council feel about setting standards for the most commonly occurring individual PCBs and for the PCB#18 mixture?

4 Would you recommend that parts of this method (i.e. the use of field data, the method for the assessment of secondary poisoning, and probabilistic modelling) also be used for the derivation of standards for other substances? If so, for which groups of substances could they be used?

Each year, in December, the INS steering committee sets a number of standards. I would therefore be most grateful if I could receive a copy of the completed report no later than the end of the year 2000.

Yours sincerely,

The Minister for Housing, Spatial Planning
and the Environment

JP Pronk

Annex **B**

The Committee

- Dr M van den Berg, *chairman*
  Professor of environmental toxicology; Institute for Risk Assessment Sciences (IRAS), Utrecht
- Dr JJM Bedaux
  statistician; *Vrije Universiteit*, Amsterdam
- Dr AC Belfroid
  ecotoxicologist; Royal Haskoning, Rotterdam (until 1-1-2002)
- Dr JP Boon
  ecotoxicologist; Netherlands Institute for Sea Research (NIOZ), Den Burg
- Dr NW van den Brink
  ecotoxicologist; Alterra, Wageningen
- Dr N van der Hoeven
  biostatistician; ECOSTAT, Leiden
- Dr SM Schrap
  environmental chemist; Institute for Inland Water Management and Waste Water Treatment (RIZA), Lelystad
- Dr MEJ van der Weiden, *consultant*
  Ministry of Housing, Spatial Planning and the Environment (VROM), The Hague
- Dr HFG van Dijk, scientific *secretary*; Health Council, The Hague

Secretarial support: TME Smith-Mets
Layout: J van Kan

Annex C

Experts consulted

From foreign countries, written consultation

- Dr JP Giesy and Dr AL Blankenship
  Michigan State University, East Lansing, USA
- Dr F Gobas
  Simon Fraser University, Burnaby, Canada
- Dr DRJ Moore
  The Cadmus Group Inc., Ottawa, Canada
- Dr EP Smith
  Virginia Tech, Blacksburg, USA
- Dr G Suter II
  EPA, Cincinnati, USA

From the Netherlands, verbal consultation

- Dr M Schipper
  Centre for Biostatistics, University of Utrecht
- Prof. W Slob
  RIVM, Bilthoven; IRAS, Utrecht

Annex **D**

Written replies from foreign experts

The Committee sent copies of the publication by Van Wezel *et al* (Wez00), together with a number of questions, to the foreign experts consulted. This appendix contains the Committee's questions and the experts' answers.

Questions addressed by the Committee to Dr JP Giesy and Dr G Suter II

General question

What is your general opinion about the method? Are the underlying assumptions and simplifications reasonable and defendable and does the method offer environmental risk limits that adequately protect ecosystems?

More specific questions

1 Are the models for calculating toxic concentrations in the soil/sediment (see page 2141) appropriate? For instance: there is no model with a BMF for aquatic predators. The model for fish eggs (model 3) does not include an egg to parent ratio, whereas the model for bird eggs (model 5) does.

2 Is it advisable or defendable to combine data from totally different animal species when calculating toxic concentrations in the soil/sediment? For example: the $NOEC_{laboratory}$ for PCB 77 of the mouse (see table 1 on page 2143) is transformed into a $NOEC_{soil/sediment}$ distribution of the mouse with model (4) on page 2141. The BMF_L-value, which is needed to do the calculation, is derived from a probability distribution based on BMF_L-values from mustelids (see table 4 on page 2145). The $BSAF_L$-value of the prey of the mouse is derived from a probability distributions based on one $BSAF_L$-value from (pooled) fish and two $BSAF_L$-values from shellfish (see table 5 on page 2146).

3 Is it advisable to derive a mixture ERL for planar PCBs without taking into account dioxins and furans, which are thought to account for a (highly variable) part of AhR-mediated toxicity in the Netherlands?

4 The authors of the paper have chosen to discard the internationally widely accepted TEF/TEQ concept for three reasons: I. The TEF/TEQ concept does not use any environmental chemical information for the derivation of the ERL; II. The TEF/TEQ concept is partly based on in vitro data, whereas the authors prefer to use only in vivo data on endpoints that are directly relevant to population development, i.e. survival, growth and reproduction; III. TEF data are only defined for three groups of vertebrates: fish, birds and mammals. Can you agree with the authors' choice?

5 Could the same method be used to derive environmental risk limits for other groups of chemicals as well?

Reply from Dr JP Giesy and Dr AL Blankenship

Dear Dr. van Dijk:

Attached you will find my review of the paper by van Wezl et al. As you can see from my comments, we would not use this approach and would prefer the TEQ approach. We feel that the proposed method, while not technically incorrect, has limitations that are greater than those of the TEQ approach.

We have sent you some hard copies of reprints. I have also attached a PDF file to this email that gives our preferred method for such analyses.

JPGiesy

Attachment:

Prof. H. van Dijk
Scientific Secretary of the Committee on Environmental Risk limits for PCBs
Health Council of the Netherlands
P.O. Box 16053
NL 2500 BB
The Hague
The Netherlands

Dear Dr. van Dijk:

I and one of my colleagues, Dr. Alan L. Blankenship have reviewed the paper entitled "Environmental Risk Limits for Polychlorinated Biphenyls in the Netherlands: Derivation with Probabilistic Food Chain Modeling". Both of us work in both the areas of PCBs in the environmental and their effects on wildlife and in the area of probabilistic risk assessment.

In general we do not think that the proposed method should be applied. We would suggest an alternative approach, similar to either one which we have developed (Blankenship and Giesy, 2002) or that of Environment Canada (, 1998) or the United States Environmental Protection Agency (USEPA, 1998), which uses the toxic equivalency approach to conduct risk assessments. We have enclosed several papers on these methods. While many of these approaches are based on a bottom-up analysis of risk, they can be adapted to derive ERLs. If you would like to have additional information on these methods please contact me.

The method proposed by van Wezel, in our opinion, is a modification of the TEQ approach that is designed to be able to make assessments of the risk of PCBs with a minimum of data acquisition. We understand the reason for developing the method and find no errors in the basic theory or application of the method. We do, however, feel that there is a great deal of uncertainty introduced by the proposed method, that is not necessary. In addition, the proposed method does not take into account the potential contribution of other residues in the environment that could contribute to the AhR-mediated mechanism of action that is considered to be the critical mechanism of action by the method of van Wezel et al. In general, the proposed method, is a simplification of the TEQ approach suggested by Blankenship and Giesy (2002). The methods employed to derive the final ERL for congener 118 is convoluted and based on a relatively small amount of data for each of the species-congener assemblages.

Specific Comments:

While we endorse the application of probabilistic methods, it is inappropriate to derive frequency distributions from one or two data points. The proposed method makes assumption of the shape of the distributions that is unsubstantiated. If the TEQ approach is used with corrections of individual congeners for relative potency factors and the inclusion of PCDD and PCDF in the data set a much better description of the cumulative frequency distribution can be obtained. We would suggest this approach, rather than the approach where each of the individual PCB congeners was considered independently and scaling factors applied. This results in a much more rigorous description of the cumulative frequency distribution.

One limitation of the method is that it assumes that the relative proportion of the 118 congener remains constant and it is well correlated with the total AhR-activity of the mixture to which organisms are exposed. The data presented in the paper indicates that this range could be approximately 25-fold for the congeners contributing to the AhR activity. This may or may not be acceptable in making regulatory decisions. This is a subjective choice.

In the derivation of the ERL, the endpoints considered NOELS, LOELs, and LC50 values. These different metrics can not combined to derive a frequency distribution of effect. It is impossible to know what effect this might have on the resulting ERLs, but we suspect that this would result in an increase (less protective) of the value.

The method seems to derive an ERL that is more appropriate for sediments than soils.

The application of BSAFs for sediment-dwelling invertebrates is appropriate, but should not be applied to higher trophic levels. This was not done in the proposed method, but we caution that it is inappropriate to apply a TEQ approach to total TEQ concentrations in sediments. Transfer of each congener needs to be estimated before the relative potency factor is applied to the concentration of each congener that would be predicted to occur in the tissues of organisms of interest.

The proposed method seems overly obtuse and cumbersome. It is very difficult to understand the methods applied. To be accepted by a wide range of parties, the method must be transparent and easily understandable. We were unable to understand the method from the description given in the manuscript. We were able to understand the derivation of the values after consulting the original report.

Answers to specific questions:

1 In general, the proposed method is scientifically defensible and appropriate. The main purpose of the proposed method is to simplify what needs to be measured in the environment. As we have indicated above, we feel that the model is obtuse and limited in applicability because of uncertainties and because of the limited data for each congener. First, it assumes that the system is at steady state. This may or may not be a good assumption, but is of minimal concern. The application of BSAF and BMF values should be separated. It is appropriate to assign values to individual congeners and to multiply the appropriate factors together as was done in the proposed method.

2 No it is not advisable to do this. For this reason, we suggest the TEQ approach and also recommend against mixing and matching different endpoints (NOEC, LOEC, LC50), different bioaccumulation factors (BMFs, BSAFs). Rather, it would be much more streamlined and transparent to focus on the species most at risk and provide the fewest possible transfer steps between these species and the sediments or soils.

3 No, it is not advisable to derive an ERL for only PCBs without considering the PCDD/DF.

4 It is our opinion that the limitations of the TEF/TEQ approach can be dealt with and that the method is more transparent and more robust than the proposed methodology.

5 I do not think that the proposed approach should be extended to other classes or chemicals. Instead relative potency methods similar to the TEF/TEQ approach should be considered for different mechanisms of action.

Sincerely,

John P. Giesy, Ph.D. and Alan L. Blankenship, Ph.D.

Enc: Reprints

Blankenship, A.L., and J.P. Giesy (2002). Use of biomarkers of exposure and vertebrate tissue residues in the hazard characterization of PCBs at contaminated sites - application to birds and mammals, in "Environmental Analysis of Contaminated Sites", G.I. Sunahara, A.Y. Renoux, C. Thellen, C.L. Gaudet (Eds.), John Wiley & Sons Inc., London.

Canadian Council of Ministers of the Environment (CCME) (1998). *Canadian Tissue Residue Guidelines for Polychlorinated Biphenyls for the Protection of Wildlife Consumers of Biota.* Prepared by the Guidelines

and Standards Division, Science Policy and Environmental Quality Branch, Environment Canada, Hull, Quebec.

US Environmental Protection Agency (USEPA) Region 9 Biological Technical Advisory Group (1998). Use of PCB congener and homologue analysis in ecological risk assessments.

Reply from Dr G Suter II

Comments by Glenn Suter on
the Proposed Method for Deriving ERLs for PCBs Presented in van Wezel et al. 2000
December 30, 2001

The problem addressed by this paper is one of the most difficult in ecological risk assessment and management. The solution proposed by the authors is consistent with the current state of science and practice in the field. Given the data and knowledge available, the authors are to be commended on their work. My comments address the questions sent to me by Dr. van Dijk, then address some issues of my own, and provide my recommendations. These comments are mine, and do not necessarily represent the policies of the U.S. EPA.

General Question

The answer to the general question depends on ones interpretation of the phrase "adequately protect ecosystems." Both the question and the paper refer to protecting ecosystems without defining what is meant by the phrase. If it refers to protecting ecosystem properties such as rates of biogeochemical processes, species diversity, trophic status, etc., then the answer is yes, because those higher level properties are little influenced by the sorts of effects seen in high trophic level organisms at most PCB contaminated sites. However, if the goal is to protect properties of sensitive organisms such as survival, growth and reproduction of piscivorous birds, as suggested by the models and data used, then the answer is not so clear.

Given the difficulty of defining ERLs for these congeners and mixtures, one must ask whether this is the best approach to managing the risks. Might it not be better to define a set of highly sensitive and susceptible species, monitor the reproductive success and contaminant burdens of those species, and take action where effect are occurring? I recognize that policy may not allow that option. Therefore, having raised it as an alternative, I will proceed to discuss the paper as if ERLs were necessary.

Specific Questions

The specific questions are insightful and highlight some of the major weaknesses of the method.

