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Following the Source to Effect Chain using PAH as a lead

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Summary

The present study addresses the question how to link sources, emissions, environmental fate, exposures, and effects of chemicals within an actual risk assessment. It focuses on the question whether existing models and data sources cover the source-effect chain. To pin methods down, polycyclic aromatic hydrocarbons (PAHs) have been chosen as an example. Each part of the present report first discusses general principles and models and then adds a specific example using PAH data to describe the source-effect chain. Most information appeared to be available for only few PAHs, notably benz[a]pyrene and fluoranthene. Two composite measures, the 10 of VROM and the 6 of Borneff, are available as indicator for total PAH emissions and environmental load.

The use of clearly described standard environments and exposure scenarios make the computer programs CSOIL, USES and EUSES very useful tools for screening risk assessment. Where actual exposures and risks are needed, these programs are less suitable, and models like AirPEx, STEM/FRIDGE, CONSEXPO, and PBPK-models are used. Insight in actual exposure demands insight in its spatial and temporal variability and its variability in the general population, requiring adequate data sources. For soil and surface water, no adequate data sources were found, while relativily adequate data sources were found for food and consumer products. For air, a concentration time series could be constructed. B[a]P exposures compared with toxicological data indicated that limit values are exceeded for exposure via air and for dermal exposures due to products or soils with high B[a]P content. Although food is responsible for more that half of total intake, tentitative oral limit values are exceeded only occasionally.

Insights from the study are more general than the PAH example. Firstly, it appeared that individual exposures to consumer products or polluted soil may cause exposures that are high compared to background exposure. Secondly, it is concluded that spatiotemporal patterns in emission should be known to assess location specific exposures and effects. Finally, the present exercise provided insight in the variability of exposure, where possible as a function of age. This proves to be valuable to discern groups at high exposure.

Samenvatting

In het rapport wordt de vraag gesteld hoe emissies, verspreiding in milieucompartimenten, blootstelling en effecten van chemische stoffen aan elkaar gekoppeld kunnen worden om te komen tot een integrale risicoschatting. Centraal staat de vraag of de bestaande modellen en gegevensbronnen te koppelen zijn en of ze dan de hele bron-effektketen dekken. Om methoden concreet te beschrijven is gekozen voor een voorbeeldstof, de polycyclische aromatische koolwaterstoffen (PAKs). In het rapport wordt per onderdeel een overzicht van methoden en modellen gegeven dat vervolgens aan een PAK-voorbeeld toegelicht wordt. Het blijkt dat slechts voor benzo[a]pyreen en fluorantheen voldoende informatie beschikbaar was. Twee indicatoren, 10 van VROM en 6 van Borneff, zijn beschikbaar als indicator voor totaal PAK. Het gebruik van duidelijk omschreven standaard omgevingen en blootstellingsscenarios maken de programmas CSOIL, USES en EUSES tot goede gereedschappen om risico's door te lichten. Als actuele schattingen nodig zijn dan zijn deze programmas minder geschikt en komen modellen als AirPEx, STEM/FRIDGE, CONSEXPO en PBPK-modellen in beeld. Inzicht in feitelijke blootstelling vereist inzicht in ruimtelijke en temporele variaties van blootstelling en de variatie van blootstelling in de algemene bevolking, zodat adequate gegevens een vereiste zijn. De gegevens over PAKs voor bodem en water lieten te wensen over. Daarintegen werden voor voedsel en consumentenproducten relatief adequate gegevens gevonden. Voor lucht werd een concentratie-tijdreeks samengesteld uit monitoring gegevens en meetstudies in de stad. Als B[a]P blootstellingen tegen toxicologische gegevens aan gehouden worden wordt gesuggereerd dat grenswaarden voor lucht en voor dermale blootstelling aan producten en bodems met een hoog PAK gehalte overschreden kunnen worden. Alhoewel voedsel voor meer dan de helft van de inname zorgt, ligt de blootstelling rond een voorlopige orale grenswaarde.
De studie levert inzichten in de ketenbenadering op die algemener zijn dan de voorbeeldstoffen. Ten eerste blijkt dat individuele blootstellingen aan producten of bodems met hoge (PAK)gehalten kan leiden tot relatief hoge belastingen. Ten tweede wordt geconcludeerd dat ruimtelijke en temporele patronen in emissie bekend moeten zijn voordat lokatie specifieke blootstellingen en effecten geschat kunnen worden. Als laatste levert de studie inzicht in variabiliteit van blootstelling op, waar mogelijk als een functie van leeftijd. Dit maakt het mogelijk groepen met een hoge blootstelling te onderscheiden.

