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Selection of substances, deserving policy attention

A.P. van Wezel, D. Kalf

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RIVM, P.O. Box 1, 3720 BA Bilthoven, telephone: 31 - 30 - 274 91 11; telefax: 31 - 30 - 274 29

Abstract

In the current report an inventory is made of chemicals that may require extra policy attention. The focus is on chemicals that are of relevance for the Netherlands, and that have not been the subject or are not planned to be the subject of (inter)national risk assessment programmes. Chemicals that are encountered and identified during analytical-chemical surveys are listed. As a second category groups of potentially hazardous chemicals that are frequently mentioned in recent literature are discussed. Finally, information from the Dutch registration on emission of substances is used to identify substances of possible concern.

Preface

Mrs. Ellen Siebel and Dick Jung, both attached to the ministry of housing, spatial planning and the environment (VROM-DGM/SVS) are acknowledged as being contact persons and for their interest in the subject. Jack de Bruijn (RIVM/CSR) is thanked as being coördinator of the project 'Coördination and policy advice towards risk assessment and -management of existing substances', and John Janus for being the project leader of RIVM project 601503, 'General Assistance for the National Policy towards Substances'.
Furthermore, we want to thank Hans Klamer, Remi Laane, Willem van Loon, Jannie Peijnenburg (all RIKZ), Pim Leonards (RIVO), Gert-Jan de Maagd, Jan Hendriks, Hein Barreveld (RIZA), and Eric Verbruggen (RIVM) for their comments on an earlier version of this report and for providing additional information.

Contents

Summary

The numbers of chemicals that occur in our environment are estimated to be higher than 100.000. Approximately 600 of these chemicals are under (inter)national attention (for an overview see [Van Wezel, 1999]). Thus, for the majority of chemicals no measures are taken. The aim of policy on substances is to reduce risks for humans and the environment, so should be focused on those compounds that give a high risk on adverse effects. The purpose of this report is to give some fresh input on (groups of) chemicals that might need policy concern for their possible ecotoxicological risks. As this report is prepared on behalf of the Dutch ministry for Housing, Spatial Planning and the Environment, it is focused on compounds that may be of concern for the Netherlands. Three types of information are gathered for this purpose, see Figure I.

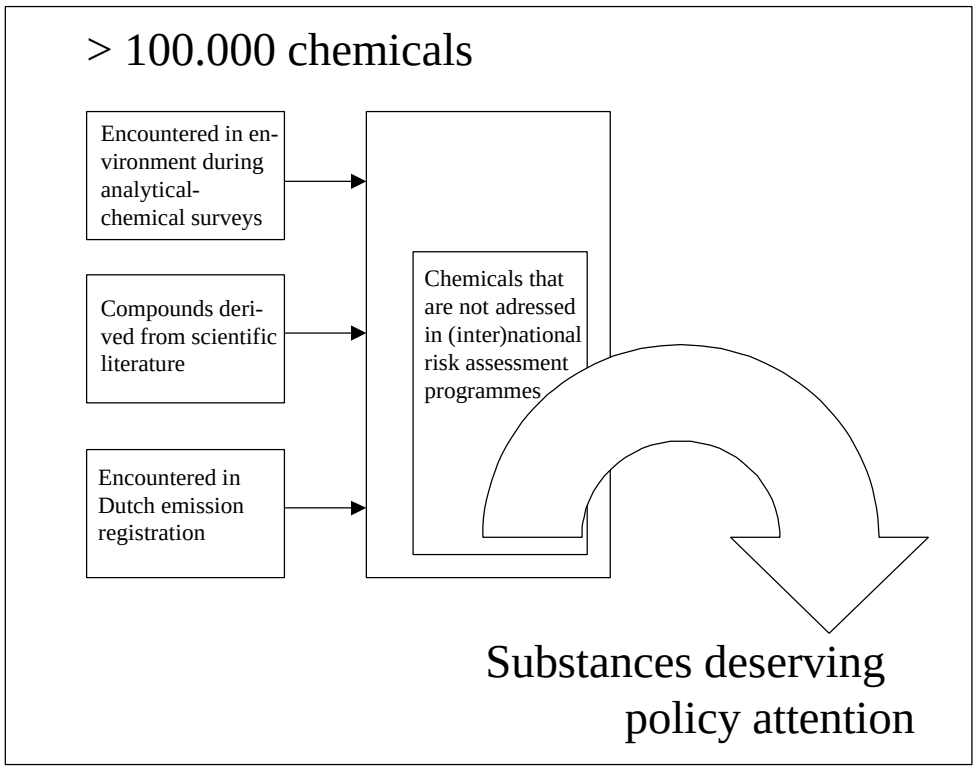

Figure I. Schematic overview on the current report

Several authors present surveys of Dutch surface waters. Water extracts, biota or sediments are analyzed with help of different analytical techniques to identify as many compounds as technically possible. An overview of the non-priority compounds that are detected in significant amounts in various Dutch environmental matrices is given in Table I.

The compounds that are in the focus in recent scientific literature are summarized. Major compound classes are pharmaceutical substances, disinfectants, (anti-) estrogenic compounds, biotransformation products of pesticides, fluorescent whitening agents, flame retardants and aromatic substances. These compounds are compared with the list of chemicals

Table I. Compounds measured in significant amounts in environmental matrices, that are not subject of (inter)national risk assessments (see for more detailed information Table 2.1.)

Environmental matrix	**Non-priority compounds encountered**	**Reference**
Biota (mussel, eel)	octachlorostyrene	Hendriks et al., 1998
Effluents from sewage treatment plants	2,6-diisobutylphenol	Van Loon et al., 1997
	HHCB (1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-gamma-2-benzopyran)	
	limonene	
	AHTN (6-acetyl-1,1,2,4,4,7-hexamethyltetraline)	
Surface waters	HHCB	Verbruggen et al., 1999
	AHTN	
Effluents from sewage treatment plants	galaxolide	Leonards et al. (unpublished results)
	tonalide	
	traseolide	
	celestolide	
	phantolide	
	vertofix	
	triclosan	
	triclosanmethyl	
	chlopyrifos	
	butylated hydroxytoluene	

for which a risk assessment is finished or planned in any (inter)national framework. It is concluded that the majority of the mentioned compounds do not occur in the lists of (inter)national organizations, except for simazine, musk ketone, musk xylene and limonene.

In the Netherlands information on compounds that are emitted is collected in the emission register. Until 1995, 700 companies were questioned each year. About 1700 substances or groups of compounds are registered. The compounds in the emission register were subdivided in several categories:

1. Groups of compounds considered as non-relevant for the purpose of the current report. Examples are wastes of certain uses, general environmental parameters such as pH or heat, complex mixtures such as cement or milk powder, or compounds for which the expected problems do not occur via toxicological mechanisms (592 -groups of- compounds).
2. Compounds that are relevant in terms of ecotoxicological risks; the risks are generally known (262 chemicals, 15%).
3. Compounds that are not expected to bring about high ecotoxicological risks to ecosystems, for reasons of high biodegradability or low bioavailability (137 compounds).
4. Compounds that are expected to bring about ecotoxicological risks for ecosystems, which do not seem to be well-realized based on the information found in open literature (87 substances).
5. Compounds on which the authors do not have an opinion (621 compounds).

The nature of the 1700 (groups of) compounds of the emission register is rather diverse, and therefore also the frameworks in which legislation and policy for these compounds takes place. Categories 4 and 5 probably contain compounds that deserve policy attention.
Only for few compounds in the Dutch emission register risk assessments are performed within national or international programs, see figure II.
Many brominated and fluorinated compounds are listed. Chlorinated compounds have received much attention in the past. However, fluorinated or brominated substances are comparable in their behavior and toxicological endpoints to chlorinated compounds.