1 The lack of a model for piscivorous fish is a potentially significant problem. The clearest case of effects of dioxin-like chemicals on fish is that of the lake trout (*Salvelinus namaycush*) in the Laurentian Great Lakes. This is a piscivorous salmonid which has experienced reproductive failure associated primarily with PCBs in adults and eggs. I doubt that Eq. 2 would predict PCB levels in those fish. I feel certain that Eq. 3 would not predict levels in their eggs, or the eggs of any non-migratory fish (i.e., it might work if fish from a clean habitat spawn in a contaminated habitat). The cases of high observed

concentrations in eggs are clearly related to maternal contamination, not exposure to ambient PCB as suggested by Eq. 3.

2 This question raises the combination of data for different species in one model as a problem. I would rephrase the question in terms of the endpoint to be estimated. That is, what is the endpoint species (or set of species), and in what sense is it (are they) represented by a mouse toxicity value, a mustelid biomagnification factor, and fish and bivalve prey? If, for example, the endpoint is river otter fecundity, one would have to assign an extrapolation model to the mouse toxicity data to estimate otter toxicity which would include a large uncertainty. The fish to otter data would be directly applicable, with some experimental uncertainty due to duration and conditions of the test. The BSAF data are applicable to much of the otter's diet, but would need to have uncertainty applied due to lab-to-field extrapolations, unrepresented dietary components, experimental error, etc. This is the simplest case, but it raises the issue of incomplete accounting for uncertainty if distributions of model parameters are based simply on distributions of available data. If the models are intended to represent entire taxa or communities, the interpretation of the data as estimators of the model parameters becomes more difficult. However, that would seem to be necessary since the authors combined toxicity data for all taxa for PCB 77.

3 It would certainly make sense to develop an ERL for all AhR mediated chemicals. However, a PCB ERL could be useful in the interim for those sites where the contribution of dioxins and furans is negligable.

4 I would favor the use of TEFs. The limitation of TEFs to vertebrates is not a problem, since effects on invertebrates were not modeled and invertebrates and plants are not sensitive. The use of in vitro data is not a problem if the degree of AhR induction determines the relative toxicity of congeners, a proposition that the authors seem to accept. See, for example, p. 2150, third paragraph. The obvious advantage is the ability to incorporate more congeners.

5 The same general approach could be used whenever persistent bioaccumulative toxicants are assessed.

Other Comments

As suggested above, I found it difficult to review the model because it was not clear what was being predicted. Is it the NOEC for the fifth percentile species of an entire ecosystem? If so, is it assumed that, except for PCBs 77 and 105, birds and mammals represent entire ecosystems? If so, does the addition of aquatic species for PCB 77 make it a better estimator of the ecosystem effects or does it simply make the ERLs inconsistent?

In addition, it would be good to define the conceptual models underlying the mathematical models. For example, the most direct interpretation of the model implementations for aquatic organisms is that there is no dietary accumulation and for mammals and birds is that they feed on benthic organisms that are directly exposed to contaminated sediments or on earthworms. However, they may mean to include other routes. For example, they may assume that the BSAF include dietary bioaccumulation.

The authors do not indicate what their distributions are meant to represent, and the data combined into distributions make them hard to interpret. Is it variance among species or among exposure conditions, or is it uncertainty, or maybe subjectivist degree of belief?

The prior three paragraphs address a common theme: without better specification of the goals one can not determine whether the models and their implementation are conceptually correct or verified by field data. The authors are to be commended for comparing their model results to field data, but the cases are too few (one mammal and one bird) and ambiguous. How do the concentrations causing reproductive effects in otters relate to those causing increased disease incidence? It is certainly not reassuring that the sediment ERLs result in body burdens seven times that needed to apparently cause adverse effects in otters. Perhaps they should not "focus on field studies from the Netherlands" (the mammalian case is not from the Netherlands any way). The models should work in any PCB-contaminated temperate ecosystem and verification is much more convincing when there are multiple cases. The authors could also break the models down and verify their ability to estimate body burdens, independent of the ability to predict effects of mixtures.

The use of statistical tests to determine whether to combine data in a distribution violates standard statistical inference. Failure to reject the null hypothesis does not allow one to accept it. For example, just because the small and highly inconsistent data sets do not allow the authors to prove that mammals are different from birds does not mean that they are the same. To show that they are the same (i.e., are unlikely to differ by more than a prescribed amount), you must estimate beta.

The text refers to BMF data for birds when there is none in table 4. In fact, there are only mustelid AhR mediated chemicals data

Recommendations

If I were performing this analysis, I would base it on the observation that birds are the most sensitive organisms (p. 2149), that piscivorus birds are the most exposed to aquatic contaminants, and that birds that feed on soil invertebrates are the most exposed to terrestrial contaminants. I would make the criterion apply to all AhR mediated chemicals and use avian TEFs to normalize to your best avian toxicity data set for AhR mediated chemicals. I would base the exposure model on the partitioning and uptake data that best represent the endpoint birds. This would, in my opinion, make the assessment clearer, simpler, and more defensible. This approach would leave out the PCB congeners that do not have AhR mediated toxicity, but we do not have good information on those less toxic congeners in any case.

I realize that these recommendations constitute a fundamentally different approach than that taken by the authors, and that they may be unacceptable for either policy or technical reasons. However, I feel that critical comments should be accompanied by a positive alternative.

Questions addressed by the Committee to Dr F Gobas

General question

What is your general opinion about the method? Are the underlying assumptions and simplifications reasonable and defendable and does the method offer environmental risk limits that adequately protect ecosystems?

More specific questions

1 Is it advisable or defendable to combine data from totally different animal species when calculating toxic concentrations in the soil/sediment? For example: the $NOEC_{laboratory}$ for PCB 77 of the mouse (see table 1 on page 2143) is transformed into a $NOEC_{soil/sediment}$ of the mouse with model (4) on page 2141. The BMF_L-value, which is needed to do the calculation, is derived from a probability distribution based on BMF_L-values from mustelids (see table 4 on page 2145). The $BSAF_L$-value of the prey of the mouse is derived from a probability distributions based on one $BSAF_L$-value from (pooled) fish and two $BSAF_L$-values from shellfish (see table 5 on page 2146).
2 The sediment/soil-to-water partition coefficient (K_{oc}) is hard to measure. Therefore, the authors replaced it by the ratio $BCF_L/BSAF_L$. Is this replacement advisable if BCF and BSAF values come from different studies and even from different animal species? Is biotransformation implicitly taken into account be using this ratio instead of the K_{oc} (see page 2141 below the heading '*Calculation of toxic concentrations in soil/sediment*')?
3 The authors appear to assume independence among the variables EBR, BCF_L, BMF_L and $BSAF_L$, when making the Monte Carlo analysis (see page 2142 below heading '*Probabilistic modeling to account for variability*'). Is this assumption reasonable?

Reply from Dr F Gobas

In general, I think that is a useful and a defensible approach. Its strength is that it recognizes the relationships that exists between PCB concentrations in the various media. It further makes use of empirical data for those substances for which the ERLs are developed. The uncertainty in the data are taking into account through Monte Carlo simulations. Also, variations in sensitivity among species are recognized in the approach and it makes use of all relevant toxicity data available. The downside of the method is that biomagnification and food-chain bioaccumulation are not well represented in the method (see question 2) and that inherent error to the approach itself (errors inherent to the model rather than the input parameters used) are not translated in some kind of conservancy or caution in the ERL numbers selected. Also, the use of the 5^{th} percentile of data that include both effects and non-effects data does not translate in my view into a cautious approach.

Question 1

I would say that it is defendable to combine data for different animal species. It is the necessary outcome of choosing for an empirical approach. The way the data are combined is crucial to the outcome. I think that the authors have done a good job combining the various data sets and choosing good values for the BMFL and BSAFL for the aquatic environment. As for your specific example in the question, I think that the authors go too far extending the approach to soil. The inherent model that is used by the authors is an aquatic model, where chemicals generally partition between water, sediments and biota and magnify in the food-chain. These processes are well understood and in my view reasonably well captured by the authors. However, the same processes are less well understood for terrestrial food-chains. In particular, organism-to-soil accumulation factors (rather than organism-to-sediment) and the partitioning to air are not considered in this approach. In my view the approach is best applied to sediments, not soil.

Question 2

I have some reservations about how this BCFL/BSAFL is executed as it has a tendency to ignore food-chain accumulation in the food-chain. Figure 1 (left) shows the model the authors follow illustrated by a numerical example. In the example, the NOECW = 0.0001 and BCFL=10,000 and the BSAFL is 1. The BCFL is based on lab data, which does not involve dietary uptake, and only a few field data (for some lower trophic level organisms). Hence, the NOECfish = 10,000 * 0.0001 = 1 and following eq. 2, one arrives at a

NOEC-OC/NOEC-W = 10,000/1 = 10,000, which is indeed the OC-water partition coefficient.

However, in real food-chains the relationships are closer to that depicted in Figure 1 (right) where as a result of biomagnification, levels in the fish will be higher than those in the benthic organisms. So, assuming a

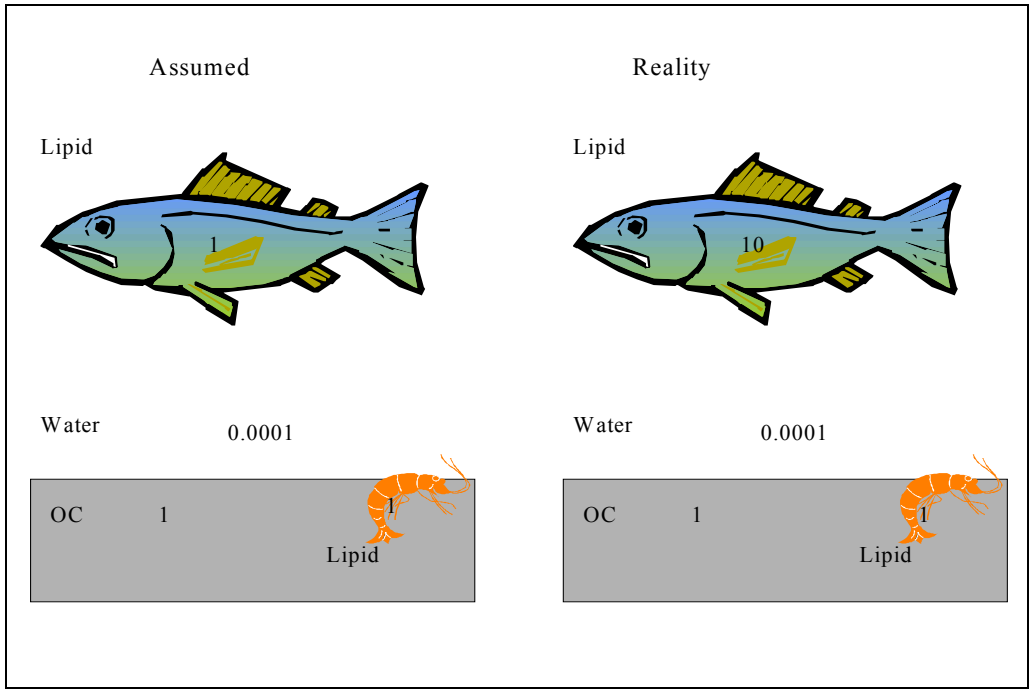
BMFL of 10 and given the same NOECOC of 1 one will get a NOECfish of 10, i.e. a ten times greater internal body burden than the no-effect body burden. To ensure that the NOECfish remains a 1, the NOECOC has to be 10 times lower than calculated using equation 2.

This effect is not captured in the BCFL and BSAFL. Over an entire aquatic food-chain the BMF can be between 10 to a 100. So, given a NOECOC of 1 one gets an upper trophic level fish body burden of 100, i.e. 100 times greater than the no-effect concentration. To incorporate the food-chain biomagnification of PCB congeners in the calculations, one has to lower the NOECOC below what is calculated in equation 2 by the total amount of biomagnification that takes place in the food-chain:

NOEC-OC = NOEC-W x (BCFL / (BSAFL x BMFL))

I am not sure what is meant by taking metabolic transfromation into account. However, if the BSAFL and BCFL belonged to the same species, he ratio NOECOC/NOECW would not be independent on the metabolic transfromation rate. I think that the authors are referring to situations where the BSAFL would refer to a species unable to metabolize the PCBs while the fish, to which the BCF applies, would. In that case, I agree that the NOECOC/NOECW ratio includes the metabolic transfromation that occurs in the fish.