1. INTRODUCTION

When chemicals are suspected to cause health problems, exposure and hazard assessments should be performed to make a rigorous risk assessment. Exposure assessment should include the chain from emission to exposure as experienced by the human population. Several approaches have been taken at the RIVM to stepwise describe the process from emission to effect. The State of the Environment and Environmental Outlooks ('Milieubalans and Milieuverkenningen', see RIVM, 1996; 1997) describe the chain from emission to effect to monitor environmental status and to compare that to environmentals goals. Since most goals are defined in terms of environmental quality, these documents focus on emission and distribution in environmental compartments. The step to effects is bridged by relations between concentration in environmental compartments and human effects. It largely concerns the air compartment, for which most epidemiological studies have been done.
Another approach is the use of models for risk screening purposes. A number of models have been developed to describe fate of chemicals following emission. The models USES 1 (RIVM et al., 1994) and CSOIL (Van den Berg, 1995) were among the first. USES models fate of a chemical from emission to exposure, while CSOIL focuses on soil pollution and is based on chemical levels actually found in soil. USES recognizes the life cycle of a product and incorporates emission during both production and use. The successors of USES, EUSES (EC, 1996) and USES 2 (RIVM, 1998), also use life cycle emissions as a starting point to estimate environmental fate and human exposure.
Both approaches have their own domain of application with few links. Links are provided by some exposure models that have been developed to describe actual exposure, such as AirPEx (Freijer et al., 1997). These models are used both for regular risk assessments and for Environmental Outlooks and related documents. To find out which models and data exist to describe the chain from emission to effect and whether or not these provide a comprehensive picture, a number of experts were invited to cooperate on the subject. To pin down methods, polycyclic aromatic hydrocarbons (PAHs) were chosen as example chemicals because they cover a range of sources and exposure routes. Details on PAH risks will be reported in a separate document (Kroese et al., in prep.), here we will describe the methods, models and data sources that were used to carry out the exercise.
The present report describes available methods and data to follow sources, emissions, environmental fate, exposures to effects of chemicals within risk assessments at the RIVM. The chain from emission to effect is described first by the screening approach of USES and CSOIL, and second by more sophisticated models and data sources. Each part of the report first discusses general principles and then adds a specific example using PAH data.

2. THE CHEMICALS OR 'WHY PAHS AS A LEAD?'

2.1 The chemical and mixture under study

In order to explore the steps that are necessary to provide an overview of the emission-effect chain, a group of chemicals is chosen. Polycyclic aromatic hydrocarbons (PAH) were selected because

1. There are many sources of emission,
2. Measurements and monitoring data are claimed to be available for soil and air,
3. Exposure takes place via all routes,
4. Information on PAH was already gathered in a parallel project and that information could be used here.

Polycyclic Aromatic Hydrocarbons: background

Slooff et al. (1989) published the 'Basisdocument PAK' as a comprehensive document describing sources, distribution, and effects of PAHs as apparent at that time. For general and physico-chemical information on PAHs we refer to the basisdocument. The main general information from the basisdocument can be summarized shortly as follows.

Industrial processes, wood preservation, heating and indoor burning, mobile sources (traffic), and agricultural activities are the main Dutch sources and emissions. Smaller emissions are expected from e.g. preparation of food, and disposal of oil in the sewage. In addition to Dutch sources, PAHs enter the Netherlands via air, mainly from Great Britain and the German Ruhr-area, and water, mainly via the large rivers.

Emissions of PAHs occur to water, soil and air. Redistribution between these compartments occurs by mass transport in water and air, by deposition from air to water and soil, and by volatilization from water and soil to air. PAHs are degraded by physico-chemical processes and by organisms. In the soil, biodegradation is most important. For water and air physico-chemical degradation is most important, although significant biodegradation occurs in water.

An overview of environmental concentrations known upto 1988 is given in the basisdocument (Slooff et al., 1989: Chapter 4). Concentrations of PAH in soil, water and air are not uniform over The Netherlands. For soil and water, hot spots exist, where concentrations far exceed background. For air, it is important to consider the proximity to sources and to differentiate indoor and outdoor. Sites close to sources, for example streets with high traffic density, attain higher concentrations, while sites remote from sources, rural areas, attain lower concentrations. Indoor concentrations tend to exceed outdoor concentrations because a number of significant sources, smoking and fireplaces, occur indoor and ventilation is lower inside than outside.

2.2 Indicators and model chemicals

Complex mixtures such as PAHs exhibit a chemical diversity that hinders risk assessment of the mixture as a whole. Mixtures may consist of chemically similar components, such as polychlorbifenyls, dioxins and polycyclic aromatic hydrocarbons, or they may consist of chemicals that have no chemical similarity, such as exhaust gas or sludge. For complex mixtures, monitoring programs and measurements will necessarily capture only a few individual chemicals.

A subset of chemicals from a complex mixture could

1. serve as *indicator chemicals*. If a small set of chemicals is used as indicator, they serve to summarize exposure to the full group by a small selection. The selected set of chemicals should have a clearly defined relation to the full set, in the sense that high concentrations of the indicator imply high concentrations of the full set and vice versa. The chemical composition differs per environmental compartment and per source and one has to be aware that air has a different composition than, for example, food. An indicator therefore has to be constructed for a particular environmental compartment and a particular source. Sometimes, indicators are used in an abstract way, for example to indicate for 'traffic related pollution'. In the latter case, the full composition of the pollution is not specified
2. serve as *model chemicals*. In toxicologal research, few chemicals are studied intensively and the results are extrapolated to similar chemicals. When extrapolating the toxic action of a model chemical, the reasons for similarity of toxic action should be clarified. Quantitative structure activity relations are used for extrapolations based on chemical similarities and statistical relations (see for example Hermens and Opperhuizen, 1991).

For both indicator and model chemicals, the relevance of the chemical as an indicator or model chemical should be made clear.

Indicators and model chemicals in case of PAHs

For PAHs, it appeared customary to make the following choices for measurement in the Netherlands as indicated by various sources (e.g. Slooff et al., 1989; TCB, 1998; Van Velze, 1996). These represent existing measurement suites in The Netherlands.

1. Measurement of benzo[a]pyrene, being regarded as the most toxic of the PAHs.
2. Measurement of the sum of the 6 of Borneff: fluoranthene, benzo[a]pyrene, benz[b]fluoranthene, benz[k]fluoranthene, indeno[123cd]pyrene, and benz[ghi]perylene.
3. Measurement of the sum of the 10 of VROM: fenanthrene, antracene, fluoranthene, chrysene, benz[a]antracene, benzo[a]pyrene, benz[k]fluoranthene, indeno[123cd]pyrene, and benz[ghi]perylene. Selection criteria and discussion is found in Slooff et al. (1989).