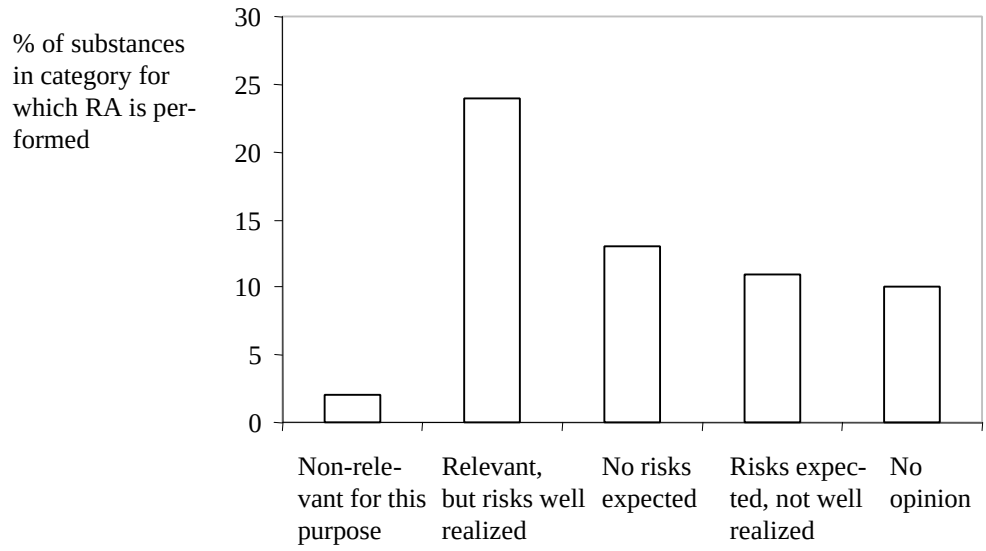

Figure II. Percentage of substances per categories for which a risk assessment is (being) performed in any (inter)national program

Next to chemicals that are emitted directly from industrial sources, chemicals that are emitted diffusely for instance after their use by consumers are gaining more attention. This can also be noticed from the type of chemicals that are mentioned in this report. These chemicals often enter the environment via sewage treatment plants.

Other ways of identifying compounds that deserve more policy attention is by applying priority setting schemes. Blok et al. (1999) identified 301 substances that score high on criteria related to persistence, toxicology and bioaccumulation (PTB) from a set 28.600 substances. It should be noted that information on use and emission is not included in the PTB-criterion. Little of the chemicals mentioned in this report as deserving more policy attention appeared to be classified by Blok et al. as a PTB-substance. It is concluded that the approach followed in the current report is a valuable addition to the approach as followed by Blok et al. [1999].

1. Introduction

Chemicals are produced, imported, formed unintentionally as a by-product or during transformation processes, or appear in our regional environment originating from remote sources as a result of environmental fate processes. The numbers of chemicals that occur in our environment are estimated to be higher than 100.000. A little less than 2000 chemicals are produced or imported in the European Union in more than 1000 tons per year, the so-called high production volume chemicals (HPVCs). Approximately 600 of these chemicals are under (inter)national attention (for an overview see [Van Wezel, 1999]); the ecotoxicological risks of these chemicals are assessed more or less extensively, sometimes the compounds are monitored, risk reduction measures are taken, environmental quality criteria are set or other policy is made. Thus, for the majority of chemicals no measures are taken.
The aim of policy on chemicals is to reduce risks for humans and the environment. It is shown [Hendriks et al., 1994] that concentrations of known and identified compounds only explain a minor part of the ecotoxicity that is observed in environmental samples. Policy should be focused on those compounds that give a high risk on adverse effects. The purpose of this report is to give some fresh input on (groups of) chemicals that might need policy concern for their possible ecotoxicological risks. As this report is prepared on behalf of the Dutch ministry for Housing, Spatial Planning and the Environment, it is focused on compounds that may be of concern for the Netherlands.

1.1 Identifying (groups of) compounds with probable risks

The approach that is followed to identify (groups of) compounds that might be of ecotoxicological relevance in concentrations as may occur in the environment, can be multifarious.

1.1.1 Priority setting schemes

Several systems have been developed to set priorities [e.g. Hansen et al., 1999; Eisenberg and McKone, 1998; Halfon et al, 1996; Blok et al., 1999]. These classification systems vary in complexity; some only consider toxicity, others include only exposure factors such as persistence, fate and exposure pathways, and several systems include both exposure and toxicity related parameters. In general, methods are believed to be better predictors of risks when both toxicity and exposure indicators are included.
The systems that are most in line with elaborate risk assessment schemes [Hansen et al., 1999; US-EPA, 1996], are often rather complex and based on models with a large number of required inputs. If thousands of chemicals are to be evaluated, time to search for and judge data for the underlying parameters is limited. For reasons of missing data, calculations (and thus priority setting) are sometimes based upon default values. This hampers the credibility of the produced lists of chemicals with highest concern.
Alternatively, simple quantitative approaches exist which are based on a (weighed) multiplication of a limited number of factors; these are often intrinsic properties of the

chemical. This approach is not necessarily based upon a mechanistic understanding and factors may be neglected or weighed improperly.
As can be expected based upon the aforementioned, method selection is critical for the ranking obtained; Hertwich et al. [1998] showed that when the same compounds are analyzed with help of four recently developed models the relative toxicity scores vary by three orders of magnitude. This is partly explained as all methods rely in part on subjective, value-laden choices; e.g. the treatment of data gaps, setting of default values, choices among models etc. [Hertwich et al., 1998]. Also the choice to use one method and not another is, next to scientific considerations, value-driven.
In the assessment of the chemical fate, and therefore also in the classification of chemicals if fate is considered, prescribed models are used which are originally developed for a certain type of chemicals (mostly nonpolar organics). However, as stated by Mackay et al. [1996], different type of physico-chemical data may be required to understand or predict the fate of different type of chemicals. Basically, chemicals partition between different phases i.e. air, water, solid organic matter, biological media and the pure phase of the substance. It depends on the chemical properties if the chemical in question really will be present in all these phases. Mackay et al. [1996] put forward five classes of chemicals (see Table 1.1), for which different types of environmental fate models should be used. Only environmental fate models for the first class of chemicals (that partition to all phases) are well developed and validated. For the other type of compounds, a sound understanding on the important fate processes and on the (values of) parameters that describe these processes is lacking.
As priority setting with help of model-based ranking methods already attains much attention, and because of the above-mentioned drawbacks of these methods, model-based ranking methods are not used in the present report.

Table 1.1. Different classes of chemical (other fate models should be used), adapted from Mackay et al. [1996]

Type	**PHASES TO WHICH THE CHEMICAL PARTITIONS**	**Proposed criterion/remarks**	**Example**
1	All phases		Chlorobenzene
2	All phases but air	Vapor pressure < 10^{-7} Pa or $K_{air/water}$, 10^{-5}	Lead Linear alkylbenzene sulfonate
3	All phases but water	S < 10^{-6} g/m^3 or $K_{ow} > 10^8$	Eicosane
4	All phases but air and water	Vapor pressure < 10^{-7} Pa and S < 10^{-6} g/m^3	Polyethylene
5	Speciating chemicals	Each species has own set of partition coefficients	Mercury Pentachlorophenol

1.2 Methods used in this report to select (groups of) compounds with probable risks

This report is based on information from various sources. In chapter 2, information from measurements and survey programmes in surface water and effluents is summarized. In chapter 3, information on specific compound classes is given, as derived from recent literature in international journals on environmental toxicology and chemistry. This chapter is partly based upon information from several scientists in the field which were asked to mention compounds which are currently not under the regulatory attention, which possibly pose risks. Finally, in chapter 4 information from the Dutch registration on emission of substances was used to identify compounds of possible concern.