3 I think that this is reasonable as the data refer to independent observations.



Questions addressed by the Committee to Dr EP Smith and Dr DRJ Moore

General question

What is your general opinion about the method? Are the underlying assumptions and simplifications reasonable and defendable and does the method offer environmental risk limits that adequately protect ecosystems?

More specific questions

1 The authors appear to assume independence among the variables EBR, BCF_L, BMF_L and $BSAF_L$. If this assumption is false, how does this influence the answers obtained by the Monte Carlo analysis? (see page 2142 below heading '*Probabilistic modeling to account for variability*')
2 Is it advisable to fit a (log) normal probability distribution to data that have been extracted by simulation from several different probability distributions? (see page 2142 below the heading '*Deriving ERLs*')
3 Should variability and uncertainty be separated more clearly when deriving ERLs?
4 The sensitivity distributions used to derive the ERLs of individual PCBs have varying SDs (see table 6 on page 2147). A large SD means that animal species show considerable differences in their sensitivity to that congener, whereas a small SD means that all species are approximately equally sensitive. Doesn't this conflict with the assumption of toxicity additivety, which is made when deriving the mixture ERL?

Reply from Dr EP Smith

Comments on the method for estimating environmental risk levels for PCBs as described in the paper "Environmental risk limits for polychlorinated biphenyls in the Netherlands…" published in Environmental Toxicology and Chemistry 19(8): 2140-2153.

General

The approach that is used is fairly standard. Define equations that model the mechanisms of interest, pick distributions for the parameters of interest then simulate outcomes. Use the outcomes to define lower limits. The lower limits are usually assumed to be the maximum values to be tolerated.

While this approach is standard, there are a number of assumptions that need to be evaluated. These include

Choice of method: Monte Carlo uncertainty analysis is the standard amongst a variety of approaches. In this case it may not be necessary. The authors produce log transformed estimates of EC_{oc}. If the log is applied to the equation describing the EC_{oc} the result is a linearization of the model i.e.

$$Log(EC_{oc}) = log(ED_o) - log(L_m) - log(BMF_L) - log(BSAF_L)$$

If the quantities all follow lognormal distributions, the log of the quantities is normal. These distributions may then be added together and Monte Carlo is not required. This approach was suggested by W. Slob quite a while ago but does not seem to be used much. The authors assume normal distributions several quantities rather than lognormal though.

Choice of distributions: the authors have used data from the literature to try to estimate these distributions. They also seem to run a small sensitivity analysis to check that the choices made are not overly influential (in the case of mammals).

Independence of parameters: Since parameters are treated as random in the models, the distribution and relationships between parameters is important. A common assumption is that the parameters are independent. This is often a critical assumption that is not checked or even discussed. If the correlations are high, ignoring them will sometimes lead to large effects on the estimates of variance. Since the variance is a critical factor in determining the percentiles, it is important to think about the correlation and evaluate its effect on the models.

Choice of parameter values for distributions. The parameter values are often chosen based on the literature. This can be a severe limitation, especially when the data are limited. On reading the paper I was confused

by how the quantities were actually selected for the distributions. For example, the quantities selected for lipid % egg (table 2) for birds (L_b) is 7.7 with a standard deviation of 0.8. In looking over the table, this appears to reflects data on one taxa from one study. Other values in the table indicate considerable variation for example 8.2 to 9.9 for another taxa and 3.5-4.5 for the last one.

This problem leads to a concern about modeling of between versus within variation. It is not clear if the ERL that is produced is to be protective of all species. I think that is what is implied but I did not see it directly stated in the paper. If the purpose is protection of species then the variation with the species (between individuals from the same taxa) is not relevant. What is relevant is the variation between species and this is what should go into the model. With this approach the parameters that are species specific would be correlated and the correlation should be taken into account in the Monte Carlo. The quantities that were used seem sometimes to be within species and sometimes between. I see this as an error (or at least a major assumption) in the modeling process. For example, if you consider the bird lipid %egg data in Table 2. there is considerable differences between taxa P. sinensis and L. argentatus. Based on my experience the standard deviations that are used for the normal distributions seem too small.

Your specific questions

1 Independence – if the parameters are species specific then I think correlation is a considerable problem. It should be investigated.

2 Fitting the lognormal – if I understand what was done, artificial data were generated using normal distributions then the ratio formed. The ratio will probably not have a normal distribution. It is appropriate to fit a log normal to the resulting data if the ratio is skewed. It looks like the authors check the fit (do more then just estimate parameters) so I think this is not a problem. Given they have 1000 simulated observations, I probably would have calculated the 5% percentile directly. It is not clear if they do this or just use the value calculated from the normal distribution.

3 I think variability and uncertainty need to be better integrated into the model. There is not a clear statement of what is uncertainty and what is variability. For example, is variability the individual variation or taxa variation. By the way, a statistical view is that variability is part of uncertainty.

4 I am not sure what the right answer is here. I think the answer is that it does not matter but I am not sure what they actually do (have not been able to reproduce their numbers). Scaling the quantities is a good thing to do if you are forming an overall index. Another concern is whether you should add these quantities on the log scale or the original scale. I would be inclined to add on the log scale. It looks like that is what they did but it is not at all clear. Is there a good reason to drop 153 from the analysis? I again don't quite see what they are doing but I would do take a simple approach and compute standardized values for the log transformed data then sum these. This approach puts the numbers on a log scale that may be a problem for some. I also have a bit of a problem with combining these together unless they are correlated.

Reply from Dr DRJ Moore

Dear Dr. van Dijk

I finally had a chance to review the paper yesterday. My responses to your questions are below. Please note that I did not read the extended report on which the van Wezel et al. paper was based. Thus, some of my concerns about lack of information about how certain methods were applied may have been addressed there.

General Opinion

I thought the methods employed to develop the ERLs were creative and generally well applied. Given the complexity of the methods and the many assumptions involved, however, I wonder whether the effort was worth it. The alternative would be to develop a TEQ benchmark, a relatively easy task because data and TEFs are available for many congeners, as well as 2,3,7,8-TCDD. TEQs are easily calculated for environmental samples and, unlike the mixture ERL developed here, can be applied to samples that differ in congener composition. TEFs are currently available for fish, birds and mammals (van den Berg et al. 1998 paper done for WHO), so have the same applicability as ERLs.

Specific Questions

1 It seems highly unlikely that BCF_L, $BSAF_L$, BMF_L and EBR are all completely independent of one another. However, the dependencies may not be all that strong. It is our experience that high BCF substances tend to have high BMFs because the former are generally less readily metabolized than are low BCF substances. However, there are plenty of exceptions to that rule of thumb (e.g., some high Kow PAHs are readily metabolized and hence have low BMFs). I would guess that EBR is not related to partitioning behaviour (like BCF) because it is a lipid:lipid ratio. More likely other factors are involved, such as ability of the substance to cross the placenta. So independence assumption of EBR to other three variables is likely reasonable. Nevertheless, I would recommend that the authors take two courses of action: (1) compare relationships between 4 variables for congeners that have appropriate data (likely to be limited), and (2) conduct "what if" analyses that explore the consequences of no, moderate and strong dependencies between variables (likely EBR can be ignored in these comparisons).

2 I have no problem with fitting lognormal distributions to data that have been extrapolated by simulation from several different probability distributions. It is well known that when several variables are multiplied together that the product will have an underlying lognormal shape, even when the distributions on the input variables are not lognormal (or even right skewed). Similarly, when input variables are added together, the sum will have an underlying normal shape, even when the input variables are

not themselves normal. Many of the equations used in this paper had input variables that were combined via multiplication.

3 For the purpose of deriving ERLs, I see no compelling reason that variability and uncertainty (a better term here would be "incertitude" because uncertainty includes both variability and incertitude) be separated. The two major reasons for separating variability and incertitude are: (i) to determine how confident we should be about the output distribution (the spread of the 2nd dimension bounds is an indication of how much incertitude exists about where the output distribution should be), and (ii) to identify whether research would be useful to reduce incertitude about particular variable distributions (i.e., if the environmental decision is clear even with the existing incertitude (e.g., benchmark is above upper bound distribution) then research is of little value). Neither of these two reasons appears to apply here.

4 I see no reason why sensitivity distributions with different slopes some how invalidates the assumption of toxicity additivity.

Cheers,

Dwayne

Annex **E**

Glossary

Ah receptor

Aryl hydrocarbon receptor; a receptor for polycyclic aromatic hydrocarbons which is located in the cytoplasm of cells of vertebrates. Is closely associated with the toxic action of both planar PCBs and dioxins and furans. See also receptor.

BCF_L

Bioconcentration factor standardised for fat (lipids); partition coefficient which, in an equilibrium situation, illustrates the ratio between the concentration of a substance in an animal's body fat and the concentration of the same substance in the surrounding water.

BMF_L

Biomagnification factor standardised for fat (lipids); partition coefficient which, in an equilibrium situation, illustrates the ratio between the concentration of a substance in a predator's body fat and the concentration of the same substance in the body fat of its prey. It is a measure of bioaccumulation via the food chain.

$BSAF_L$

Biota-to-soil accumulation factor standardised for fat (lipids) and organic carbon or, in the case of aquatic soils, the biota-to-sediment accumulation factor; partition coefficient which, in an equilibrium situation, illustrates the ratio between the concentration of a substance in the body fat of an animal

and the concentration of the same substance in the organic-substance fraction of the soil or sediment.

Concentration-addition model

Model in which the concentrations of substances with a common mechanism of action, weighted according to their relative toxicity, are added up to derive the total toxicity of a mixture of such substances.

Congeners

Substances with identical carbon skeletons but with different numbers of chlorine atoms (or those of another halogen). See also dibenzodioxins, dibenzofurans and polychlorinated biphenyls.

Dibenzodioxins

Chlorinated aromatic hydrocarbons with the general structural formula $C_{12}H_{8-n}O_2Cl_n$, in which n (the number of chlorine atoms) can vary from 1 to 8. There are 75 different possible compounds, which are referred to as congeners.

Dibenzofurans

Chlorinated aromatic hydrocarbons with the general structural formula $C_{12}H_{8-n}OCl_n$, in which n (the number of chlorine atoms) can vary from 1 to 8. There are 135 different possible compounds, which are referred to as congeners.

Dioxin-like PCBs

Planar PCBs (see this term for details).

EBR_L

Egg-to-bird ratio standardised for fat (lipids); partition coefficient which, in an equilibrium situation, illustrates the ratio between the concentration of a substance in the body fat of the mother bird and the concentration of the same substance in the fat contained in the egg (mainly the yolk).

EC_x (ED_x)

Concentration (dose) of a substance where x% of the investigated test organisms show an effect after a given period of exposure or where the test organisms experience an average effect of x%.

Equilibrium partitioning

Distribution of a substance across various environmental compartments (soil, water, air, organisms), such that its concentrations in the various environmental compartments are in a constant relationship to one another.

Frequency distribution

Ranking data in such a way as to illustrate the incidence of certain values or value classes.

HC_p (HC_5)

Hazardous concentration for p% (5%) of the species of organisms. The value is based on the p%(5%) percentile of a species sensitivity distribution (SSD). This is the exposure concentration of a substance in the environment that is considered to protect (100-p)% (95%) of the species of organisms.

Probability distribution

The theoretical frequency distribution (see this term for details) when all possible elements have been observed or when an infinite number of observations have been made.

K_{oc}

Partition coefficient standardised for organic carbon content which, in an equilibrium situation, illustrates the ratio between the concentration of a substance in the organic-substance fraction of the soil or sediment and the concentration of the same substance in the pore water or surface water.

Kolmogorov-Smirnov test

A statistical test used to determine how well an observed frequency distribution corresponds to a given probability distribution.

LCx (LDx)

The concentration (dose) of a substance at which, after a given duration of exposure, x% of the test organisms under investigation are dead.

LOEC

Lowest-observed-effect-concentration. This is the lowest exposure concentration in a toxicity test at which, after a given duration of exposure, a statistically significant effect is found on the selected measurement goal, thereby causing the null hypothesis (‘there is no effect’) to be rejected.

Lognormal distribution

An asymmetric probability distribution which produces a normal distribution when the logarithmns of each value is plotted instead.

Mono-ortho PCBs

PCBs with a chlorine atom at one of the four ortho positions (see figure 1 in section 1.1).