Whatever choice is made from the above three, it is apparent that not all PAHs are taken into account. A selection of PAHs serves as either indicator or as model chemical. The following indicates the use of the above mentioned measurement suites.

1. Benzo[a]pyrene alone, the 6 of Borneff or the 10 of VROM are used as indicator and then they serve to summarize the exposure to total PAH by a small selection. The PAH composition differs per environmental compartment and per source and one has to be aware that air has a different PAH composition than, for example, food. Therefore, a PAH indicator has to be constructed for a particular environmental compartment and a particular source. Only the toxicological relevant PAHs for humans are taken into account.
   Van Velze (1996) proposes PAHs that may serve as indicator for traffic related air pollution. His best indicators for traffic pollution were benzo[e]pyrene, chrysene, and benz[a]anthracene. Also benz[a]pyrene appeared to be a reasonable indicator, certainly when carcinogenic potency is taken into account as weighting factor.
2. Benzo[a]pyrene is often used as a model chemical to study dose-effect relations for PAHs.

3. SOURCE-TO-EFFECT CHAIN

In line with the approaches chosen by Environmental Outlook, State of the Environment (RIVM, 1997) and EUSES (ECB, 1996), the route from sources to effect can be represented by the components sources, environmental fate, exposure, and effect (fig. 1). Consumer (and occupational) products escape environmental fate because they are transported to the site of use and pass, as product, environmental distribution. It is the so called 'direct' path of exposure, in contrast to 'indirect' exposure via the environment (EU, 1996). Sources and environmental fate are linked by location of source and subsequent distribution of chemicals over various parts of the environment. Environmental concentrations in air, water, and soil are linked to exposure by human contacts to them. Exposure is linked to effect by the dose rate derived from external exposure. The fate of a chemical inside the body connects the dose rate to concentrations in target tissue inside the body.
The environmental compartments comprise air, soil (and ground water) and water (and sediment) (Slooff et al., 1989; EC, 1996; Van den Berg, 1995), together with food and drinking water. The latter are not environmental compartments themselves, but are closely linked to one of the compartments. Although they are consumed, they are not consumer products, which refer to nonfood products. The routes of exposure comprise the inhalatory, dermal, and oral route. These routes define entries into the human body. Properties of the body boundary

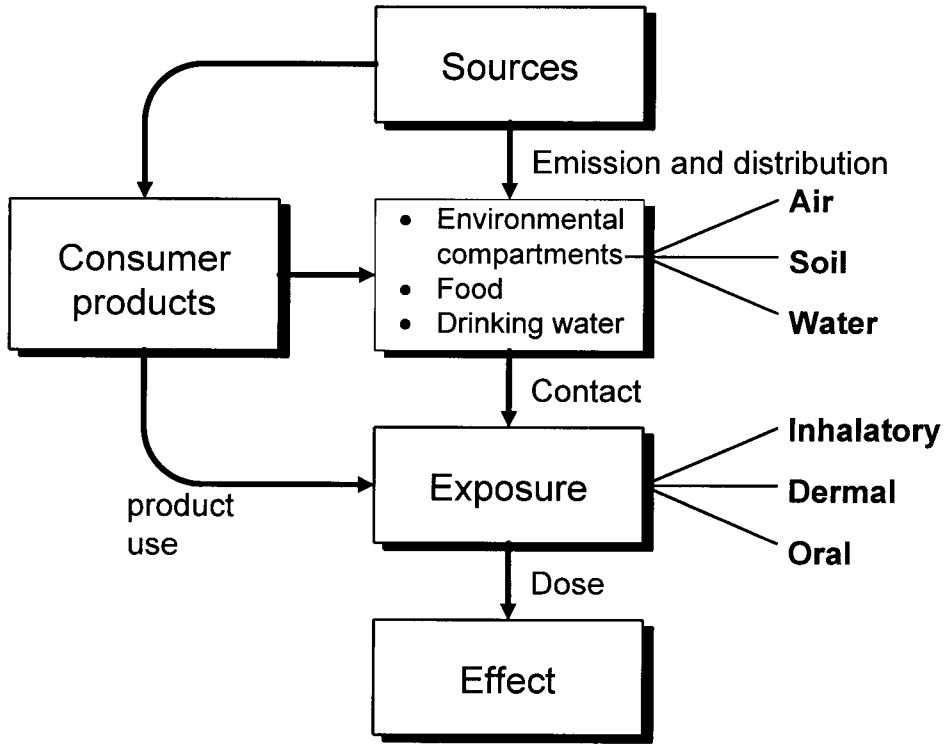

Figure 1. source-to-effect chain.

in the lung, the gastrointestinal tract and of the skin determine the absorption rate of the chemical and thereby dose rate.
A number of mathematical models are available to model parts of source-to-effect chain (Vermeire et al., 1997). Models that cover the entire chain are screening level models suitable for preventive risk assessment such as USES, EUSES and CSOIL. Assessments that aim at actual risks are more sophisticated and involve a suite of models which each cover only part of the chain and require more input data. For chemicals, Vermeire et al. (1997) mention CONSEXPO for consumer exposure, AirPEx for air pollution, and STEM for food exposure, while Slob and Pieters (1997) present a probabilistic model for deriving human intake limits. These models are to be used together to cover environmental compartments, exposure, and effect.