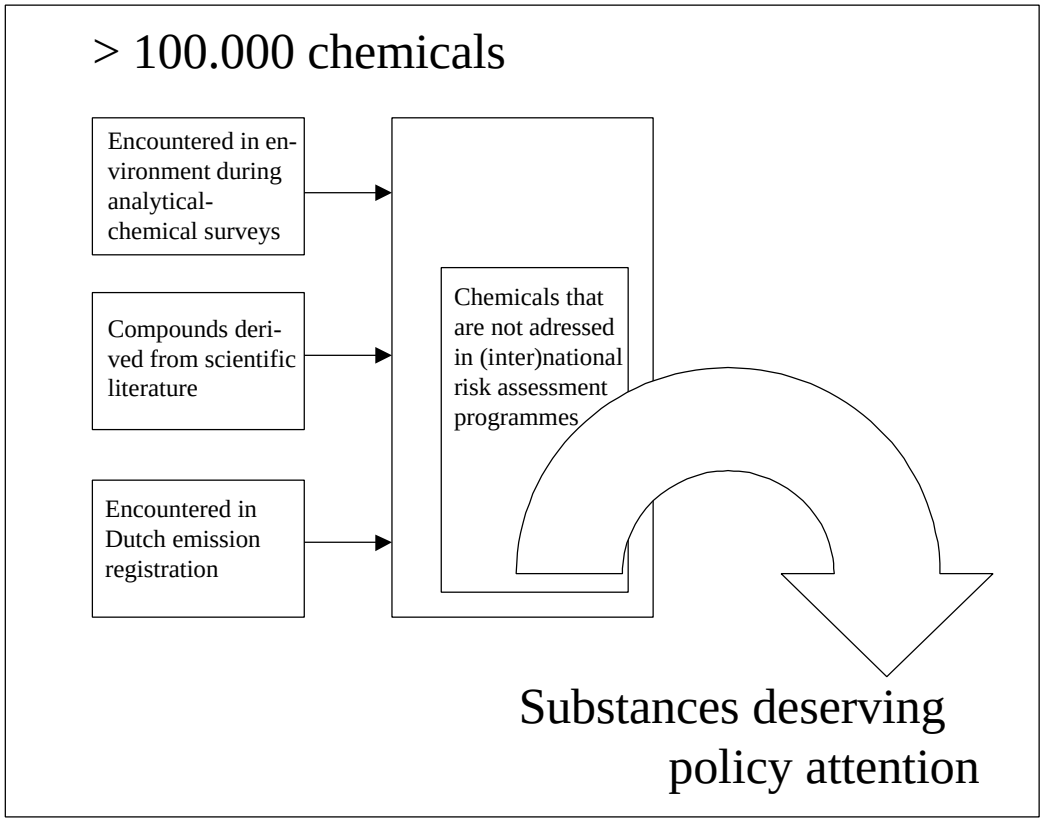

Figure 1.1. Schematic overview on the current report

2. (Groups of) compounds deserving more policy attention: information from survey studies

Several authors present surveys of Dutch surface waters. Water extracts, biota or sediments are analyzed with help of different analytical techniques to identify as many compounds as technically possible. These studies are summarized in the below, an overview of the non-priority compounds that are detected in significant amounts in various Dutch environmental matrices is given in Table 2.1.

2.1 Survey in biota

Hendriks et al. [1998] performed a study in which mussels and eel from the rivers Rhine and Meuse were analyzed for heavy metals and organic microcontaminants, with the purpose to demonstrate the presence of priority as well as non-priority compounds. Eleven heavy metals, 15 PAHs, 2 polybrominated diphenylethers and 6 polybrominated biphenyls, 8 chlorobenzenes, octachlorostyrene, 7 chloronitrobenzenes, 35 polychlorinated biphenyls, 23 chlorobiocides, 2 chloroanisoles, chloroterphenyls, tetrachlorodifon, tetrachlorobenzyltoluenes, 4 carbamates, 21 nitrogenbiocides, 14 phosphorbiocides, 8 nitrogen PAHs, chlordenes, and organotins were analyzed. In addition chlorophenols and phthalates were analyzed, but these results were considered as less reliable. All chemicals are expressed as molar concentrations in the organism lipids, and these concentrations are summed. This summed concentration can be directly related to the so-called 'critical body residue' at which adverse effects occur, and which is more or less a constant value for chemicals that act via the mechanism of narcosis [Van Wezel and Jonker, 1998]. Well-known and classically studied chemicals such as PAHs, PCBs and chlorobiocides cause the largest contribution to the overall burden. The compounds 4,4'-DDE, toxaphene, trichlorophenylmethane and ?-HCH turned out to be the most important chlorobiocides. From the non-priority compounds brominated biphenyls, bromodiphenylethers and octachlorostyrene significantly contributed to the total burden. Carbamates, nitrogenbiocides, phosphorbiocides and nitrogen PAHs turned out to occur in the eel and mussel at concentrations below the detection limit. The total body burden measured was 0.003-0.004 mmol/kg wet weight, or 0.05 to 0.07 mmol/kg fat weight. For comparison; a body burden of 20 to 60 mmol/kg lipid yields acute lethality, and around 5 mmol/kg lipid sublethal effects are exerted [Van Loon et al., 1997; Van Wezel et al., 1995].

2.2 Survey in surface waters and effluents

In comparable surface waters and in effluents as were used in the aforementioned study by Hendriks et al. [1998], Van Loon et al. [1997] performed a biomimetric extraction with 'empore disks' composed of C-18 material. In biomimetic extracts, compounds that only have a minor contribution to the total amount in exhaustive extracts, can become very prominent due to their bioaccumulative properties. For more details on the methods used it is referred to

Van Loon et al. [1996] and Verhaar et al. [1995]. Subsequently the total molar concentration on these disks was measured using GC-MS or vapor pressure osmometric techniques. Using this method, the total body residue in biota exposed to the same water can be estimated. This body residue is on its turn directly related to toxicity. The total body residue that was estimated using this method varied from 0.05 mmol/kg lipid (Wadden Sea) to 2.7 mmol/kg lipid (Scheldt) for the different surface waters tested. These body residues are higher than that in the study by Hendriks et al. [1998]. This indicates that in the study by Hendriks et al. [1998] not all relevant accumulating chemicals were analyzed, or that not all chemical accumulated on the empore disk are able to bioaccumulate in the same extent in biota due to biotransformation or steric hindrance.

The compounds that turned out to attribute to a major part of the total molar concentrations in the various effluents were identified and quantified. As expected, the results differ per effluent type. Effluents from chemical, polymer, paper, metal or pesticide industry and from sewage treatment plants were studied. For the sewage effluents, major organic micropollutants turned out to be 2,6-diisobutylphenol, and the fragrances HHCB (1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-gamma-2-benzopyran), limonene and AHTN (6-acetyl-1,1,2,4,4,7-hexamethyltetraline)[Van Loon et al., 1997].

Using a comparable technique, in a number of Dutch and Belgian surface waters and effluents again HHCB and AHTN were analyzed [Verbruggen et al., 1999]. In surface waters concentrations were 0.5-180 ng/L for HHCB and 1-180 ng/L fir AHTN, in STP effluents concentrations varied from 2 to 630 ng/L for both compounds. Together, both fragrances compromised up to 25 % of the ' Critical Body Residue' that exerts toxic effects due to narcosis.

Recently, compounds in effluents of various sewage treatment plants have been identified (unpublished results by P.Leonards et al.). The research goal was to identify as many substances as possible. Several synthetic fragrances have been identified (galaxolide CASnr.1222055; tonalide CASnr.1506021; traseolide CASnr.68140487; celestolide CASnr.13171001; phantolide CASnr.15323350 and vertofix CASnr.32388559). Also the desinfectant triclosan (a chlorinated hydroxydiphenylether, CASnr. 338035) and its methylated metabolite triclosanmethyl (CASnr. 4640011) were identified. Also chlopyrifos (CASnr. 5598152) and the antioxidant butylated hydroxytoluene (CASnr. 128370) were identified.

Table 2.1. Compounds measured in significant amounts in environmental matrices and are not subject of (inter)national risk assessments

Environmental matrix	**Location**	**Non-priority compounds encountered**	**CAS-numbers**	**Reference**
Biota (mussel, eel)	Rhine, Meuse	octachlorostyrene	29082-74-4	Hendriks et al., 1998
Effluents from sewage treatment plants		2,6-diisobutylphenol	52348513	Van Loon et al., 1997
		HHCB (1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylcyclopenta-gamma-2-benzopyran)	1222055	
		limonene	138863	
		AHTN (6-acetyl-1,1,2,4,4,7-hexamethyltetraline)	1506021 or 21145777	
Surface waters	Rhine, Meuse, Eem, Drentsche AA, Scheldt, IJsselmeer, Ketelmeer, Markermee,	HHCB	1222055	Verbruggen et al., 1999
		AHTN	1506021	
Effluents from sewage treatment plants		galaxolide	1222055	Leonards et al. (unpublished results)
		tonalide	1506021	
		traseolide	68140487	
		celestolide	13171001	
		phantolide	15323350	
		vertofix	32388559	
		triclosan	338035	
		triclosanmethyl	4640011	
		chlopyrifos	5598152	
		butylated hydroxytoluene	128370	

3. (Groups of) compounds frequently addressed by scientists as deserving more policy attention

In this chapter, information on specific compound classes is given. The compound classes that are discussed, are catching much attention in the recent international literature on environmental toxicology and chemistry. Furthermore, this chapter is partly based upon information from several scientists in the field, which were asked to mention compounds that are currently not under the regulatory attention, which possibly pose risks. For some compound classes, specific compounds are mentioned as an illustration. The non-priority compounds of these are listed in Table 3.2. It should be mentioned that this Table is not exhaustive.