Monte Carlo simulation

A statistical technique which is used to estimate a given value and its probability distribution by repeatedly extracting a set of values for the variables from which the value is calculated. The values for the variables are extracted from a theoretical, expected probability distribution, or from an observed frequency distribution.

NOEC

No-observed-effect-concentration. This is the highest exposure concentration in a toxicity test at which, after a given duration of exposure, no statistically significant effect is found on the selected measurement goal, thereby causing the null hypothesis ('there is no effect') not to be rejected.

Non-ortho PCBs

PCBs with no chlorine atoms at any of the four ortho positions (see figure 1 in section 1.1).

Normal distribution

The classic statistical bell-shaped, continuous probability distribution. It is symmetrical and can be fully characterised by two parameters, the mean and the variance. A normal distribution is often observed in situations where numerous independent influences determine the value of a variable.

Partition coefficient

Constant ratio of the concentrations of a substance in two compartments at equilibrium.

PCBs

Polychlorinated biphenyls (see this term for details).

p% percentile

That measured value which is larger than p% of all values measured, and smaller than (100-p)% of them.

Planar PCBs

Polychlorinated biphenyls in which both phenyl rings can rotate so easily relative to one another that they can occupy a common plane without needing a large amount of energy input to do so. The energy required for this purpose increases with the degree of chlorination at the four ortho positions. It is almost impossible for PCBs with three or four ortho-chlorine atoms to achieve such a planar configuration at room temperature since they always have two chlorine atoms from different rings positioned opposite one another. Planar PCBs are also known as dioxin-like PCBs since, in dioxins, both phenyl rings always lie in the same plane. This is because they are linked together by two bridges, each consisting of a single oxygen atom.

Polychlorinated biphenyls

Chlorinated aromatic hydrocarbons with the general structural formula $C_{12}H_{10-n}Cl_n$, in which the number of chlorine atoms (n) can vary from 1 to 10 (see figure 1 in section 1.1). In all, there are 209 different possible compounds, which are referred to as congeners.

Receptor

Binding site with high affinity for a given toxic substance.

Species sensitivity distribution

Probability distribution of the sensitivities (expressed as NOEC, LC_{50}, EC_x, etc.) of species of organisms to a toxic substance.

SSD

Species sensitivity distribution (see this term for details).

TEF

Toxicity Equivalency Factor. This is the factor that relates the toxic efficacy of a substance to that of a reference substance. In the case of planar PCBs, dibenzodioxins and dibenzofurans, 2,3,7,8-TCDD is generally used as the reference substance, since this is the most poisonous of the substances that exert their effect via this particular toxicity mechanism.

TEQ

Toxicity Equivalent. This is a specific compound's individual contribution to the toxicity of a mixture of related compounds. It is calculated by multiplying the concentration of the compound in question by its TEF value.

Annex **F**

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Hazard/Risk Assessment

ENVIRONMENTAL RISK LIMITS FOR POLYCHLORINATED BIPHENYLS IN THE NETHERLANDS: DERIVATION WITH PROBABILISTIC FOOD CHAIN MODELING

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Abstract—Environmental risk limits (ERLs) for individual congeners of polychlorinated biphenyls (PCB 77, 105, 118, 126, 153, 156, 157, and 169) are derived. After lipid normalization, toxicity data for birds, mammals, and aquatic organisms were converted to equivalent concentrations in soil or sediment organic carbon (OC). Accumulation in the food chain was taken into account. Field-derived data on the environmental fate of PCBs, e.g., biomagnification factors and biota-to-sediment accumulation factors, were used in the calculations. The variability in these data was incorporated by using probabilistic techniques. Parameters that are difficult to measure for these hydrophobic compounds, such as the bioconcentration factor or the sediment/water partition coefficient, were avoided where possible. Probability distributions for various species were combined per congener when statistically appropriate; ERLs were based on the fifth percentile of these combined distributions. Congener patterns occurring in various sediments and invertebrates in The Netherlands were used for determining a mixture ERL for non- and mono-*ortho* PCBs. The PCB 118 was selected as a guiding congener. If the concentration of PCB 118 is less than 5 μg/kg OC, Dutch ecosystems are assumed to be protected for effects of the whole mixture of non- and mono-*ortho*-substituted PCBs. Concentrations associated with adverse effects in field studies were comparable to concentrations that would result if all congeners would be present at the ERL level.

Keywords—Polychlorinated biphenyls Environmental risk limit Probabilistic Food chain

INTRODUCTION

Polychlorinated biphenyls (PCBs) have been banned in industrialized countries since the 1980s but still enter the environment by leakage, recycling, transboundary influx via the major rivers, and long-range atmospheric transport [1]. Relatively high concentrations can still be encountered in sediments and soils as an inheritance of the past. The PCBs are biomagnified in the food chain and are found in top predators such as otters, seals, and fish-eating birds [2,3]. Many toxic responses have been described for the planar dioxin-like PCBs as well as for the nonplanar PCBs. The toxic responses include hepatotoxicity, body weight loss, thymus atrophy, impairment of immune responses, reproductive toxicity, disruption of the endocrine system, alterations in vitamin A and thyroid hormone metabolism, (developmental) neurotoxicity, teratogenicity, and promotor activity in carcinogenesis [4–8]. The non-*ortho* PCBs and, to a lesser extent, the mono-*ortho* PCBs are thought to exert their toxicity via the cytosolic aryl hydrocarbon receptor (AhR) [9,10]. The structure-dependent effects of these congeners are believed to be concentration additive. Multiple *ortho*-substituted PCBs and hydroxylated PCBs show effects like reproductive toxicity, promotor activity, neurotoxicity, effects on vitamin A metabolism, and alterations in thyroid hormone levels [5,11–13]. These latter effects probably are not directly exerted via the AhR-mediated pathway. For the non-*ortho* and mono-*ortho*-substituted PCB congeners (such as, respectively, 77, 126, 169 and 105, 118, 156, 157), much more toxicity data are available than for the multiple-*ortho*-substituted congeners. Concerning information on environmental fate (e.g., the *n*-octanol/water partition coefficient, the aqueous solubility, the bioconcentration factor, and the biomagnification factor) and on environmental concentrations (e.g., in sediment), information is available on the congeners that are included in routine monitoring programs. In The Netherlands, these are congeners 18, 28, 44, 49, 52, 101, 118, 138, 153, 170, 180, and 187, which occur in relatively high concentrations and can be analyzed with high accuracy. Of these, only PCB 118 is a planar AhR-binding congener.

For proper management of contaminated sediments and soils, environmental risk limits (ERLs) are needed to evaluate the possible risk of PCBs to the ecosystem. In The Netherlands, ERLs are based on information concerning the ecotoxicology and the environmental chemistry of substances. In The Netherlands, ERLs have been derived for several compound classes, including heavy and trace metals, several volatile compounds, substances with a potential for secondary poisoning, chlorophenols, pesticides, polycyclic aromatic hydrocarbons, and aniline derivatives [14]. The purpose of the present work is to derive ERLs for PCBs. These ERLs for PCB should protect the ecosystem and are derived for sediments and soils. Sediments and soils are considered as the major sinks, and exposure of any organism occurs via (pore) water and food from those sinks. In addition, most monitoring activities for PCBs focus on sediments and soils.

The ERLs are derived for those congeners that exert their effects by binding to the AhR, and in addition for congener 153. It is recognized that not all the possible toxic responses of PCBs are being considered. However, the lack of data on these responses and on the additivity of these effects does not justify an integral risk assessment. The individual congeners 77, 105, 118, 126, 156, 157, and 169 were selected. To account

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for the concentration addition of those congeners working via the AhR, a mixture ERL was derived and expressed as the concentration of PCB 118 that is routinely monitored. In addition, an ERL for PCB 153 was derived. This congener is thought to represent other toxic mechanisms exerted by PCBs that cannot adopt a planar configuration. Also for these mechanisms, concentration addition with other congeners is plausible. Because of a lack of toxicological data for other congeners, however, no mixture toxicity could be taken into account for these effects.

Toxicity data were converted into an equivalent toxic concentration in the organic carbon of sediment/soil [15]. For the compartments water and air, no ERLs were derived. Water and air, in contrast to organic carbon, are not important primary routes of exposure for highly hydrophobic compounds [16–19] and levels in water and air are extremely low. Accumulation via the food chain was taken into account. Data on environmental fate of PCBs, such as biomagnification factors and biota-to-sediment accumulation factors, were used in the calculations. Probabilistic techniques were used to incorporate the variation in the above-mentioned environmental fate data in the ERLs.

METHODS

Data collection and selection

The ERLs were derived for congeners 77 (3,3′,4,4′-CB), 105 (2,3,3′,4,4′-CB), 118 (2,3′,4,4′,5-CB), 126 (3,3′,4,4′,5-CB), 153 (2,2′,4,4′,5,5′-CB), 156 (2,3,3′,4,4′,5-CB), 157 (2,3,3′,4,4′,5′-CB), and 169 (3,3′,4,4′,5,5′-CB). Data were collected on the acute and chronic toxicity of these individual PCB congeners to aquatic and terrestrial organisms, mammals, and birds. Effects on growth, reproduction, and survival were used in the derivation of ERLs. Data on adverse biochemical or histopathological effects were not included in the derivation of ERLs. No observed effect concentration values (NOEC), but also other percentages of effect such as median effective concentrations (EC50s), were included. We included different dosing methods (diet studies, dosing per gavage or per injection). A toxicity study was considered reliable if it was in agreement with internationally accepted guidelines such as the Organization for Economic Cooperation and Development (Paris, France) guidelines or with criteria developed at the National Institute of Public Health and the Environment (Bilthoven, The Netherlands). Per compound, the most sensitive toxicity test was selected for each species to form the basis to derive the ERL.

Information about the lipid content of organisms was collected to lipid normalize the toxicity data. Data were collected on the environmental fate of the PCBs, i.e., data on the bioconcentration factor (BCF_L, the lipid normalized concentration ratio between an organism and the surrounding water), the biomagnification factor (BMF_L, the lipid-normalized concentration ratio between predator and prey), the biota-to-sediment/soil accumulation factor ($BSAF_L$, the lipid- and organic carbon-normalized concentration ratio between an organism and sediment or soil), the organic carbon-normalized partition coefficient between sediment/water or soil/water (K_{oc}), and the partition coefficient between *n*-octanol and water (K_{ow}).

Data sources

Sources used for the collection of data were the library of the National Institute of Public Health and the Environment's (Bilthoven, The Netherlands), on-line databases containing evaluated data ([20] available free through http://www.epa.gov/ecotox [21–23]), and on-line bibliographic databases Biosis® (Biosis, Philadelphia, PA, USA) and Toxline and Chemical Abstracts (http://toxnet.nlm.nih.gov) as well as literature searches of the open literature and reviews.

Calculation of toxic concentrations in the soil/sediment

The toxicity data of the different species were converted to equivalent toxic concentrations in the organic carbon of soils or sediments using the procedures described below.

Uptake of administered dose. For all studies with dosing per injection or per single oral gavage, it was assumed that 100% of the administered dose was taken up. For diet studies and multiple oral gavage studies for mammals, the effective concentration in the organism (ED_o, mg/kg) was estimated using the following one-compartment bioaccumulation model [6]:

$$ED_o = \frac{A \cdot R \cdot C_f}{K}(1 - e^{-Kt}) \quad (1)$$

in which A is the assimilation efficiency (dimensionless), R is the daily ration of food (kg/kg/d), and C_f is the concentration of PCBs in the food (mg/kg). For studies with dosing via multiple oral gavage, $R \cdot C_f$ was replaced by the daily gavage concentration (mg/kg/d). K is the elimination rate (per day). For mustelids, the secretion rate via the anal gland (0.0165/d [5]) was added to K. Finally, t is the duration of the diet (days). Values for K and A were taken from Leonards et al. [6].

Aquatic organisms. Toxicity data expressed as water concentrations ($NOEC_w$), were converted into equivalent (no) effect concentrations in the organic carbon fraction of the sediment ($NOEC_{oc}$) by using the ratio $BCF_L/BSAF_L$, i.e.,

$$NOEC_{oc} = NOEC_w \frac{BCF_l}{BSAF_l} \quad (2)$$

By using $BCF_L/BSAF_L$ rather than the sediment/soil-to-water partition coefficient (K_{oc}), biotransformation of the compound is implicitly taken into account.