The source-effect chain can be approached from two points of view.
1. Risk assessment. For assessment of risks, it is essential to know exposure to the chemical, uptake and effects. Exposure can either be measured by personal monitoring or it can be estimated from the environmental concentrations. Risk assessment focuses on the exposure and effect parts of the source-to-effect chain.
2. Risk reduction. Reduction may aim at reductions in environmental immisions and at reduction during product use. To reduce environmental risks, knowledge of sources and emissions and their contribution to concentrations in environmental compartments is essential in addition to risk assessment. Emission sources should be characterised by type and rate, in order to prioritize actions. Risk reduction by interfering with environmental levels focuses on the sources and environmental compartments, the first part of the source-to-effect chain.
   To reduce risks during product use, measures can be taken that focus directly on exposure, for example the concentration of a chemical in a product or the amount released by the package. These risk reduction measures focus on consumer products and the exposure part of the chain.

The two points of view are part of the same approach, including the full chain. Effective risk reduction should ideally not be decided upon without risk assessment, because risks need to be described and assessed first before reduction measures will be effective in terms of costs and results.
In the following, the route through the source-effect chain will be exemplified for PAHs. All information on PAHs available at 1988 has been incorporated in Slooff et al. (1989). An update to that information will be given in the 'evaluation document PAH' (Kroese et al., in prep.). Here, focus will be on data and model sources used and relation between source, environmental distribution, exposure and effect.

3.1 Screening the route from source to exposure

The Uniform System for the Evaluation of Substances USES (RIVM et al., 1994, version 1; RIVM, 1998, version 2) and its European branch the European Union System for the Evaluation of Substances EUSES (ECB, 1996) quantify risks of chemicals for humans and the environment. Likewise, CSOIL (Van den Berg, 1995) quantifies risks pertaining to soil. USES and EUSES both calculate environmental exposure, exposure of humans through the environment, worker exposure and consumer exposure. Predicted exposures finally result in a margin of safety, when they are compared to no-effect or lowest-effect dose levels. CSOIL

only calculates the risks due to soil pollution and use of the polluted area. It results in a predicted intake of contaminants as long-term average daily dose and is used to derive human toxicological limit values for soil concentrations in mg per kg dry matter.
USES and EUSES rely on a number of scenarios. Their world consists of three spatial scales: continental, regional and local (fig. 2). The continental scale encompasses a territory such as the European Union or Europe. The regional scale encompasses a region like a country or larger part of a country. The risk assessment for the regional scale uses steady state concentrations in a standard environment taking into account release of the chemical followed by distribution. On the local scale, substances released from point sources are assessed for a standard local environment, being a hypothetical site embedded within the regional scale.
CSOIL is also a scenario based model, but has no spatial scales other than the local area. It calculates first the partition of a chemical over the phases in the soil (solid, fluid and gas), then calculates concentrations in contactmedia and exposure to those contactmedia, and finally calculates intakes and human toxicological limit values for soil.
The USES approach has recently been compared by Guinée et al. (1996) to methods applied in life cycle assessment (LCA). Essentially, LCA assess chemicals from a single product in order to characterize the impact of a product. On the other hand, USES assesses a chemical which may be released from multiple products in order to characterize the impact of a chemical. Both, however, try to incorporate emissions during the full life cycle of one or more products and use these emissions to characterize exposure and risk. Guinée et al. (1996) explore the similarities of USES and LCA, and propose a mechanism to use USES for LCA types of assessments. A main difficulty is that LCA considers multiple chemicals which may act on widely diverging time scales with respect to distribution, exposure and effects.
The use of clearly described standard environments and exposure scenarios make CSOIL, USES and EUSES excellent tools for screening risk assessment. Where actual exposures and risks are needed, these programs are less suitable. Insight in actual exposure demands insight in spatial and temporal variability of exposure and analysis of exposure distributions in the general population. Because of the use of standard scenarios and spatially and temporally averaged concentrations, USES, EUSES and CSOIL cannot easily be used. Rather, a more accurate description of emission, distribution and exposures through the inhalatory, dermal and oral route is necessary, as explored in the remainder of this chapter.

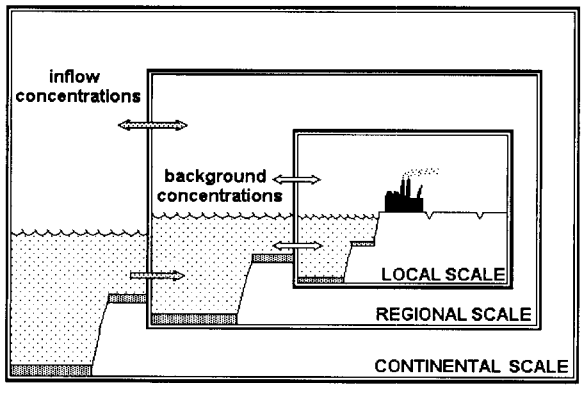

Figure 2. The spatial scales of USES and EUSES and their exchange of chemicals.

PAH example: Screening estimations

Mennes et al (1995a) and Teewisse and Van den Hout (1996) use USES to screen emission and distribution of and exposure to benzo[a]pyrene. Likewise, Vissenberg and Swartjes (1996) use CSOIL to screen risks of benzo[a]pyrene pollution of soil. Both Mennes et al. (1995) and Teeuwisse and Van den Hout (1996) only consider exposure through the environment, and not through consumer products. Mennes et al. (1995a) strictly adhere to the standard USES approach and they only use additional emission estimates for B[a]P. For the regional scale, the estimated intake of B[a]P is 62.9 ng/kg bw/day. Total intake is dominated by intake of 'plant roots' such as potatoes, which accounts for 70% of total intake. Intakes of meat and milk each account for another 10%. Intake by the inhalatory route is minor, accounting for only 0.02% of total intake. The estimate for the local scale, simulating an anode bakery, refers to a specific local exposure scenario and it is, consequently, much higher than the regional estimate, 16.42 mg/kg bw/day. For the local scale, plant shoots, meat, and milk account for nearly 100% of total intake.