3.1 Pharmaceutical substances

Medical substances, designed for either for human or veterinary use, are developed with the intention of performing a biological effect. The pharmaceutical will also be potent towards nontarget organisms sensitive to the pharmaceutical's mode of action. Pharmaceuticals often have bioaccumulative properties; they are hydrophobic as they must be able to pass through membranes and they are often relatively persistent. All together, these compounds can be considered as having a PTB-profile that gives reason to be precautionary. A PTB-profile gives information on the persistence, toxicity and bioaccumulative properties of a chemical [Sijm et al., 1999].

3.1.1 Fate and exposure

Pharmaceutical used by humans will enter the environment generally after passing an sewage treatment plant (STP), veterinary medicines may enter the environment directly (e.g. by spraying, use in fish farms) or via manure. Some compounds, e.g. chlortetracyclines, are excreted as metabolites but are reconverted in the manure or in the STP in the active form [Warman and Thomas, 1981]. Al-Ahmad et al. [1999] report on ready biodegradability tests for 5 antibiotics (cefotiam, ciprofloxacin, meropenem, penicillin G. and sulfamethoxazole). They showed that none of the compounds is classified as ready biodegradable and that only penicillin was degradable to some degree. On the other hand available data on ibuprofen [Buser et al., 1999] show that this compound is efficiently degraded in waste water treatment plants, leading to concentrations in surface water lower than 8 ng/L while concentrations in the influents of the plants are up to 3 µg/L.

Not much is known about the exposure in the environment to these substances, although there is a growing interest in the subject. Pharmaceuticals are found in the environment depending on the substance in ng/l or µg/l range in water, see for an overview on measured concentrations Halling-Sørensen et al. [1998]. Al-Ahmad et al. [1999] calculated concentrations in surface waters of around µg/l range for five commonly used antibiotic drugs. Some high volume medical substances are probably released into the environment at the same order of magnitude as other xenobiotics. For example in Denmark, over 200 tons of antibacterial agents are used annually in Denmark for human and veterinary purposes.

3.1.2 Toxicity

In a review on occurrence, fate and effects of pharmaceuticals in the environment [Halling-Sørensen et al., 1998], it appeared that only acute toxicity data are available in the open literature. Due to their persistent nature, more chronic testing would be very relevant. It was shown by Henschel et al. [1997] that a limitation to the standard ecotoxicity tests (algae, Daphnia and fish) would have underestimated the toxicity for three out of the four tested pharmaceuticals (i.e. paracetamol, clofibrinic acid, methotrexate, not salicylic acid). These authors recommend to choose a test strategy adapted to the expected specific mode of action of the substance.

3.1.3 Risk assessment

Information on this class of contaminants is in general too sparse to conduct thorough environmental risk assessment. Both on the exposure as on the effect sides, knowledge is lacking. Commonly used models for performing risk assessment such as USES [RIVM et al, 1998], may not be applicable as the models therein are based on hydrophobicity driven partitioning. Many of the pharmaceuticals are relatively big molecules with ionizable groups. Other partitioning processes such as ion-ion pair formation may play an important role in the environmental chemistry of these compounds.

In Europe directive 92/18/EEC regulates the environmental risk assessment for veterinary products in a two-phase process. Environmental concentrations are to be predicted (see for models on the exposure assessment Montforts et al. [1999]). When trigger values (e.g.10 µg/kg in soil) are not exceeded no further assessment will take place. This is not in line with the risk assessment as conducted for new and existing chemicals - council regulation 793/93, technical details in commission regulation 1488/94 - in which both the toxicity as the exposure are considered. In addition, the EU guideline 92/18/EEC calculates the PEC according to the estimated production or consumption quantity of the product concerned. However the total quantity of the active ingredient originating from different products with the same active ingredient, might be much higher resulting in a higher PEC, as shown in calculations by Henschel et al. [1997].

In view of the fact that livestock breeding and rearing is an important industry in the Netherlands, these classes of chemicals can be considered as very relevant for the Netherlands.

3.2 Disinfectants

Disinfecting products are utilized in high amounts in hospitals, household, and livestock breeding. In many of them phenolic antiseptics are used. Examples are biphenylol (CAS nr. 90437), 4-chloro-m-cresol (CAS nr. 59507), chlorophene (CAS nr. 120321), bromophen (CAS nr. 15435297), 4-chloroxylenol (CAS nr. 88040), tetrabromo-o-cresol (CAS nr. 576556), phenylsalicylate (CAS nr. 118558), 5-chlorosalicylic acid (CAS nr. 321142), 5-bromosalicylic acid (CAS nr. 89554) [Ternes et al., 1998]. In German municipal STP effluents, rivers, and stream waters, concentrations of approximately 0.030 to 0.050 µg/l are encountered for biphenylol and chlorophene [Ternes et al., 1998].

Antibacterial agents are applied in fish farming to prevent and to treat microbial infections among the fish. They are a direct source of exposure to the aquatic environment, and

sometimes applied in rather large quantities. Especially algae seem to be sensitive to antibacterial agents, compared to crustaceans and fish [Holten Lützhøft et al., 1999]. Some of these antibacterial agents are relatively stable in the environment (t½>100 d) [Hektoen et al., 1995]. Examples of these compounds are amoxicillin, flumequine, oxolinic acid, oxytetracycline, sarafloxacin, sulfadiazine and trimethoprim.

Disinfectants can be presumed to be used in high amounts in the Netherlands, due to the high population density. The compounds are often acids which due to their acidic properties, will have a lower tendency to accumulate in biota than the aforementioned group of pharmaceuticals. The toxicity will depend on the pH of the environment; in general the products will be more in the nonionic form, and thus their bioavailability and toxicity will be higher if the pH is lower [cf. Van Wezel, 1998]. It can be presumed that the pH in the environment is higher than in the situation where these acidic products are used.
Together, the emission in the Netherlands of disinfectants is estimated to be considerable. Although no quantitative measurements in surface waters or other environmental matrices exist to the authors' knowledge, detectable concentrations are expected. Literature would have to be reviewed to give a satisfactory prediction on the 'PTB-properties'. On a first glance, toxic and bioaccumulative properties are not expected to be worrisome on account of the acidic properties of most disinfectants.
Regulation occurs via directive 98/8/EC concerning the placing of biocidal products on the market. The decision making for authorization as far as environmental effects are concerned is based on the PEC/PNEC ratio. As for veterinary medicines, authorization takes place per product. If the active substance is present in a variety of products, the PEC used in the decision making will be an underestimation from the actual environmental concentration.

3.3 (Anti-) estrogenic compounds

For a recent overview on contaminants which disrupt hormonal balance and affect reproduction, it is referred to Janssen et al. [1998], Tyler et al., [1998] and Gillesby and Zacharewski [1998]. Various mechanisms of action to obtain those effects are possible; i.e. interaction with the hormonal receptor, interaction with hormonal synthesis and metabolism, and (de)activating hormone-related gene sequences via non-hormone receptors, e.g. the Ah-receptor. Xeno-estrogens are compounds that can act as (anti-)estrogens. Although the strength of binding to the estrogen receptor of xeno-estrogens is by far lower than that of natural estrogen, they can occur in higher concentrations and/or be effective in their kinetics to have access to the receptor. Compounds that are often mentioned as being xeno-estrogens are listed in Table 3.1., which is adapted from aforementioned reviews.