Aquatic toxicity data obtained in fish egg injection studies ($LD50_o$, concentration injected in the fish eggs exerting 50% effect) were converted to an equivalent toxic concentration in the organic carbon ($LC50_{oc}$) by

$$LC50_{oc} = \frac{LD50_o}{L_f \cdot BSAF_L} \quad (3)$$

where L_f stands for the lipid fraction in the fish eggs.

Mammals. The effect concentration in the mammal (ED_o) was lipid normalized with help of the lipid content of the mammal, L_m, and a one-level food chain was assumed for calculating the effect concentration in the organic carbon (EC_{oc}) as

$$EC_{oc} = \frac{ED_o}{L_m \cdot BMF_L \cdot BSAF_L} \quad (4)$$

Birds. Almost all data on toxicity of PCBs to birds were obtained in studies with dosing by egg injection. The dose in the egg ($ED50_{egg}$) was first lipid normalized using the lipid content of the bird egg (L_b). Then a correction for the transfer of PCBs from the parent bird to the egg was applied (EBR; the concentration ratio between the egg and the parent on a lipid weight basis). In this way, a lipid-normalized concentra-

tion in the parent was obtained. Then, a one-level food chain was assumed:

$$EC50_{oc} = \frac{ED50_{egg}}{L_b \cdot EBR \cdot BMF_L \cdot BSAF_L} \quad (5)$$

Probabilistic modeling to account for variability

Considerable variability in the literature data on the parameters as used in equations 2 through 5 ($L_{fish\ egg}$, $L_{bird\ egg}$, L_m, EBR, BCF_L, BMF_L, and $BSAF_L$) was encountered because of intra- and interspecies differences, sediment differences, use of different test methods, etc. The variability in these data can be included in the calculations using probabilistic modeling.

Distributions were fitted to the literature data of the mentioned parameters using the software package Crystal Ball 4.0 (Decisioneering, Denver, CO, USA). These distributions, instead of discrete values, were used as input to the calculations. For the parameters BCF_L, BMF_L, and $BSAF_L$, whether there were significant differences among congeners was tested by single-factor analysis of variance ($\alpha < 0.05$) or by a two-sample *t* test assuming equal variances. If there were statistically significant differences among congeners, these fits were performed per congener.

The calculations using equations 2, 3, 4, or 5 were then performed; the distributions for the different parameters used in the equations were sampled with a Latin hypercube sampling. Each calculation was performed 1,000 times. This resulted in probability distributions of the equivalent toxic concentration in the organic carbon of soil/sediment for each original toxicity value. In this way, all types of toxicity studies could be readily compared as all data were expressed in the same concentration axis (in organic carbon) and integrated into one ERL.

Deriving ERLs

ERLs for individual congeners. From each individual probability distribution of the equivalent toxic concentration in the organic carbon, 1,000 data points were extracted. All data were combined per congener, and new distributions were fitted to the combined data. These were normal distributions based on the log-transformed data. Combined distributions were fitted for all toxicity data together or only for the data on birds and mammals. The goodness of fit of the distributions to all data or to all mammal and bird data was tested by the Kolgomorov–Smirnov test. If the *s*-value was less than 0.1, the distribution was judged to be an acceptable basis for the ERL. Otherwise, the most sensitive probability distribution was chosen as the basis for the ERL.

The ERL values reported are the fifth percentiles of the selected distributions, back transformed into μg/kg OC.

Mixture ERL. The mixture ERL is supposed to be protective for the mixture of AhR-binding PCBs that were considered in this study (i.e., congeners 77, 105, 118, 126, 156, 157, and 169). The mixture ERL aims to protect ecosystems from these planar congeners. It was expressed on the basis of PCB 118 since this planar congener is monitored routinely. The fraction of the toxicity of the mixture of planar PCBs that is explained by PCB 118 was calculated, and the ERL for the single congener PCB 118 was multiplied by this fraction to yield the mixture ERL.

For calculating the fraction of the toxicity explained by PCB 118, both information on the relative concentrations of the congeners and information on the relative potency is needed. For deriving the mixture ERL, the congener pattern of planar PCBs in The Netherlands was used. The concentration of each individual AhR-binding PCB was expressed as a percentage of the summed concentration of planar PCBs. The distributions forming the basis for the ERL of the individual congeners were used to scale the toxicological importance of the congeners. Means were used instead of ERLs (fifth percentiles) since means are not influenced by the dispersion (as, e.g., measured by standard deviation) in the distributions.

RESULTS

Toxicity data

The toxicity data used to calculate the ERL values are listed in Table 1. For an extensive overview of all the toxicity data collected, we refer to the underlying report [24].

Lipid content of the different species

The BCF_L, $BSAF_L$, and BMF_L data are expressed on a lipid basis, while toxicity data (except for L[E]C50s) are expressed on a wet weight basis. So toxicity data must be lipid normalized before converting them into equivalent toxic concentrations in the organic carbon (equations 3–5). Lipid content varies between species but also within a species depending on the season, reproductive phase, food availability, etc. [25]. In addition, the lipid extraction method used influences the amount of lipids found [26]. Table 2 shows extractable lipid contents in various species and their eggs and the variability therein.

For the lipid content of fish eggs, a normal distribution with a mean of 10.1 and a standard deviation of 0.2% was used in the calculations [27]. For lipid content of bird eggs, a normal distribution with a mean of 7.7 and a standard deviation of 0.8% was used [28]. These values are consistent with the values reported in Table 2. Concerning the lipid content of mammals, two alternative distributions were considered. First, a normal distribution with a mean of 9.4 and a standard deviation of 7.7%, based on a compilation of literature data on laboratory-raised test organisms [29], was used. This value is high compared to the range of lipid contents observed in mammals taken from the field (Table 2). The laboratory-raised organisms as used in toxicity studies are generally well fed and do not have much movement, so they can be assumed to have a higher lipid content than free-ranging organisms. Second, a uniform distribution of the lipid content between 2 and 30% was used. These two alternatives were included to check the importance of the mammal lipid content; the variability in the literature data is high, so uncertainty in the distribution assumed is a consequence.

The PCB concentrations in bird eggs are translated to concentrations in the parent birds by assuming an egg-to-parent ratio of a mean of 0.60 with a standard deviation of 0.11 on a lipid basis. This value is derived from a field study on herring gulls [28]; no significant differences between homologue groups of PCBs were reported in that study. Few data on egg-to-parent bird ratios are available for PCBs (see also [30,31]). However, the absence of an influence of the substitution pattern on the partitioning between parent and egg lipids implies that the PCBs partition nonselectively between the various lipid pools in the avian body. The cited value of 0.60 is also assumed to be applicable to other bird species [31].

Data on environmental fate

Bioconcentration. Data on bioconcentration for fish, mollusks, and crustaceans derived from laboratory studies and

Table 1. Overview of the toxicity data used in the derivation of the environmental risk limits (ERL) for selected polychlorinated biphenyl (PCB) congeners[a]

PCB	Aquatic organisms			Mammals			Birds		
	Species	Toxicity endpoint	Ref.	Species	Toxicity endpoint	Ref.	Species	Toxicity endpoint	Ref.
77	*Salvelinus namaycush*, eggs	Survival, LD50	[56]	*Mus musculus*	Reproduction, NOEC	[57]	*Falco sparverius*	Survival, LD50	[58]
	Oncorhynchus mykiss, eggs	Survival, LD50	[59]				*Meleagris gallopavo*	Survival, LD60	[47]
	Daphnia magna	Growth, NOEC	[60]				*Gallus gallus*	Reproduction, NOEC	[61]
105	*Brachydanio rerio*	Survival, LC50	[62]	*Rattus rattus*	Growth, ED50	[63]	*Gallus gallus*	Growth, LOEC	[45]
118				*Rattus rattus*	Growth, NOEC	[64]	*Gallus gallus*	Survival, LD45	[47]
126	*Oryzias latipes*	Survival, NOEC	[65]	*Rattus rattus*	Growth, NOEC	[66]	*Meleagris gallopavo*	Survival, LD36	[46]
	Oncorhynchus mykiss, eggs	Survival, LD50	[59]				*Gallus gallus*	Reproduction, NOEC	[61]
							Falco sparverius	Reproduction, NOEC	[61]
153				*Rattus rattus*	Growth, NOEC	[67]			
				Mustela vison	Growth, NOEC	[68]			
156				*Mus musculus*	Reproduction, LOEC	[69]	*Gallus gallus*	Survival, LD50	[70]
				Rattus rattus	Growth, NOEC	[71]			
157				*Rattus rattus*	Growth, ED50	[63]	*Gallus gallus*	Survival, LD50	[70]
169				*Cavia porcellus*	Survival, LD50	[72]	*Gallus gallus*	Survival, LD80	[47]
				Mus musculus	Reproduction, NOEC	[48]			
				Rattus rattus	Reproduction, NOEC	[73]			
				Mustela vison	Growth, LOEC	[74]			

[a] NOEC = no observable effect concentration; LOEC = lowest observable effect concentration.

Table 2. Extractable lipid content in various species and their eggs as percentage of wet weight

Species	Lipid % whole body, mean ± SD	Lipid % egg, mean ± SD	Ref.
Birds			
Larus argentatus	10.3 ± 2.2	7.7 ± 0.8	[28]
Larus argentatus		8.2–9.9	[75]
Aythya fuligula	3.6 ± 0.7		[76]
Podiceps cristatus	4.2 ± 0.5		[76]
Ardea cinerea	2.7 ± 1.5		[76]
Phalacrocorax carbo sinensis	3.5 ± 0.5		[76]
Phalacrocorax carbo sinensis		3.5–4.5	[77]
Birds	8.9 ± 9.0		[29]
Altricials		5.9 ± 1.5	[78]
Semialtricials		6.3 ± 0.7	[78]
Semiprecocials		9.5 ± 2.3	[78]
Precocials		10.3 ± 1.4	[78]
Mammals			
Martes martes (muscular tissue)	3.4 ± 1.8		[79]
Stoat (liver)	4.1 ± 0.7		[80]
Weasel (liver)	3.2 ± 0.6		[80]
Polecat (liver)	5.4 ± 2.0		[80]
Red vole	2.9 ± 0.5		[80]
Wood mouse	4.6		[80]
Common vole	2.7		[80]
Shrew	2.7		[80]
Common hare	0.95		[80]
Mammals	9.4 ± 7.7		[29]
Fish			
Silver bass		5.5	[75]
Smallmouth bass		11.4	[75]
Walleye		10.1 ± 0.2	[27]

field studies were reviewed (Table 3). In Figure 1, lipid-normalized BCF_L values from laboratory or field studies were related to log K_{ow} values (data from [32]). For the congeners considered, there was a significant relationship between BCF_L and log K_{ow} ($F > F_{critical}$, $p = 0.01$, $r^2 = 0.63$). Data points were within the range where, according to the literature, linearity is no longer observed [33–37]. In addition, standard deviations for the individual congeners were rather high (Fig. 1). For PCB 153, no significant differences were observed in BCF_L values derived from laboratory or field studies (*t* test). Therefore, laboratory and field data were combined for fitting distributions. The available lipid-based BCF_L data did not differ significantly between congeners (analysis of variance, $\alpha < 0.05$) both for laboratory data only and for the combination of laboratory and field data. Therefore, the log-transformed laboratory and field BCF_L data for fish and mollusks were combined for all congeners.

Biomagnification. Data on biomagnification can be found in Table 4. All available laboratory studies concerned fish species. Field studies concentrated on biomagnification in mammals and birds. In Figure 2, the BMF_L values for the different congeners are depicted for both the laboratory and field studies. Significant differences between the congeners were observed for the field-based BMF_Ls. For birds, less data were found than for mammals. The largest number of BMF data available was for PCB 153. No significant differences between the BMF_L for birds or mammals were observed for this congener. For each congener, the probability distributions for BMF_L were fitted to the data, combining data for birds and mammals. The distributions were log normal and based on the field data.