The exercise of Teeuwisse and Van den Hout (1996) takes the regional scale of USES as a starting point, and suppletes it with data on lifestyle and refined calculations on air quality. Lifestyle was quantified in terms of time-activity patterns and food consumption. Time activity patterns define where someone resides and their level of exertion. Food consumption data were derived from the food consumption survey (WVC and LNV, 1988) and attributed to the 7 food categories discerned by USES. Teeuwisse and Van den Hout (1996) estimate total B[a]P intake to be 83 ng/kg bw/day, suprisingly comparable to the regional scale result of Mennes et al. (1995a). Teeuwisse and Van den Hout (1996) also conclude that food is the main route of intake, while air accounts for a minor part of intake. The fact that exposure via air is marginal and their food consumption is not too different from the default USES assumptions will explain the similarity of the Teeuwisse and Van den Hout (1996) and Mennes et al. (1995a) estimates. Food intake and mobility of people do not appear to be discriminative for exposure to B[a]P.

Vissenberg and Swartjes (1996) perform sensitivity analysis of CSOIL and take benzo[a]pyrene as model chemical. Departing from soil with 1110 mg per kg benzo[a]pyrene, a median intake of 2.8 and a 95 percentile intake of 7.4 μg per kg bodyweight per day is calculated. Total intake is dominated by ingestion of soil (84%), at distance followed by consumption of crops from polluted soil (10%).

3.2 Sources and emission

Emissions may occur during the whole life cycle of products. The life cycle consists of the stages production, formulation, processing, private use and waste/recovery. The relevance of each stage in the life cycle depends on the intention of the production. If a substance is produced on purpose, all life stages may be relevant. However, if a substance is produced as a byproduct which is immediately released, various life stages as processing and private use, may not be relevant because the substance does not reach that stage.

Table 1. PAH emissions (Emissieregistratie Nederland, 1997) during 1995 in the Netherlands in tonnes per year.

	Air	*Water*	*Soil*
10 of VROM	1130		
6 of Borneff		25.7	26.6
benzo[a]pyrene	5.9	3.17	1
fluoranthene	103	16.7	21.8

During production stage, the substance is synthetised from its constituents. If produced on purpose, production may involve substantial quantities at chemical plants under controlled circumstances. If the substance is a contaminant or a byproduct, it may emerge anywhere, and not always under controlled circumstances.
During the formulation stage, a number of substances are mixed to arrive at the formulation. The formulation is typically a raw product, that needs to be processed further. During the processing stage, the formulation is processed to get the final product. Processing may involve the process from the blending of raw materials to the final shaping of a product. At the moment a product leaves the processing stage, it is ready to be used. The private use stage includes the use of products by workers and consumers. The waste stage is entered when products are disposed of, enter landfills and incinerators or are recovered.
General data sources for emissions are the database of the emission registration (see Emissieregistratie Nederland, 1997) at LAE (Laboratory for Waste Materials and Emissions, RIVM), substance monographs (eg Slooff et al. (1989) for PAH and monographs produced as a result of the European Union and OECD existing substances programs), and RIVM (1997). EUSES (EC, 1996: appendix IV; Van der Poel, 1997) uses default emission tables to estimate emission per industrial category and use category. Industrial categories designate where the substances and products are produced, including typical production processes. Use categories designate how products are used, including typical use environments.

PAH sources and emissions

To exemplify how sources are designated and how their emission rates are estimated, an overview of PAH sources is given. Emissions strengths are coarsely estimated, using the summary measures 10 of VROM and 6 of Borneff, supplemented with detail on benzo[a]pyrene and fluoranthene only. The emission database allows for a further specification of the summary measures. The sources are summarized in categories as used by RIVM (1997) and a further specification of these categories is potentially possible.

Table 2. Emissions to air during 1995 differentiated according to target groups in the RIVM emission database. For each target group, the category accounting for most emission is separated out, and its contribution is set in parentheses in the emission columns.

Target group	*main category*	*10 VROM tonnes*	*Fluoranthene tonnes*	*Benzo[a]Pyrene kg*
Waste disposal		0.196	0.0105	0.95
Construction	Creosoted wood	292 (197)	30	47 (28)
Consumers	wood burning	85 (83)	16 (16)	2800 (2800)
Energy	natural gas production	6.5 (2.8)	0.212	25 (11)
Trade, tertiary sector, and government	(un)loading and transfer	4.2 (3.1)	0.024	2.2 (0.010)
Industry	cokes and steel industry; wood and furniture industry	348 (224)	30 (16)	950 (490)
Agriculture	glass warehouses	1.4 (1.3)	0.0025 (0.0024)	0.16 (0.15)
Traffic and transport	road traffic	393 (380)	27 (13)	2100 (1700)

The emission registration (Emmissieregistratie Nederland, 1997) estimated PAH emissions to air, water and soil (table 1).Differentiation of the emissions to surface water is reported by Wagemaker and Verstappen (1997) for the 6 of Borneff. They estimate that road traffic (18%), atmosferic deposition (23%), and inland shipping (50%) constitute the main sources of emission to surface water, in increasing order of importance. The emission database reports that 65-82% of the PAK emission consists of fluoranthene.
The emission database enables differentiation for emissions to air (table 2). Emissions of the 10 of VROM are dominated by three sources, being building activities, industry, and traffic/transport, in increasing order of importance. This top 3 of emissions is also valid for fluoranthene. Benzo[a]pyrene exhibits a different pattern of emission where consumers and traffic/transport dominate emission. Table 2 also lists the main source of emission within a category, which makes up 43-97 % of all emissions within the category. The energy category appears to be the most divers, and production of natural gas makes up 43 % of the emissions. On the other hand, emissions in the consumers, agriculture, and traffic and transport categories are dominated for more than 90% by a single source. The latter categories all cause diffuse emissions by e.g. cars. For benzo[a]pyrene, large consumer emissions are attributed to use of fire places and burners, which account for as much as 99% of the consumer emission (RIVM, 1997). Other consumer emissions, due to use of consumer products, appear to be minor and will be given in more detail in the paragraph on consumer products.