Table 3.1: (Groups of) compounds that are suspected of (anti-)estrogenic action (adapted from Janssen et al. [1998], Tyler et al., [1998] and Gillesby and Zacharewski [1998])

Application	Group name	Examples
Synthetic oestrogen		diethylstilbesterol (DES)
		17∃-ethinyloestradiol (used as anticonceptive in 'the pil)
		Gestodene
		Norgestrel
Phyto-oestrogen	Isoflavones	Daidzein
		Genistein
		Equol
		Naringenin
		Formomonetin
		Biochanin A
	Coumestans	Coumestol
	Lignans	Enterolactone
Myco-oestrogen	Zearalones	Zearalone
Pesticide	Dichlorodiphenyl-ethanes	DDT
		DDD
		DDE
		Dicofol
		Perthane
		Methoxychlor
	Hexachlorocyclohexanes	a-HCH
		?-HCH
	Cyclodienes	Aldrin
		Dieldrin
		Endosulfan
		Chlordecone
		Trans-nona-chlor
		Heptachlor
	Toxaphenes	
	Chlorotriazines	Atrazin
		Simazin
	Fungicide	Vinclozolin
	organotins	TBT
		TPT
Industrial chemicals	Alkyl phenoles	Nonylphenol
	Alkylphenole polyethoxylates	Octylphenol
	PCBs, PCDDs, PCDFs, PAHs	
		Bisphenol A
	phthalates	butylbenzylphthalate
		di-n-butylphthalate

It should be noted that not only xenobiotics explain the adverse effects as observed in the field. Desbrow et al. [1998] show with help of fractionation in combination with an *in vitro* assay for detecting estrogenic activity, that natural and synthetic hormones might be responsible for vitellogenin synthesis in caged male fish downstream of STP effluent discharges. In various British domestic STP effluents, estrone occurred in concentrations of 1-80 ng/L, 17ß-estradiol occurred in concentrations of 4-50 ng/L and the synthetic hormone 17a-ethynylestradiol occurred in concentrations between below detection limit (~ 0.2 ng/L) up to 7 ng/L. In subsequent 21-d experiments with rainbow trout and roach [Routledge et al., 1998] it was shown that environmental relevant concentrations of the natural hormones 17ß-estradiol and estrone are sufficient to account for the levels of vitellogenin synthesis observed in fish exposed in the field. Comparable results are obtained in Sweden [Larsson et al., 1999]. For comparison, Belfroid et al. [1999] showed that in Dutch surface water estrogenic hormones can be detected at concentrations up to 6 ng/l. In general however, concentrations are below

1-5 ng/l. The detected hormones are17a-estradiol, estrone, 17ß-estradiol, and the synthetic anticonceptive 17a-ethynilestradiol. In domestic effluents as well as in surface waters, the highest concentrations were found for estrone (up to 47 ng/l for effluents). 17a-estradiol and 17a-ethynilestradiol were only found occasionally.
(Eco)toxicological scientists currently spend a lot of effort on these types of compounds and effects. Some of these xenobiotics mentioned in Table 3.1. are already covered in various (inter)national programs on risks of chemicals. Also, some of the substances mentioned to be (anti-)estrogens can hardly be regulated, such as phytoestrogens. The pesticides as mentioned in Table 3.1. are regulated by authorization, in the Netherlands by the Board of the authorisation of pesticides. The industrial chemicals are regulated via the EU regulation for existing or new chemicals, the technical details of the risk assessment are embodied in the so-called 'Technical guidance document on risk assessment for new and existing substances' (EC 1488/94). Until now no risk assessment techniques are applied that explicitly integrate risks on hormonal disturbance. Effects on endpoints related to reproduction are commonly taken into account though. For the suspected xeno-estrogens phthalates it was shown that risk assessment techniques currently in use are sufficiently protective against these types of effects [Van Wezel et al., in press].

3.4 Biotransformation products of pesticides

Once entered in the environment, the majority of pesticides degrade into transformation products. If over 20% of a transformation product is formed within a limited time under laboratory circumstances, the toxicity of the transformation products is taken into account in the authorization of pesticides. However, for the majority of transformation products little is known on toxicity, environmental fate or risk [Belfroid et al., 1996]. Only for a very limited number of transformation products, the environmental concentrations are measured. Especially for triazines, carbamates and phenoxypropionic acids, a first survey on literature data shows that the transformation products of these compounds can pose a similar to higher risk to the environment than their parent compounds [Belfroid et al., 1996].
If it is known from the information given in the dossiers supplied by the industry that one metabolite is formed for more than 10% of the parent compound within a given time frame, this metabolite and its effects is considered in the authorization of the pesticides. This is not the case for metabolites formed in a lower percentage. It must be noted that the formation of metabolites in a field situation can differ markedly from the situation in a laboratory degradation study, as explained by the type of organisms that are involved and environmental circumstances.

3.5 Fluorescent whitening agents

These are high volume chemicals used in detergents and the manufacturing of paper and textiles. There are many types of fluorescent whitening agents (FWAs). Most commonly used are stilbene derivatives. Emission from textiles is low compared to emission from paper industry and use in detergents. Especially for use in paper industry, some estimated

PEC/PNEC ratios exceeded 1. For a recent overview on sources, occurrence, effects and risk evaluation of this compound class it is referred to Van de Plassche et al. [1999].

3.6 Aromatic substances

Aromatic substances (musk ketone, musk xylene, polycyclic musks (AHTN, HHCB, ADBI, AITI and AHMI), limomene and acetylcedrene) have been observed in several environmental matrices (surface waters, fish etc.) (e.g. Rimkus and Wolf [1995]).
Musk xylene and musk ketone are the major components of the nitro musk group. It are in general hydrophobic substances (log K_{ow} > 4). The compounds seem to biotransformed relatively fast, resulting in a lower bioconcentration factor than predicted based on their hydrophobicity [Tas et al., 1997]. Preliminary measurements of concentrations in surface waters show levels around 0.1 µg/L [Balk and Rutten, 1998]. Based on the available toxicity data, predicted no effect concentrations (PNEC) have been derived by dividing the lowest NOEC by a factor of 10, resulting PNECs for these compounds of 1-7 µg/L [Balk and Rutten, 1998]. Tas et al. [1997] performed a risk assessment for musk ketone and musk xylene (CAS nrs. 81141 and 81152). They concluded that risks for aquatic species, sediment organisms and fish-eating birds and mammals are low, however risks for soil organisms could not be excluded.
It might be concluded that although the compounds are not very persistent, they are used in such high amounts and are emitted in such quantities that a considerable environmental concentration can be maintained.

3.7 Flame retardants

Flame retardants are produced in high quantities, and include over a hundred different products [WHO, 1997]. They are used mainly in plastics, and also in the textile and furnishing industry, so are expected to be emitted diffused. Some of the flame retardants, especially the brominated diphenylethers and diphenyls are already subject to programmes on risk assessment and for the brominated diphenyls subsequent measures have been taken. However, the risks of many other types of flame retardants have been paid little attention to. It is remarkable that many of the substances that are recently encountered in environmental matrices with help of analytical-chemical methods are identified as flame retardants (Pim Leonards, personal communication).

3.8 Further compound classes to be mentioned

a-Terpineol; a terpenoid alcohol widely used in detergents and cosmetics was shown to be one of the major components of sewage effluents [Desbrow et al., 1998].
Lots of fluoro or iodio-substituted compounds can be found in the Dutch emission register (see chapter 5). Several authors mention the mutagenicity of these compounds, especially substituted nitrobenzenes and substituted PAHs, in *in vitro* systems [Diamond et al., 1984; Kerklaan et al., 1987; Shimizu et al., 1983].

3.9 Conclusions

The compounds that are mentioned in this chapter are summarized in Table 3.2., together with their CAS-nrs. following EINECs numbering. These compounds are compared with the list of chemicals for which a risk assessment is finished or planned in any (inter)national framework. It is concluded that the majority (75%) of the mentioned compounds do not occur in the lists of (inter)national organizations, except for simazine, musk ketone, musk xylene and limonene. For few (groups of) compounds information was lacking to make the comparison.