Table 3. Overview of available literature data on bioconcentration factors for selected PCB congeners[a]

	Laboratory studies			Laboratory studies, crustaceans			Field studies		
PCB	Organism	log BCF_L, l.w.	Ref.	Organism	log BCF, wet wt	Ref.	Organism	log BCF_L, l.w.	Ref.
77	*Dreissena polymorpha*	6.63	[81]	*Daphnia magna*	4.12	[60]			
	Brachydanio rerio	6.89	[82]		4.04	[60]			
	Poecilia reticulata	5.92	[83]	*Hyalella azteca*	3.54	[84]			
		6.11	[85]		3.58	[84]			
					3.38	[84]			
					3.41	[84]			
105	*Brachydanio rerio*	6.53	[86]						
	Gadus morhua	6.72	[86]						
118				*Daphnia magna*	3.84	[60]	*Mytilus edulis*	7.20	[21]
					4.42	[60]		7.11	[21]
								6.70	[21]
								6.60	[21]
126	*Brachydanio rerio*	7.34	[82]						
153	*Crassostrea virginica*	6.64	[61]	*Selenastrum capricornutum*	4.48	[87]		6.82	[88]
	Dreissena polymorpha	7.71	[81]	*Daphnia magna*	4.11	[60]		7.62	[88]
		6.58	[81]		4.16	[60]	*Platichtus flesus*	7.85	[88]
	Mytilus edulis	7.66	[89]	*Mysis relicta*	5.64	[90]			
	Strophitus rugosus	5.72	[91]	*Potoporeia hoyi*	5.00	[90]			
	Brachydanio rerio	7.18	[82]						
	Cottus bairdi	5.99	[91]						
	Cyprinodon variegatus	6.65	[92]						
	Oncorhynchus mykiss	6.20	[93]						
	Pimephales promelas	7.23	[94]						
		7.23	[94]						
		6.18	[94]						
		7.11	[94]						
	Poecilia reticulata	6.78	[95]						
		7.00	[83]						
		6.15	[96]						
		6.78	[95]						
		6.36	[85]						
169	*Brachydanio rerio*	7.51	[82]						

[a] BCF = bioconcentration factor; BCF_L = lipid-normalized bioconcentration factor; l.w. = lipid weight.

Biota-to-sediment accumulation. Data on biota-to-sediment accumulation ($BSAF_L$) are listed in Table 5. Most laboratory studies used the bivalve *Macoma nasuta.* For PCB 153, $BSAF_L$ data were found for other species as well; these did not differ significantly from the *Macoma* data. For $BSAF_L$ values derived from field studies, data for various species were found. No clear relationship was observed between type of species and $BSAF_L$ values. For biota-to-soil accumulation, few data were found, and these did not seem to deviate much from the sediment data.

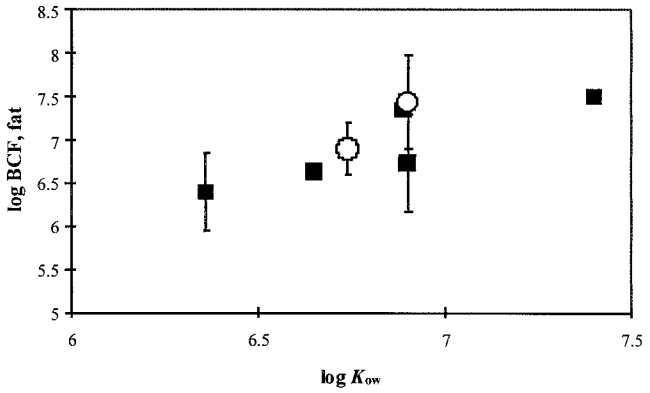

Fig. 1. The bioconcentration factor (BCF_L) (± SD) of selected polychlorinated biphenyls (PCBs) for fish and mollusks related to the log K_{ow}. ■, data from laboratory studies; ○, data from field studies.

The $BSAF_L$ values derived from field studies were higher than those from studies conducted in the laboratory (Fig. 3). There were significant differences between the congeners for the field data. Normal distributions were fitted to the field-derived $BSAF_L$ data for each congener. For congeners 126 and 169, no standard deviation could be determined because of a lack of data. For these congeners, the standard deviation was estimated on the basis of the variation in the data for other congeners, as described by Luttik and Aldenberg [38]. For several congeners (especially 153 and 169), a significant part of the left tail fell below zero in the normal distribution. This resulted in an unrealistically high probability density at and near zero. Therefore, as an alternative, a log-normal distribution was fitted to the data and was included in the calculations (equations 2–5).

Environmental risk limits for individual PCB congeners in organic carbon

Probability distributions of effect concentrations in organic carbon. For each individual congener, probability distributions were calculated for concentrations in the organic carbon associated with adverse effects on survival, growth, or reproduction. Examples are given in Figure 4 for PCB 126 and in Figure 5 for PCB 169. It can be seen that probability distributions for different species sometimes overlapped (PCB 169, Fig. 5), indicating a lack of differences in sensitivity among species. For other congeners (see Fig. 4 for PCB 126), sensitivity differences between the species were more distinct.

Table 4. Overview of available literature data on biomagnification factors for selected polychlorinated biphenyl (PCB) congeners

	Laboratory studies			Field studies		
PCB	Organism	BMF_L,[a] lipid/lipid	Ref.	Organism	BMF_L, lipid/lipid	Ref.
77	*Oncorhynchus kisutch*	4.2	[97]	Fish to otter	2.5	[98]
				Fish diet to otter	1.4	[2]
				Mammal/amphibians to weasel	17	[80]
				Mammal/amphibians to stoat	6	[80]
				Mammal/amphibians to polecat	4	[80]
105				Fish to otter	7.9	[98]
				Fish diet to otter	12	[2]
				Mammal/amphibians to weasel	10	[80]
				Mammal/amphibians to stoat	38	[80]
				Mammal/amphibians to polecat	31	[80]
118	*Oncorhynchus mykiss*	6.00	[82]	Fish to otter	35	[98]
				Fish diet to otter	15	[2]
				Mammal/amphibians to weasel	7	[80]
				Mammal/amphibians to stoat	25	[80]
				Mammal/amphibians to polecat	20	[80]
126	*Gasterosteus aculeatus*	4.94	[99]	Fish to otter	130	[98]
				Fish diet to otter	70	[2]
				Mammal/amphibians to weasel	20	[80]
				Mammal/amphibians to stoat	112	[80]
				Mammal/amphibians to polecat	31	[80]
153	*Gasterosteus aculeatus*	12.0	[99]	Fish to otter	28	[98]
	Oncorhynchus kisutch	9.2	[97]	Fish diet to otter	15	[2]
	Poecilia reticulata	46.5	[100]	Mammal/amphibians to weasel	5	[80]
		22.5	[100]	Mammal/amphibians to stoat	26	[80]
	Oncorhynchus mykiss	16.0	[82]	Mammal/amphibians to polecat	180	[80]
156				Fish to otter	37	[98]
				Fish diet to otter	30	[2]
				Mammal/amphibians to weasel	7	[80]
				Mammal/amphibians to stoat	37	[80]
				Mammal/amphibians to polecat	64	[80]
157				Fish to otter	84	[98]
				Fish diet to otter	19	[2]
				Mammal/amphibians to weasel	3	[80]
				Mammal/amphibians to stoat	22	[80]
				Mammal/amphibians to polecat	58	[80]
169	*Gasterosteus aculeatus*	4.65	[99]	Fish to otter	108	[98]
				Fish diet to otter	348	[2]

[a] BMF_L = lipid-normalized biomagnification factor.

It was found for congener 77 that using either a normal or a uniform distribution for the parameter L_m in the calculations yielded comparable results (data not shown). In addition, it was found for PCB 77, 153, and 169 that using a normal or a log-normal distribution for the parameter $BSAF_L$ did not lead to different results (data not shown). Apparently, the calculated probability densities are not sensitive to parameters that are uncertain. In further calculations for all congeners, normal distributions for $BSAF_L$ and lipid content were used. For all congeners for which toxicity data on aquatic organisms were available (77, 105, 126), mammals and especially birds appeared more sensitive than aquatic species (see Fig. 4 for PCB 126).

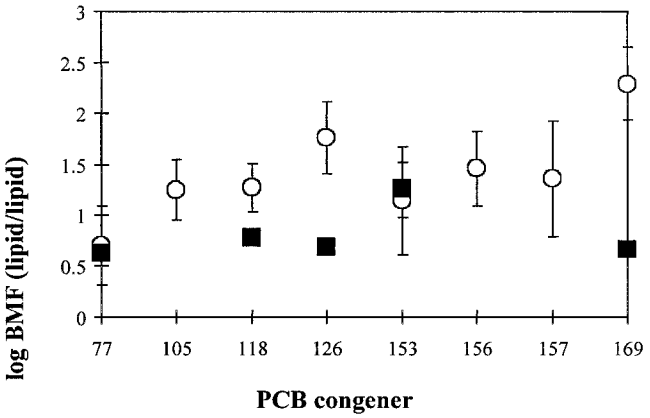

Fig. 2. Biomagnification factors (BMFs) (± SD) of selected polychlorinated biphenyls (PCBs). ■, data from laboratory studies on fish species; ○, data from field studies on mammals and birds.

Contribution of individual parameters to the overall variance. An analysis was conducted to determine the relative contribution to the variance by the various underlying parameters, as used in equations 2 through 5. For the conversion of aquatic toxicity data into equivalent effect concentrations in OC (equation 2), the BCF_L was most important. For the fish egg injection studies (equation 3), the $BSAF_L$ contributed most to the variance. For the transformation of mammal toxicity studies into effect concentrations in OC (equation 4), all the parameters used (L_m, BMF_L, and $BSAF_L$) contributed to the variance. The importance of the various parameters varied by congener. For equation 5 used for the bird toxicity studies, BMF_L and $BSAF_L$ were most important for the resulting variance.

Derivation of ERLs. As a result of the Kolgomorov–Smirnov test (see Methods), the ERLs for all individual congeners

Table 5. Overview of available literature data on biota-to-sediment/soil accumulation factors for selected PCB congeners

	Laboratory studies			Field studies		
PCB	Organism	$BSAF_L$,[a] lipid/organic carbon	Ref.	Organism	$BSAF_L$, lipid/organic carbon	Ref.
In sediment						
77				*Dreissena polymorpha*	3.32	[80]
				Pseudanodonta complanata	3.21	[80]
				Pooled fish	1.10	[101]
105	*Macoma nasuta*	1.63	[101]	*Dreissena polymorpha*	5.09	[80]
		2.87	[101]	*Pseudanodonta complanata*	4.56	[80]
		3.85	[101]	Pooled fish	5.50	[101]
		0.22	[102]			
		0.39	[102]			
118	*Macoma nasuta*	2.02	[101]	*Anodonta cygnea*	3.80	[103]
		3.28	[101]	*Pseudanodonta complanata*	0.51	[103]
		4.74	[101]	*Dreissena polymorpha*	7.02	[80]
		0.73	[102]	*Pseudanodonta complanata*	3.55	[80]
		0.54	[102]	*Mercenaria mercenaria*	1.32	[104]
				Yoldia limatula	4.26	[104]
					5.73	[104]
				Anguila anguila	4.57	[103]
					4.88	[103]
					5.88	[103]
				Abramis brama	5.47	[103]
					4.00	[103]
				Esox lucius	5.06	[103]
					4.75	[103]
				Rutilus rutilus	4.71	[103]
					6.63	[103]
					1.75	[103]
					7.00	[103]
				Pooled fish	7.10	[101]
126				*Dreissena polymorpha*	4.17	[80]
				Pooled fish	5.70	[101]
153	*Macoma nasuta*	1.57	[101]	*Anodonta cygnea*	6.75	[103]
		2.66	[101]	*Pseudanodonta complanata*	0.78	[103]
		4.05	[101]	*Dreissena polymorpha*	4.95	[105]
		0.71	[102]		0.003	[80]
		0.40	[102]	*Pseudanodonta complanata*	6.36	[80]
		1.75	[89]	*Mercenaria mercenaria*	1.49	[104]
	Ictalurus nebulosus	0.23	[106]	*Yoldia limatula*	5.10	[104]
		0.93	[106]		8.25	[104]
		0.76	[106]	*Anguila anguila*	14.34	[105]
		5.94	[106]		5.97	[103]
					5.87	[103]
					7.69	[103]
				Abramis brama	9.23	[103]
					5.38	[103]
				Esox lucius	4.20	[103]
					3.92	[103]
				Rutilus rutilus	6.43	[103]
					10.08	[103]
					2.69	[103]
					11.33	[103]
				Pooled fish	10.00	[101]
156	*Macoma nasuta*	0.61	[102]	*Dreissena polymorpha*	5.00	[80]
		0.16	[102]	*Pseudanodonta complanata*	3.22	[80]
				Pooled fish	6.10	[101]
157				*Dreissena polymorpha*	20.00	[80]
				Pseudanodonta complanata	10.35	[80]
				Pooled fish	3.00	[101]
169				Pooled fish	2.50	[101]
In soil						
118	*Eisenia andrei*	4.3	[17]			
153	*Eisenia andrei*	4.1	[17]			
156	*Eisenia andrei*	3.9	[17]			

[a] $BSAF_L$ = lipid-normalized biota-to-sediment/soil accumulation factor.