3.3 Environmental compartments

Air, soil, and surface water comprise the environmental compartments (fig. 3). The environmental compartments are all interconnected, and chemicals will be exchanged by diffusion and advection. The soil and air compartment are connected to food. The soil compartment because chemicals are taken up from the soil by animals and plants, the air compartment because material and chemicals in air deposit on plants which are subsequently taken up by those plants and the animals feeding on them.
Direct information on the levels of chemicals in the environmental compartments can be gathered by monitoring systems that regularly measure a predefined set of chemicals. Levels of 'hot spot' areas, for example soil pollution areas, are measured when they (are suspected to) form a problem. The latter levels presumably represent the upper limit of environmental levels.

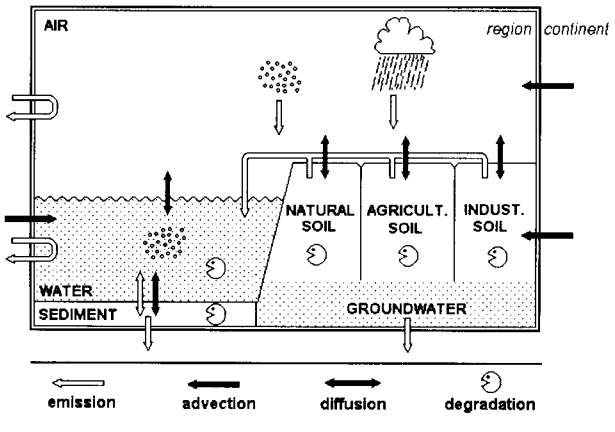

Figure 3. Schematic overview of the environmental compartments and their exchange of material.

Air

The air compartment comprises that part of the atmosfere that is in reach of humans. It is a heterogeneous compartment, with spatially and temporally fluctuating levels of chemicals. Environmental monitoring reveals levels of selected chemicals on a coarse grid in The Netherlands and is performed by RIVM and TNO (see Slooff et al., 1989). The LML (Landelijke Meetnet Luchtkwaliteit, LLO/RIVM, see Buijsman and Stolk, 1995; LLO, 1997) monitors at a number of sites in both rural and urban areas. To predict air concentrations from emissions and environmental conditions, the OPS-model (Operationeel Prioritaire Stoffen Model; Van Jaarsveld, 1995) estimates outdoor concentrations based on emission rates and climatological data on a spatial resolution of 5x5 km^2.

Spatial and temporal variability of levels of airborne chemicals necessitate an approach where levels in the air compartment are a function of time and space. Monitoring programs typically deliver measurements that are averaged over 15 minutes (ozone) to 24 hours (PAH, Particulate Matter). Where averaging times over 24 hours are used, within day variability is masked completely. In order to cope with spatial variability, the air compartment is commonly subdivided into micro-environments (Ryan et al., 1983; Freijer et al., 1997). Each microenvironment is supposed to represent a spatially homogeneous environment, retaining temporal variability. Using microenvironment models allows for an estimate of personal exposure. Personal exposure can exceed the mean environmental concentration if concentration peaks co-

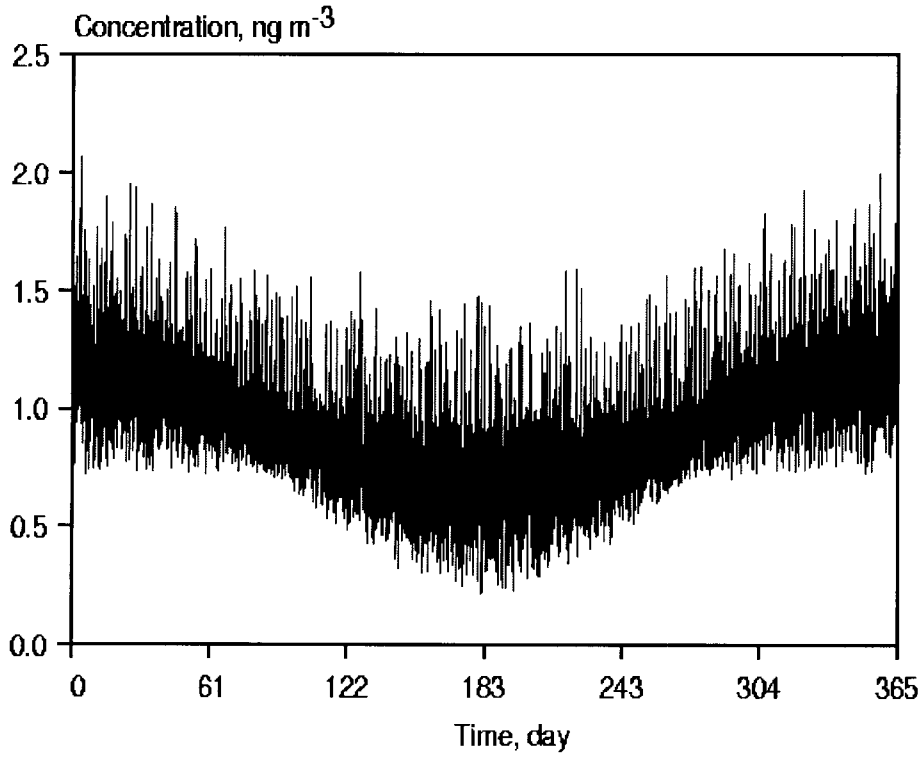

Figure 4. Hypothetical time series of B[a]P in urban areas generated by Freijer and Bloemen (pers. comm.) from measurements reported by Van Velze (1996), LLO (1997) and SAVIAH.