Table 3.2.: An illustrative, non-exhaustive list of compounds that are not subject of (inter)national risk assessment programs of the compound classes described in the above

Compound class	Chemical name	CAS-nr.	Reference
Pharmaceutical substances	chlortetracycline	57625	Warman and Thomas, 1981
	cefotiam	66309691	Al-Ahmed et al., 1999
	ciprofloxacin		
	meropenem		
	penicillin G.	61336	
	sulfamethoxazole	723466	
	ibuprofen	15687271	Buser et al., 1999
	paracetamol	103902	Henschel et al., 1997
	clofibrinic acid	882097	
	methotrexate	59052	
	salicylic acid	69727	
	overview		Halling-Sørensen et al., 1998
Disinfectants	biphenylol	90437	Ternes et al., 1998
	4-chloro-m-cresol	59507	
	chlorophene	120321	
	bromophen	15435297	
	4-chloroxylenol	88040	
	tetrabromo-o-cresol	576556	
	phenylsalicylate	118558	
	5-chlorosalicylic acid	321142	
	5-bromosalicylic acid	89554	
	amoxicillin	26787780	Hektoen et al., 1995
	flumequine	42835256	
	oxolinic acid	14698294	
	oxytetracycline	79572	
	sarafloxacin		
	sulfadiazine	68359	
	trimethoprim	738705	

(Anti-)estrogenic compounds	Dicofol*	115322	Janssen et al. 1998, Tyler et al., 1998, Gillesby and Zacharewski 1998
	Perthane	72560	
	Chlordecone*	143500	
	Trans-nona-chlor*		
	Vinclozolin	50471448	
Biotransformation products of pesticides	transformation products of triazines, carbamates and phenoxypropionic acids		Belfroid et al., 1996
Fluorescent whitening agents	Stilbene derivatives		Van der Plassche et al., 1999
Aromatic substances	AHTN		Rimkus and Wolf, 1995
	HHCB		
	ADBI		
	AITI		
	AHMI		
	acetylcedrene	91053337	
Remaining	a-terpineol	98555	Desbrow et al., 1998

*: Identified as PTB-compound by Blok et al. [1999], see chapter 5

4. Compounds in the Dutch register on emission of substances

4.1 Introduction on the Dutch emission register

In the Netherlands information on compounds that are emitted is collected in the emission register. Until 1995, 700 companies were questioned each year which substances they were wittingly emitting. Note that all kinds of by-products of industrial processes and transformation products cannot be taken into account in this procedure. About 1700 substances or groups of compounds are registered in the emission register. At the moment a different system is being introduced; about 350-400 companies have to register if they emit substances from a list consisting of approximately 500 compounds.
The emissions from the questioned companies are extrapolated to total emissions for 550 substances. For the extrapolation methods used it is referred to Van de Most et al. [1998]. The accuracy and reliability of these extrapolations is higher for substances on which there is an active policy, or which are emitted during combustion processes. Emissions resulting from product use by consumers are estimated. In general there is little empirical information on those kinds of losses, so emission data are based upon emission factors from literature combined with information on product uses. For about 250 compounds of the originally registered 1700 compounds, emissions are presented yearly in reports [Draaijers et al., 1997; Van der Auweraert et al., 1997].
Emission reduction goals are derived for relatively few compounds, for which there are many sources.

4.2 Methods

The compounds in the emission register were subdivided in several categories:

1. Groups of compounds considered as non-relevant for the purpose of the current report , i.e. selecting new substances which deserve policy attention. Examples are wastes of certain uses (e.g. waste of paving or car wrecks), general environmental parameters such as pH or heat, complex mixtures such as cement or milk powder; compounds for which the expected problems do not occur via toxicological mechanisms (e.g. global warming compounds).
2. Compounds that are relevant in terms of ecotoxicological risks; the risks are generally known based on information from scientific literature (examples are chlorinated alkanes, - alkanols, - benzenes etc., PAHs, PCBs, well-known pesticides, heavy metals etc.).
3. Compounds that are not expected to bring about high ecotoxicological risks ecosystems, for reasons of high biodegradability or low bioavailability (examples are non-halogenated alkanes or alkanols, silicates, cellulose).
4. Compounds that are expected to bring about ecotoxicological risks for ecosystems which do not seem to be well-realized, based on the information found in open literature (e.g. fluorinated alkanols).

5. Compounds on which the authors do not have an opinion.

For each category, it was checked which percentage of the compounds have been undergoing a risk assessment in (inter)national frameworks [based on an overview by Van Wezel, 1999]. In addition, ecotoxicological data were searched for compounds of category 4 and 5. To this end, an extensive 'meta-database' is used. This database was developed at the National Institute for Human Health and the Environment [De Zwart, personal comm.; De Zwart and van de Meent, 1998], and is a combination of different databases (AQUIRE, pesticide database of EPA, database developed in RIVM project 'Setting Integrated Environmental Quality Standards'). This database consists of approximately 100.000 observations on 1700 species and 3500 chemicals. Finally, the yearly emission in kilograms to the air in the Netherlands were checked.

4.3 Results

The division of the 1700 (groups of) compounds from the emission register into the categories as mentioned in 5.2. is depicted in Figure 3.1. In category 1, non-relevant, 592 (groups of) compounds were classified. 15 % of the compounds, 262 chemicals were classified as having high but well-known ecotoxicological risks. For 137 compounds in the emission register no ecotoxicological risks are expected. For 87 substances risks are expected, but do not seem to be well-realized. For the remaining 621 compounds the authors do not have enough information to classify the substance in one of the aforementioned categories. The nature of the 1700 (groups of) compounds of the emission register is rather diverse, and therefore also the frameworks in which legislation and policy for these compounds takes place. Approximately half of the compounds (categories 4 and 5), are of possible interest for the current report, as these categories probably contain compounds that deserve policy attention. Categories 1 and 3 are not of interest as these wastes or (groups of) compounds are not expected to bring high ecotoxicological risks to the ecosystem.

Only for few compounds in the Dutch emission register risk assessments are performed within national or international programs, in the whole 10%. Note that substances can have various synonyms and can be treated as a group with comparable substances or as a specific substance. This hampers the analysis for which of the compounds in the emission register a risk assessment is performed, and makes that the figures mentioned should be interpreted as indicative figures. As expected, the percentage of the compounds for which risk assessment is performed varies per category. In Figure 3.2 it can be seen that for category 2, compounds that are having high but well-known risks, as expected relatively the most risk assessments are performed.

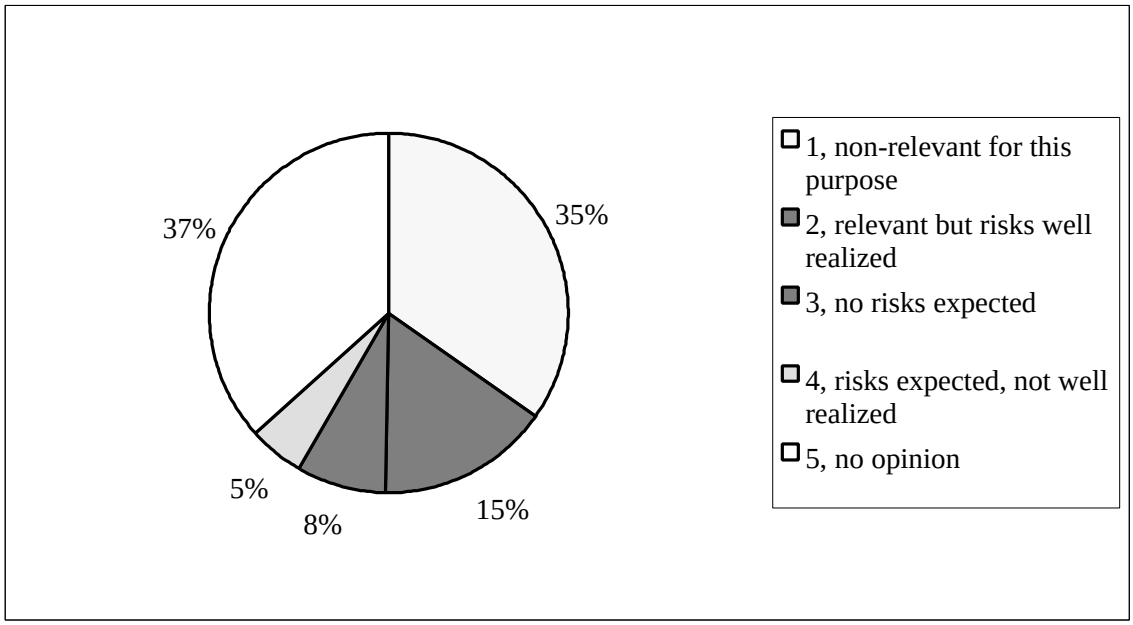

Figure 3.1. Categories (see legend) in which the 1700 (groups of) compounds from the emission register were divided.