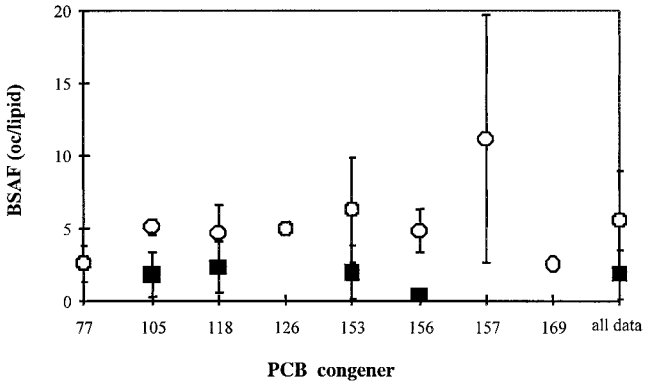

Fig. 3. Biota-to-sediment accumulation factors BSAFs (± SD) of selected polychlorinated biphenyls (PCBs). ■, data from laboratory studies; ○, data from field studies.

were based on a distribution of all mammal and bird data combined. One exception was congener 77, where a combined distribution based on all toxicity data showed a good fit. Another exception was congener 105, for which neither of the combined distributions showed a good fit. The ERL for congener 105 was calculated from the most sensitive probability distribution based on a single toxicity value. The ERLs and the statistics of the underlying distributions are presented in Table 6.

Environmental risk limit for the mixture of planar PCBs

Congener pattern of planar PCBs in The Netherlands. The congener pattern provides the contribution of a specific congener to the total concentration of planar PCBs. Both the congener pattern and the toxicological potency of each congener determine the toxicity of the mixture of AhR-binding PCBs.

The PCB patterns normalized to PCB 153 in sediments from different areas in The Netherlands are given in Figure 6. The most toxic congeners, 126 and 169, occur at the lowest concentrations (10^3–10^4 times less than PCB 153). There is less than a sevenfold difference in 153-normalized concentrations between different locations (except for congener 180, for which 153-normalized concentrations differ up to 23-fold).

Non- or mono-*ortho* PCBs occur in low concentrations and are rarely measured. Only four datasets on planar PCB in sediment were available for The Netherlands. More information, and from different locations, was available on concentrations in organisms low in the food chain. Congener patterns in arthropods and mollusks should reflect those in the sediment because of their low metabolic capacity [39]. When congener patterns in sediments, arthropods, and mollusks from various Dutch locations were compared (Fig. 7), patterns were highly similar and consistent.

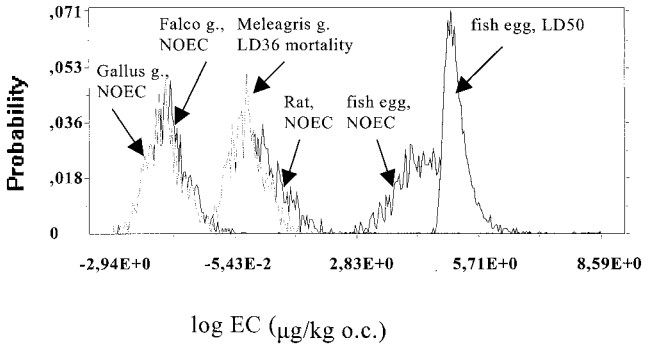

Fig. 4. Probability distributions of organic carbon concentrations (OC) in sediment or soil associated with critical levels of polychlorinated biphenyl (PCB) 126 in different species. On the *x*-axis, the logarithm of the equivalent adverse effect concentration (in μg/kg organic carbon) is given; on the *y*-axis, the probability is given that this concentration has a certain value.

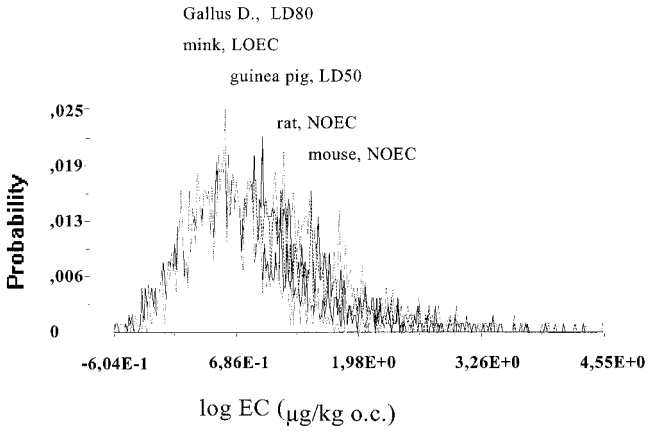

Fig. 5. Probability distributions of organic carbon concentrations (OC) in sediment or soil associated with critical levels of polychlorinated biphenyl (PCB) 169 in different species. On the *x*-axis, the logarithm of the equivalent adverse effect concentration (in μg/kg OC) is given; on the *y*-axis, the probability is given that this concentration has a certain value.

Deriving the mixture ERL. The mixture ERL addresses the toxicity of the mixture of congeners 77, 105, 118, 126, 156, 167, and 169. To derive this mixture ERL, the data depicted in Figure 6 were averaged and expressed as percentage of the summed concentration of AhR-binding PCBs (second column in Table 7). To scale the toxicological importance of each congener, the mean of the distribution that was the basis for the ERL (see Table 6) was back-transformed (third column in Table 7). The fractions was divided by the scaling factor of that specific congener (fourth column in Table 7). The ERL for the single congener 118 (25 μg/kg OC, Table 6) was then multiplied by the fraction of the total toxicity explained by 118 (0.21), yielding the mixture ERL. The mixture ERL for 118 of 5 μg/kg OC aims to protect the ecosystem for the total mixture of planar PCB congeners.

It should be noted that, at a specific location, the congener pattern of planar PCBs may deviate from the congener pattern used here. A mixture ERL for that specific situation can then be calculated in a similar way as described here.

Table 6. The environmental risk limits (ERL) (fifth percentile, in μg/kg organic carbon [OC]) for each polychlorinated biphenyl (PBC) congener and the mean ± SD of the underlying distribution

PCB	ERL (μg/kg OC)	Mean ± SD of log-transformed data	Based upon
77	7.2	4.04 ± 1.93	All toxicity data
105	26	1.87 ± 0.28	Most sensitive toxicity value
118	25	2.57 ± 0.72	All mammal and bird data
126	0.042	0.07 ± 0.88	All mammal and bird data
153	151	3.86 ± 1.03	All mammal and bird data
156	55	2.87 ± 0.69	All mammal and bird data
157	32	3.00 ± 0.92	All mammal and bird data
169	0.83	0.98 ± 0.65	All mammal and bird data

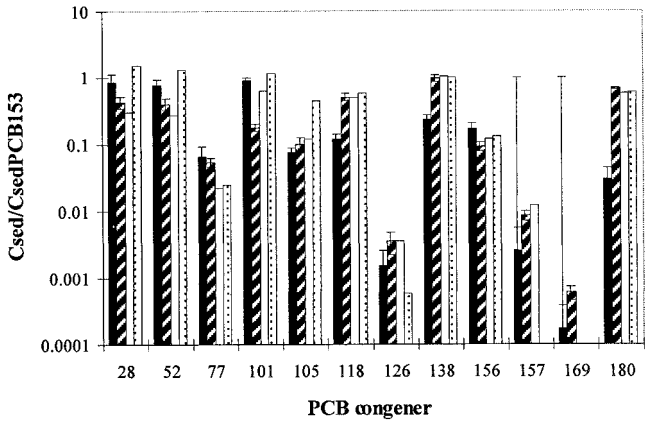

Fig. 6. Polychlorinated biphenyl (PCB) patterns in various Dutch fresh-water sediments, normalized to PCB 153. Data are from Hollandsch Diep and Bieschbosch (first two bars, B. van Hattum, unpublished data), Zandmeer (third bar, P. Leonards, unpublished data), and Ketelmeer (fourth bar, [53,54]).

DISCUSSION

Methods for including the risk for secondary poisoning

In the present study, toxicity data were transformed into equivalent toxic concentrations in the organic carbon of sediment or soil using bioconcentration factors, biota-to-sediment concentration factors, and biomagnification factors. This allowed data from different types of studies to be readily compared and integrated into one ERL. Parameters such as BCF_L and K_{oc} that are difficult to determine for hydrophobic compounds were avoided where possible. We used data from field studies to obtain biota-to-sediment accumulation and biomagnification factors because a steady state is hard to establish in the laboratory for very hydrophobic substances such as PCBs. In addition, it is difficult to simulate all potential pathways of contaminant uptake in a laboratory. The use of BCF_L/$BSAF_L$ instead of the organic carbon normalized sediment/water or soil/water partition coefficient (K_{oc}) also has the advantage that possible biotransformation of the compound is taken into account.

It should be mentioned that the food chains taken into account for this report are relatively simple ones. However, these

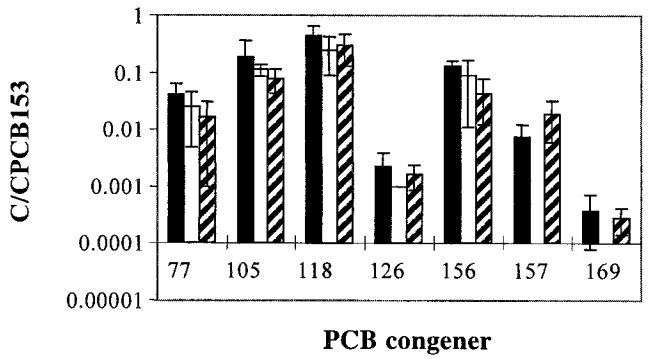

Fig. 7. Polychlorinated biphenyl (PCB) patterns in Dutch sediments, arthropods/plankton, and mollusks, normalized to PCB 153. ■, sediment; □, Arthropoda; hatched bar, Mollusca. Data for sediment are from Figure 6; data for arthropods are from [2] and Reinhold et al. (unpublished data) and are measured in lake 'Zandmeer' and the Biesbosch. Data for the mollusks are from [55] and [2] and are measured in the rivers Rhine and Meuse and in the lakes Ijsselmeer and Zandmeer.

Table 7. Information used to derive the mixture environmental risk limits (ERLs) expressed as concentration of polychlorinated biphenyl 118

PCB	(A) Fraction in pattern (% of sum)	(B) Scaling factors	(A/B) (% of sum)	Mixture ERL (μg/kg organic carbon)
77	4.73	11,000	0.06	
105	21.4	74	41	
118	56.2	370	21	5
126	0.28	1.2	34	
156	15.0	740	2.8	
157	2.29	1,000	0.32	
169	0.057	9.5	0.85	

are sufficient for estimating accumulation in the dominant aquatic food chain in The Netherlands, i.e., organic matter, herbi-detritivores (invertebrates), primary carnivores (fish), and secondary carnivores (birds, mammals) [40]. Elsewhere, additional trophic levels may be distinguished [41].

The probabilistic approach as sketched requires a sufficiently large dataset on toxicity and on the environmental behavior of the compounds studied.

Probabilistic modeling

The variability in the environmental fate parameters was taken into account. Distributions were fitted based on literature information, and these distributions (rather than absolute values) were incorporated in the calculations. Considerable spread in literature data on these parameters was encountered because of intra- and interspecies differences, sediment differences, differences in test methods, etc.

Inclusion of different dosing methods in the derivation of ERL

For toxicity studies on mammals and birds, diet studies are considered most reliable. Other and more common dosing methods include gavage or injection. The validity of using these data is evaluated by comparing the results among different types of studies.