incide with someone being there when a peak occurs. Figure 4 shows that such concentration peaks are expected to occur (see also Van Velze, 1996).
The contribution of traffic to outdoor contaminant levels, especially in urban areas, has been given considerable interest and is taken into account by various (inter)national studies in urban areas, such as SAVIAH (Fischer, pers. comm.), Van Velze (1996), and EXPOLIS. The CAR (Vissenberg and Van Velze, 1998) and CAR Parking (Gofferje, 1997) programs estimates air concentrations resulting from traffic, using parameters like car density, speed, composition of cars, wind &c. These models are able to predict levels at a timescale in the order of minutes to days, depending on the dynamics implemented in the model.

PAH in air
Historical and recent time series of B[a]P concentrations with a high temporal resolution are not available for the Netherlands, because measurements have been taken at a limited number of locations with a coarse resolution. To assess exposure to airborne PAHs, a time series has been composed following the approach of Janssen et al. (1997), who use seven 'rules of thumb' to estimate the distribution of PM_{10} in The Netherlands. The present exercise uses results from Van Velze (1996), LLO (1997), and the SAVIAH project to generate a B[a]P time series that compensates the lack of historical and actual data with a one hour time resolution. These reports show that, in the Netherlands, rural concentrations of B[a]P are in the range of 0.1-0.25 ng/m^3, urban concentrations are in the range of 0.2-0.4 ng/m^3, and along roads concentrations are in the range of 0.4-2.0 ng/m^3. Because B[a]P emissions increase during winter due to heating, B[a]P concentrations in winter will exceed those of summer by a factor two. In addition, a significant daily rise of benzo[a]pyrene levels is caused by the rush hour in the morning (Van Velze, 1996). To be able to use environmental monitoring data for exposure analysis, the daily pattern of Van Velze (1996) was superimposed on the 24 hour averaged PAH measurements. Further, seasonal variation was superimposed on this daily sequence by using a sine function that sets winter level to twice the summer levels. Finally a B[a]P time series was constructed for urban areas (fig. 4) which includes both daily and seasonal variation. This procedure to obtain a time serie of sufficient time resolution is not optimal, rather one hour measurements throughout the year in both urban and rural environments are needed. The generated time serie should be handled with care and be validated.
Indoor concentrations of B[a]P due to outdoor emissions are often much lower than outdoor concentrations. Measurements in the context of the SAVIAH project in nonsmokers homes reveal an indoor/outdoor ratio of 0.5-0.6. Indoor sources may elevate the indoor concentration of B[a]P beyond outdoor concentrations. For example, smoking causes indoor background concentrations of 3-20 ng/m^3 and while using fire places, B[a]P concentrations may rise to 13-370 ng/m^3 (Slooff et al., 1989).

Soil and groundwater
To interpret chemical levels in soil, it has to be taken into account that there are different types of soil, which differ in use. EUSES (fig. 3; EC, 1996) classifies soil according to land use into natural, agricultural, and industrial soils. Such a division is not set in the CSOIL model (Van den Berg, 1995). Bockting et al. (1994) propose to differentiate soils towards their use, and recognize urban-centre, urban-residential, industrial, cultural, traffic, parks, recreation, agricultural, and natural areas. Then, they apply the CSOIL modeling framework separately for each type of soil. The Environmental Outlook 1996 (RIVM, 1996) reports PAH-levels in soils in agricultural and urban areas, and background concentrations derived from natural areas.

Contaminants in soil can be taken up by crops and cause exposure by eating the crops (EC, 1996; Van den Berg, 1995; TCB, 1998). The relevance of this route for PAHs is under discussion (see TCB, 1998).

PAH in soil
PAH levels in soil are mostly determined at contaminated sites. Measurements cited by Slooff et al. (1989) show that contaminated soil exhibits widely varying PAH levels ranging from the level normally found in industrial soils upto levels that a factor 100 higher. Elevated PAH concentrations in agricultural soil will cause elevated concentrations in agricultural products, both from animal and from vegetable origin. The EUSES program (EC, 1996) differentiates products with animal origin into dairy products and meat; products with vegetable origin are differentiated into leaf crops and root crops. It calculates the expected concentrations in these food items from the agricultural soil concentrations. The TCB (Technische Commissie Bodembescherming, 1998) concludes exposure to PAHs through uptake by crops is only marginal.
In a study to the PAH burden of young children, the relation between 1-hydroxypyrene and PAH levels in front and back gardens of houses in former coal mining areas was part of the investigations (Slob et al., 1993; Van Wijnen et al., 1996). Although gardens revealed elevated PAH levels, no relation between PAH levels and urinary 1-hydroxypyrene was found, indicating that local soil contamination might not be an important factor in PAH exposure.

Water and sediment
Dutch surface water and sediments are monitored by DBW/RIZA and Waterschappen. The Inspectie Milieuhygiene (IMH) initiates specific research where appropriate (see Van der Berg, 1998). Long term monitoring data exist for the main rivers (see for example Slooff et al., 1989). Rivers and streams that enter the Netherlands are substantial sources of chemicals (see the example of Van der Berg, 1998, for PAH), importing these from abroad. No models exist to predict water and sediment concentrations other than equilibrium partitioning models such as SIMPLEBOX (Brandes et al., 1996) and the models present in EUSES (EC, 1996).