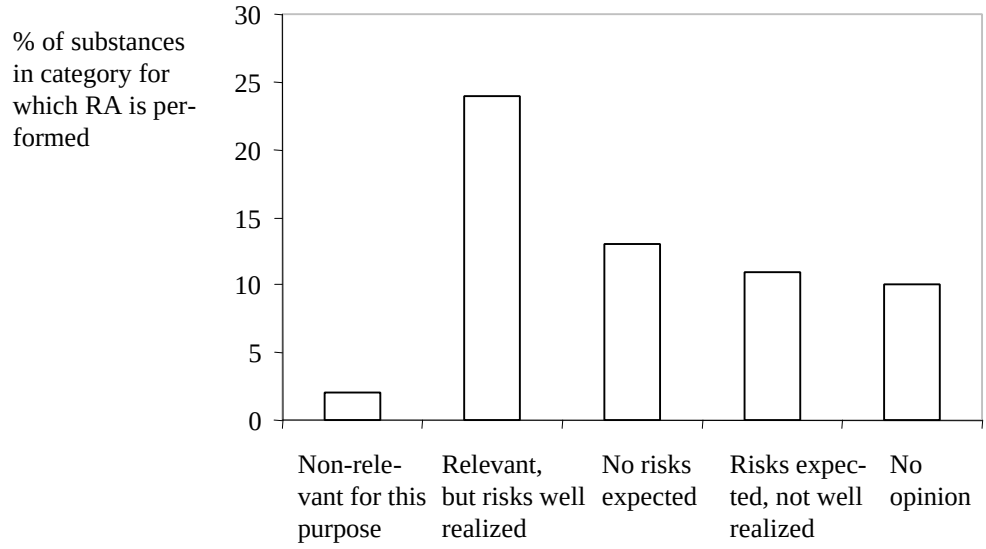

Figure 3.2. Percentage of substances per categories for which a risk assessment is (being) performed in any (inter)national program

In appendix II compounds from category 4, where risks might be expected but may not be well-realized are listed. In this appendix the chemical name is given, the CAS nr., the emission to air which is found in the inquired companies and the emission to air which is totally estimated for the Netherlands. In addition, if the compounds are treated in any (inter) national programme on risk assessment this is mentioned in the appendices. Also available toxicity data to algae, crustaceans and fish are given, as well as the total number of toxicity data. For this purpose, acute toxicity data (LC50s) are selected. The lowest value found in the database on algae, crustaceans or fish is given in appendix II.

It may be noticed that in appendix II many brominated and fluorinated compounds are listed. Chlorinated compounds have received much attention in the past. However, fluorinated or brominated substances are comparable in their behavior and toxicological endpoints to chlorinated compounds. Several chloro-fluoro-hydrocarbons are dealt with in the Montreal treaty and EC-regulation nr.3093/94 on compounds that break down the ozone layer.

5. Discussion and conclusions

For the compounds which are detected in survey studies, as described in chapter 2, the compounds that are not (planned to be) subject of (inter)national risk assessments are listed in Table 2.1. The information as given by the surveys in different environmental matrices differs in weight. For example; compounds that are measured in biota are bioaccumulative, are not readily biotransformated and steric hindrance does not obstruct the uptake. Substances that are detected in so-called biomimetric extracts are probably bioaccumulative. Compounds that are measured in effluents possibly will also be encountered in surface waters. So, the weight of the argument declines from substances that are detected in biota to substances detected in effluents. Compounds in chapter 3 are selected based on recent interest by scientists. None of the compounds mentioned in Table 3.2. is subject of assessments either. Both lists of chemicals (Tables 2.1 and 3.2.) can be concerned as compounds that may deserve more policy attention.
Next to chemicals that are emitted directly from industrial sources, chemicals that are emitted diffusely for instance after their use by consumers are gaining more attention. This can also be noticed from the type of chemicals that are mentioned in chapter 2 and 3. Examples are fragrances, disinfectants, pharmaceutical, fluorescent whitening agents etc. These chemicals often enter the environment via sewage treatment plants. In countries with a high population density, the flow of a river can be contributed for up to 50% by effluents discharged by sewage treatment plants, and in periods of low rainfall this figure can rise to 90% [Routledge et al., 1998]. So, emission reduction measures may be focused in second instance on these sources.

Other ways of identifying compounds that deserve more policy attention is by applying priority setting schemes (see 1.1.1.). Blok et al. (1999) performed a selection based on over 100.000 compounds to discern substances that score high on criteria related to persistence, toxicology and bioaccumulation (PTB). It must be noted that exposure, the amount in which a chemical is used and emitted is not expressed in the PTB criterion. Due to data limitations and mismatch between different databases used, the final screening on PTB substances could be applied to 28600 substances, so not on all existing chemicals. A number of 301 substances was classified as PTB substance. A 'list of notorious substances' was created, by aggregating different national and international lists of hazardous substances. Of these 896 notorious substances only 10% was recognized as a PTB-substance, however the majority of the generally recognized notorious substances was classified as being toxic. Of the 301 PTB substances, 209 chemicals were not identified as a notorious substance before. Many of these 209 chemicals are organo-halogen compounds (108), are applied as medicinal drugs (97) or as agricultural pesticides (81). Also 16 polyfluor organics were included. Several of these substance classes (fluorinated compounds and pharmaceuticals) are also found in chapter 2 to 4 of this report.

We made a comparison (based on CASnr.) between the compounds that were identified in chapter 2 to 4 as possibly deserving more policy attention and the compounds that were classified by Blok et al. [1999] as PTB-substances. The estrogenic compounds dicofol, chlordecone and transnonachlor from Table 2.1. are identified as PTB substances, and none of the other chemicals in Tables 2.1.and 3.2. It is concluded that the approach followed in the current report is a valuable addition to the approach as followed by Blok et al. [1999].
For the compounds in the emission register, also such a comparison was made for those chemicals of which a CAS-nr. was available. CAS nrs. were searched for extensively for the classes 4 and 5 (see 4.2.), i.e. compounds were risks are expected but does not seem to be realized, or compounds were the authors did not have an opinion. The substances quintozene (82688), lopanoic acid, dicofol (115322), dienoclor (2227170), fenbutatin oxide (13356086), hexachloro bicycloheptadiene (28680457)and fenpropimorph (67564914) were both classified as PTB substance and as a compound in the Dutch emission register for which not an (inter)national risk assessment is going on. For the compounds classified as 'non-relevant' or 'no risks expected' for the purpose of this report, none of the compounds was identified as PTB substance by Blok et al. [1999]. For the compounds of the classes 'relevant but risks are realized' several substances are classified as PTB-substances, however all these chemicals are subject of (inter)national risk assessments.

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Appendix 1. Mailing list

1) mr. A.B. Holtkamp (DGM-SVS)
2) dr. ir. B.C.J. Zoeteman (DGM)
3-13) mw. E. Siebel (DGM-SVS)
14) dr. D.W.G. Jung (DGM-SVS)
15) drs. A.W. van der Wielen (DGM-SVS)
16) dr. T. Crommentuijn (DGM-Bo)
17) drs. D.A. Jonkers (DGM.DWL)
18) dr. K.R. Krijgsheld (DGM-LE)
19) ir. J.A. Herremans (DGM-LE
20) drs. M.M. de Hoog (DGM-ICB)
21) ir. P.F.J. van der Most (DGM-HIMH)
22) dr. H. Loonen (ECB)
23) dr. E. Sneller (RWS/RIZA)
24) drs. C. van de Guchte (RWS/RIZA)
25) ing. G. Broseliske (RWS/RIZA)
26) ing. R. Faasen (RWS/RIZA)
27) ir. H.G.K. Ordelman (RWS/RIZA)
28) ing. G.B.J. Rijs (RWS/RIZA)
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30) dr. H. Barreveld (RWS/RIZA)
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32) dr. P.C. Noordam (SoZaWe-DGA)
33) drs. G. Hoube (VWS)
34) prof. dr. R. Laane (RWS/RIKZ)
35) drs. J. Peijnenburg (RWS/RIKZ)
36) drs. H. Klamer (RWS/RIKZ)
37) dr. W. van Loon (RWS/RIKZ)
38) drs. J. Lourens (RWS/RIKZ)
39) drs. C. van Zwol (RWS/RIKZ)
40) dr. T. van Brummelem (RWS/Directie Noordzee)
41) drs. M. Cerutti (RWS/HW)
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50) dr. K. de Haan (Shell Chemie)
51) KIWA
52) RIWA
53) SC-DLO
54) VNO/NCW
55) dr. D. van Well (VNCI)
56) M. Koene (Stichting Natuur en Milieu)