It is unclear for the bird toxicity studies if different dosing methods influence the results, as all studies available for the extrapolation into ERLs were based on egg injection studies. Injection took place into the yolk sac or in the air chamber of the eggs. Contaminants first have to pass membranes, and the subsequent transport of the PCBs will probably mainly occur via the blood circulation of the developing embryo. We assumed in our calculations that the injected PCBs partition over the egg (mainly the lipids) and that equilibrium was reached relatively soon after the exposure. These egg injection studies generally done on 4- to 7-d-old eggs through hatching. In a study by Näf et al. [42], it was shown for PAHs, which are hydrophobic compounds with a K_{ow} range comparable to PCBs, injected into the yolk on day 4 that 94% of the PAHs were metabolized by day 18. This indicates that the PAHs were available for uptake within this period as metabolization took place in the developing embryo.

For mammals, for those congeners where multiple studies were available (153, 156, 169), the sensitivities differed among dosing types by a maximum of 1.5 log units (means of probability distributions were compared). Therefore, the dosing method for mammals does not seem to greatly influence the results.

Concerning fish, results from different dosing methods (i.e., exposure via injection and exposure via water) for the same congener were available for PCBs 77 and 126. The results obtained by fish egg injection were more sensitive in the case of congener 77, while the opposite held for congener 126. Therefore, no conclusion can be drawn on the influence of the dosing method.

For assimilation efficiency in dietary studies with warm-blooded animals, a value of roughly 60 to 100% is often mentioned in the literature [43,44]. Less information is available for studies where dosing takes place via gavage or injection. However, assuming a 100% availability of the administered dose will probably not be a gross overestimation.

Inclusion of multiple endpoints and effect levels in the derivation of ERL

Effects on growth, reproduction, and survival were integrated in the derivation of ERLs. The most sensitive toxicity test was selected for each species and for each compound. We included NOEC values as well as other levels of effect such as EC50s. The influence of this was evaluated by studying the steepness of the dose–response curves and the differences in sensitivity among endpoints. We examined the steepness of the dose–response curve for several studies [45–48]. The steepness of the curve has to be examined within a study and not between studies, as in the latter case interlaboratory differences in sensitivities of the test animals and in the experimental design obscure the results.

For PCBs 77, 105, and 126, Powell et al. [45] showed that the ratio between the LD50 for survival and the lowest adverse effect level for growth in chickens ranged from 0.7 to 18. In a study in *Meleagris gallopavo* for congener 126, the concentration exerting 100% mortality was three times the concentration causing 36% mortality [46]. The concentrations needed to exert 17% and 100% lethality in chicken embryos exposed in ovo to PCB 77 differed by a factor of five [47]. Marks et al. [48] showed that an eightfold increase in dose resulted in an increase in response from 10 to 60% for reproduction in mice exposed to congener 169.

These results show that dose–response curves for individual congeners are steep [46–48] and that the differences in concentration needed to obtain different types of effects (survival, growth) are not overly large [45]. The differences in sensitivity between species are large (see Fig. 4) relative to the aforementioned differences within a species among endpoints or effect levels. Therefore, it is believed that the inclusion of diverse endpoints and diverse levels of effects in the extrapolation of ERLs is acceptable.

Vulnerability of different organism groups

The vulnerabilities of different groups of organisms to PCB contamination of sediments or soils can be compared directly since the equivalent effect concentrations are expressed in a comparable unit (i.e., μg/kg OC). Although different endpoints, different levels of effect, and studies with different dosing methods were combined in the derivation of the ERLs, patterns in vulnerability of different species groups could still be discerned. For those congeners where information on aquatic species was available (77, 105, 126), the aquatic organisms invariably were the least vulnerable. Avian NOECs for growth or reproduction, expressed as equivalent (no) effect concentrations in the organic carbon of soil or sediment, turned out to be the most vulnerable parameters (see 77, 105, 126). For congeners 118, 153, 156, 157, and 169, no information was available on avian NOECs for growth or reproduction, which may result in an underestimation of the ERL. New studies on these endpoints in birds may lead to adjustment of the ERL.

The number of toxicity test data used to derive ERLs for the individual congeners varied between two and seven (Table 1). If only two toxicity data were available, those data involved the relatively vulnerable mammals and/or birds.

Comparison with effects found in the field

Effects found in field-exposed fish-eating birds, otters, and minks. The ERLs as given in Table 6 can be compared with levels of PCBs associated with adverse effects in field studies. Several studies have been performed in which effects in wildlife top predators were related to the internal concentration of PCBs. This can only be done in a correlative way. Deriving a causal relationship between concentrations of (a group of) chemicals and an effect is not possible since the total composition of the mixture of chemicals in the field is unknown and other substances in the mixture may have attributed to the effects observed. We focused on field studies from The Netherlands since PCB congener patterns and the corresponding effects may be region specific.

Fish-eating birds are top predators, known to accumulate high concentrations of PCBs and related chemicals [30]. In a study by Bosveld et al. [3], eggs from the common tern were taken from seven colonies in The Netherlands. Concentrations of PCBs (including the planar PCBs), polychlorinated dibenzodioxins, and polychlorinated dibenzofurans were analyzed in the yolk, and the eggs were artificially incubated. If the concentration of PCBs was higher than or equal to 3.5 ng toxic equivalents (TEQ)/g lipid (chicken toxic equivalency factors [TEFs] were used, [3]), a significantly longer incubation period was observed. A longer incubation period in the laboratory translates into an even longer incubation period in the field [49]. The study by Bosveld et al. [3], showing a sensitive effect that is presumably relevant to population growth, was used to validate the ERLs.

In addition, an EC50 for PCBs exerting effects on reproduction in mink was derived based on a series of literature data [6]. Results were expressed as TEQ using Safe TEFs [5] and were based on whole-body concentrations calculated with a one-compartment bioaccumulation model. The lipid-normalized EC50s are 5 to 10 ng TEQ/g lipid for litter size and kit survival. It was shown that above a level of 4 ng Safe TEQ/g lipid, disease incidences were increased in Danish otters [50].

At 3.5 ng chicken TEQ/g lipid, a significantly longer incubation period before hatching was observed [3]. The ERLs for the individual congeners (Table 6) were transformed into concentrations in the lipid of the egg using the following formula:

$$C_{egg} = ERL_{oc} \cdot EBR \cdot BMF_L \cdot BSAF_L \quad (6)$$

The resulting concentrations in the eggs are expressed in TEQs using chicken TEFs and are summed. Concentrations for PCB congeners 77, 105, 118, 126, 156, 157, and 169 in the sediment at ERL level result in a chicken TEQ of 1.9 ng/g lipid in the egg. This is approximately half the lowest effect concentration observed by Bosveld et al. [3].

In analogy, the resulting Safe TEQ in the lipid of mink or otter resulting from concentrations for all planar congeners at the ERL level can be calculated via

$$C_{mammal,\ lipid} = ERL_{oc} \cdot BMF_L \cdot BSAF_L \quad (7)$$

Table 8. Statistics of the combined distribution over the probability distributions (log-transformed data) for biochemical and histopathological effects in mammals and birds

PCB	Mean ± SD of combined distribution
77	0.76 ± 0.64
105	1.85 ± 2.02
118	−0.01 ± 1.44
126	−2.89 ± 0.82
153	2.34 ± 0.88
156	0.42 ± 1.19
157	−0.76 ± 0.65
169	−1.25 ± 1.17

Concentrations for PCB congeners 77, 105, 118, 126, 156, 157, and 169 in the sediment at ERL level result in a Safe TEQ of 34 ng/g lipid. This is approximately seven times the critical level deduced from mixture and field studies [6,50].

It is concluded that the concentrations expressed in TEQ that are associated with adverse effects in field studies are comparable with the TEQ concentrations that would result if all planar congeners were present at the ERL level.

Potency rating of the different congeners: Comparison of toxicological effects with biochemical and histopathological effects

The relative potencies of the different congeners based on toxicological effects were compared with the relative potencies based on biochemical and histopathological effect data. For biochemical or histopathological effects from exposure to PCBs, more literature data are available than for effects on growth, reproduction, and survival. As toxicological and biochemical/histopathological effects are exerted via the same mechanism of action, the relative potencies are expected to be comparable for both types of effects.

The types of biochemical and histopathological effects studied are, e.g., splenic immunosupression in the mouse, ethoxyresorufin *O*-deethylase activity in the rat or mouse, free thyroxin levels in the monkey or in rat pups, liver cell abnormalities in the rat, etc. (see [24] for detailed information). Probability distributions of concentrations in the organic carbon associated with biochemical or histopathological effects were derived following methods identical to those used for toxicological effects. Again, combined distributions were fitted over all data for each congener. Statistics of these combined distributions are given in Table 8. Means of the distribution for biochemical/histopathological effects are 1.5 to 3 log units less than means of the distributions for the toxicological effects that formed the basis of the ERLs (Table 6). So, in general, biochemical or histopathological effects of PCB congeners will occur at concentrations that are 100 to 1,000 times lower than concentrations at which toxicological effects occur. Exceptions were found for congener 157, where the difference was 3.7 log units, and for congener 105, where there was no difference. The latter may be due to the fact that the distribution for toxicological effects for congener 105 was based on the most sensitive toxicity value (see Table 6).

A comparison of the relative potencies normalized to PCB 126 is shown in Table 9. The data were normalized to congener 126 since this is the most potent congener. Again, means of the distributions (Tables 6 and 8) were used. The difference between relative effect levels for toxicological and biochemical/histopathological effects were within an order of magnitude except for congener 105, where a difference of a factor 1,000 can be observed. This may again be explained by the fact that the ERL for this congener was based on the most sensitive individual probability distribution. The fact that relative potencies were comparable for toxicological effects on the one hand and biochemical or histopathological effects on the other leads to the conclusion that, although there was a paucity of toxicity data for some congeners, the dataset used is a good predictor of the toxicity.

Table 9. The effect concentrations (mean of probability distribution) in organic carbon, relative to that of polychlorinated biphenyl 126, for distributions based on toxicity data or on biochemical/histopathological effect data for birds and mammals

PCB	Normalized means of distribution for toxicological effect	Normalized means of distribution for biochemical/histopathological effect
77	0.0001	0.0002
105	0.02	0.00002
118	0.003	0.001
126	1	1
156	0.0002	0.0005
157	0.001	0.007
169	0.1	0.02

Derivation of mixture ERL

Information on the toxicity and environmental chemistry of the individual congeners was used to derive ERLs, and as a second step, a mixture ERL was derived based on this information. Toxic equivalency factors were not used in order to prevent building in circular arguments in the derivation of a (mixture) ERL due to the fact that TEFs are also based on toxicity information [5,51]. Congeners other than those listed in Table 7 were not taken into account. Multiple-*ortho*-substituted congeners show CYP1A1 induction, which points to AhR binding, although with EC50s that are 1,000 to 10,000 times less potent than PCB 126 [52]. Given their high environmental residues, these multiple-*ortho*-substituted congeners will probably contribute to AhR-mediated toxicity. Their toxicity will probably be exerted mainly via other mechanisms. Unfortunately, the lack of toxicity information prevented the inclusion of these congeners in a mixture ERL. Other types of halogenated aromatics that will have an additive effect with the AhR-binding PCBs were also not incorporated in the mixture ERL.

CONCLUSION

In the present study, toxicity data for aquatic organisms, mammals, and birds were transformed into equivalent toxic concentrations in the organic carbon of sediment or soil using bioconcentration factors, biota-to-sediment concentration factors, and biomagnification factors. This allowed data from different studies to be readily compared and integrated into one ERL. The ERLs were derived for the individual congeners 77, 105, 118, 126, 153, 156, 157, and 169 (Table 6). Parameters such as BCF_L and K_{oc} that are difficult to determine for these hydrophobic compounds were avoided where possible. The use of $BCF_L/BSAF_L$ instead of the organic carbon normalized sediment/water or soil/water partition coefficient (K_{oc}) also has the advantage that possible biotransformation of the compound is taken into account. We used data from field studies for incorporation of biota-to-sediment accumulation and biomagnification processes.

A mixture ERL addressing the toxicity of the mixture of congeners 77, 105, 118, 126, 156, 167, and 169 was derived. The mixture ERL for congener 118 of 5 μg/kg OC aims to protect the ecosystem for the total mixture of planar PCB congeners.

The probabilistic approach as sketched requires a sufficiently large dataset on toxicity and on the environmental behavior of the compounds studied.

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