57) D. van Wijk (Akzo)
58) L. Vollebregt (Chemiewinkel A'dam)
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72) ir. E. Schols (LAE)
73) drs. C. Roghair (ECO)
74) drs. D. de Zwart (ECO)
75) dr. J. Struijs (ECO)
76) drs. E. van der Velde (LOC)
77) dr. F. Swartjes (LBG)
78) ir. J. Lijzen (LBG)
79) drs. H.C. Eerens (LLO)
80) Hoofd Centrum voor Stoffen en Risicobeoordeling
81) Hoofd Laboratorium voor Ecotoxicologie
82) Hoofd Laboratorium voor Water en Drinkwateronderzoek
83) Hoofd Laboratorium voor Bodem en Grondwateronderzoek
84) Hoofd Laboratorium voor Afvalstoffen en Emissie'
85) Hoofd Laboratorium voor Effectenonderzoek
86) Sectordirecteur Stoffen en Risico's
87) Sectordirecteur Milieuonderzoek
88) Auteur
89) SBD/Voorlichting en Public Relations
90) Bureau Rapportenregistratie
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92-102) Bureau Rapportenbeheer
103-110) Reserve-exemplaren

Appendix 2. Compounds where ecotoxicological risks might be expected but may not be well-realized

Chemical name (In Dutch)	CAS nr.	Emission air, kg/yr inquired companies	Emission air, kg/yr. Total in the Netherlands	ecotox algae	ecotox crusta-ceans	ecotox fish	number of data on ecotoxi	International organization	Focus in The Netherlands
TERPENEN,NNB		15083							
HEXAFLUORETHAAN		27480							
PFK'S			302280						
DIBROOM-1-PROPANOL,2,3-PERFLUORBUTAAN									
PERFLUORPENTAAN									
OCTAFLUOR-2-METHYLPROPEEN									
HEPTACHLOORBICYLOHEPTEEN									
PCT									
RHENIUM									
METHYLBROMIDE (BROOMMETHAAN)	74839	12146	12146	3200	1700	0,6	28	OECD/SIAR	CCDM list
METHYLJODIDE (JOODMETHAAN)	74884								
ETHYLBROMIDE (BROOMETHAAN)	74964								
BROMOFORM (TRIBROOMMETHAAN)	75252			10000	26000	7100	19		
DICHLOORBROOMMETHAAN	75274								
DIFLUORETHAAN,11-	75376								
DICHLOORMONOFLUORMETHAAN	75434	23675							
CHLOORDIFLUORMETHAAN	75456	1247750	1247750					2nd prioritylist EU OECD/SIAR	
TRIFLUORMETHAAN	75467								
BROOMTRIFLUORMETHAAN	75638	9408							
TRICHLOORFLUORMETHAAN	75694	557673							
DICHLOORDIFLUORMETHAAN	75718	208937							
CHLOORTRIFLUORMETHAAN	75729								
TETRAFLUORMETHAAN	75730	274799							
PERFLUORPROPAAN	76197								
CHLOOR-1,2,2 TRIFLUORETHEEN,1-	79389								
DIBROOM-3-CHLOORPROPAAN,1,2-	96128								
BROOMFENYLFENYLETHER,4-	101553				360	5900	2		
DIBROOMETHAAN,1,2-	106934					4800	4	76/464/EEC list II	
BROOMPROPAAN,1-	106945								
BROOM-2-CHLOORETHAAN,1-	107040								
BROOMBUTAAN,1-	109659					36700	1		
OCTAFLUORCYCLOBUTAAN	115253								
TETRAFLUORETHEEN	116143								
HEXAFLUORPROPEEN	116154								
TRIBROOMFENOL,2,4,6-	118796				1310	4500	9		
CHLOORDIBROOMMETHAAN	124481					34000	1		

Chemical name (In Dutch)	CAS nr.	Emission air, kg/yr inquired companies	Emission air, kg/yr. Total in the Netherlands	ecotox algae	ecotox crusta-ceans	ecotox fish	number of data on ecotoxi	International organization	Focus in The Netherlands
DI-CL-222-TRI-F-ETHAAN,11-	306832	60	60						
BROOMCHLOORDIFLUORMETHAAN	353593								
CL-1122-TETRA-F-ETHAAN,1-	354256								
PENTAFLUORETHAAN	354336	23000							
TETRAFLUORETHAAN,1112-	354353	419569	419569						
PENTACHLOORFLUORETHAAN	354563								
TRI-CL-122-TRI-F-ETHAAN,112-	354585	1436							
TRI-CL-222-TRI-F-ETHAAN,111-	354585								
PERFLUORHEXAAN	355420								
TETRAFLUORETHAAN,1122-	359353							WHO-IPCS, CICADS document	
DIFLUORBENZOEZUUR,2,6-	385002					69000	4		
TRIFLUORETHAAN,111-	420462	17399							
HEXAFLUORPROPAAN,1111223-	431630								
CL-111333-HEXA-F-PROPAAN,2-	431878								
CHLOOR-6-FLUORBENZONITRIL,2-	668451								
DI-CL-1122-TETRA-F-ETHAAN,12-	1320372	2233							
DIFLUORBENZONITRIL,2,6-	1897521	1024							
KOBALT	2311580								
JOODTRIFLUORMETHAAN	2314978								
CL-1222-TETRA-F-ETHAAN,1-	2837890								
LANTHAANREEKSMET./-VERB.ALS LA	7439910	94				20	1		
LITHIUM/-VERBIND. ALS LI	7439932		38,4						
MAGNESIUM	7439954		3286		64700		1		
MANGAAN	7439965		606			>170 <15610	1		
NIOBIUMVERB. ALS NB	7440031								
PALLADIUM/-VERBIND. ALS PD	7440053							WHO-IPCS, EHC document	
PLATINA	7440064	0,4							
KALIUMVERB. ANORG. ALS K	7440097		13017		53200		1		
RHODIUM/-VERBIND. ALS RH	7440166								
SAMARIUM	7440199								
ZILVER	7440224		0	170	0,24	10	15	76/464/EEC list II	INS in preparation
TIN	7440315		314			>170 <15610	1	76/464/EEC list II	
TITAANVERBIND. ALS TI	7440326	0	3070					76/464/EEC list II	INS in preparation
WOLFRAAM/-VERB. ALS W	7440337	37389	37402			15610	1		
GOUD EN GOUDVERBIND. ALS AU	7440575								
VANADIUM/-VERBIND. ALS V	7440622	4460	303470			160	1	76/464/EEC list II	INS finished
ZIRKOON/-VERBIND. ALS ZR	7440677	5	387						
DIFLUORBENZAMIDE,2,6-	1806303								

Chemical name (In Dutch)	CAS nr.	Emission air, kg/yr inquired companies	Emission air, kg/yr. Total in the Netherlands	ecotox algae	ecotox crusta-ceans	ecotox fish	number of data on ecotoxi	International organization	Focus in The Netherlands
	1								
DICHLOORFLUORETHAAN	2516788 8	439720	439721						
CHLOOR-1,1-DIFLUORETHAAN,1-	2549729 4	286499	286499						
DIBROOMTETRAFLUORETHAAN	2549730 7								
TERFENYL/TERFENYLOXYDE	2614060 3	7428							
TETRACHLOORDIFLUORETHAAN	2860574 1								
HEXACHLOORBICYCLOHEPTADIEEN	2868045 7						60	2	
CHLOORPENTAFLUORETHAAN	3407787 7	2632							
BROOMOCTAAN (OCTYLBROMIDE)	5081620 1								
CL-6-FLUORBENZAMIDE,2-	6607354 9								
MONOCHLOORMONOFLUORBENZAMIDE	6607354 9								
MESSING	7935783 8								
BRONS	9169698 9								