PAH in water and sediment
Slooff et al. (1989) remark that the spatial distribution of PAH levels is largely determined by hydrodynamic factors. This indicates that there may be significant heterogeneity in water PAH composition and levels.
Van der Berg (1998) formulated a PAH mass balance for surface water and sediments in a specific area in West-Brabant (The Netherlands). Important input factors appeared to be atmosferic deposition and leaching of PAHs from PAH containing materials, together accounting for 80-86% of input. The most important output for surface water is sedimentation, accounting for 57-66% of total output. For sediments, PAH levels steadiliy increase due to sedimentation rates exceeding degradation rates.

3.4 Consumer products

Consumer products do not fit neatly in the emission-effect chain (fig. 1), because they are transported as product and cause emission of their chemicals close to users or bystanders. Therefore, they cause direct exposures bypassing environmental distribution. Emissions originating from consumer products may eventually reach the environment by waste or by drift from the site of use. Emissions and exposures from consumer products are modeled by

Van Veen (1997), while at LBO data are gathered about typical and worst case product use and emissions.

PAH in consumer products
PAHs are not regularly encountered in consumer products. They appear on purpose, as contaminants or are formed during use of the product. Meijer et al. (1992) investigated 12 consumer products for contamination with PAHs and found 2 positive products: shoe polish and furniture wax. In laserprinter and copier toners, no PAHs were detected. They traced PAH contamination in positive products to the solvent used for the product, containing naphtalene as the dominant PAH. A full inventory of consumer products containing PAH contamination is difficult to assemble, because PAHs tend to disappear from products when that fact attracts public attention.
Products that contain PAH on purpose are creosote paints, roof tiling products, mothballs, coal-tar shampoos and coal-tar ointments. Creosote is freely available, but it is predominantly used for agricultural applications (Oostergo, 1993; Broekhuizen, pers. comm. 1997). It causes human exposure during application to wood and subsequent processing of creosoted wood and cause environmental exposure during application and by leaching from creosoted wood outdoors. Roof tiling is done with products based on coal tar and bitumen. The former contain high levels of PAHs, but their use ceased in the mid eighties. The latter, bitumen based products contain low levels of PAH, upto 10 mg/kg measured as the sum of 9 PAHs (Eleveld en Toes, 1992; Concawe, 1992). Some mothballs contain naphtalene, which are used in wardrobes and, by some, in scientific collections of dead animals.
Coal-tar shampoos and ointments have mostly medical applications and products with elevated coal-tar levels are registered pharmaceuticals. These registered products may contain 7,5 g coal-tar per kg product, where coal-tar has a PAH content upto 50%. Coal-tar shampoos with low concentrations of PAH are freely available on the market (Consumentengids, 1995).

3.5 Exposure

Environmental and consumer product levels are not equivalent to exposure, because exposure involves humans in contact with environmental compartments and consumer products (Ott; 1984; Ryan, 1991; Van Veen, 1996). Because people vary in the way they contact environmental compartments and consumer products, their exposure will vary, even when in contact with, e.g., the same consumer product. Contact includes a spatial and a temporal component (Van Veen, 1996): it is essential to know where and when contact takes place in order to know exposure.
Exposure may follow the inhalatory, dermal and oral route. For the inhalatory and the oral route, chemicals are typically taken in with a medium like air or water. For the dermal route, no intake appears. Rather, a matrix contacts the skin and chemicals within the matrix have to migrate into the body. Where multiroute exposure occurs, the question how to integrate exposure and intake arises. Answering this question requires route-to-route extrapolation that involves elements like metabolism and the fraction of the chemical taken up via each of the routes.

Inhalatory
To estimate inhalatory exposure, Airpex (Freijer et al., 1997) is available as a modeling tool, which is able to use outdoor concentration time series and human time-activity patterns as input data. Airpex estimates several micro-environmental concentrations from a single main concentration time series and calculates personal exposures from the time spent in each mi-

croenvironment. Because exposures are calculated per capita and each person has a specific time-activity pattern, an exposure distribution represents population exposure. By specifying background concentrations, indoor sources can be taken into account by Airpex.
Specific indoor emissions by consumer products and subsequent exposure levels are modeled by CONSEXPO (Van Veen, 1997). At the moment, exposures to evaporating chemicals and chemicals emitted as gas from a source can be described in CONSEXPO.

Inhalatory exposure to PAHs
To calculate inhalatory exposure, B[a]P was selected as indicator. The air quality time series of B[a]P was generated from a number of studies (see paragraph 3.3 and fig. 4). The human time-activity patterns were taken from the Intomart database (see Freijer and De Loos, 1997). The time-activity patterns contain information on the micro-environments that people visit and the level of exertion during their visit. The exertion level is used to calculated the inhalation rate in a particular micro-environment, in order to allow for spatial variability of intake rates. No use was made of the CONSEXPO models, instead background concentrations were defined in Airpex.
To characterize exposure, a scenario-approach was used to capture the variability in potential exposures. It is expected that much of the variability is due to the type of outdoor environment and the presence of indoor sources. With respect to the former, a division in industrial, urban and rural areas is expected to capture most of the differences in air concentration because emissions into these areas differ markedly, for instance because traffic intensity differs. Indoor sources may significantly increase total exposure because people spend most of their time indoors. Passive smoking was added as the most important indoor source in a low and a average importance scenario. Another indoor source, fire places, was left out of the scenarios. Finally, the following scenarios were set:

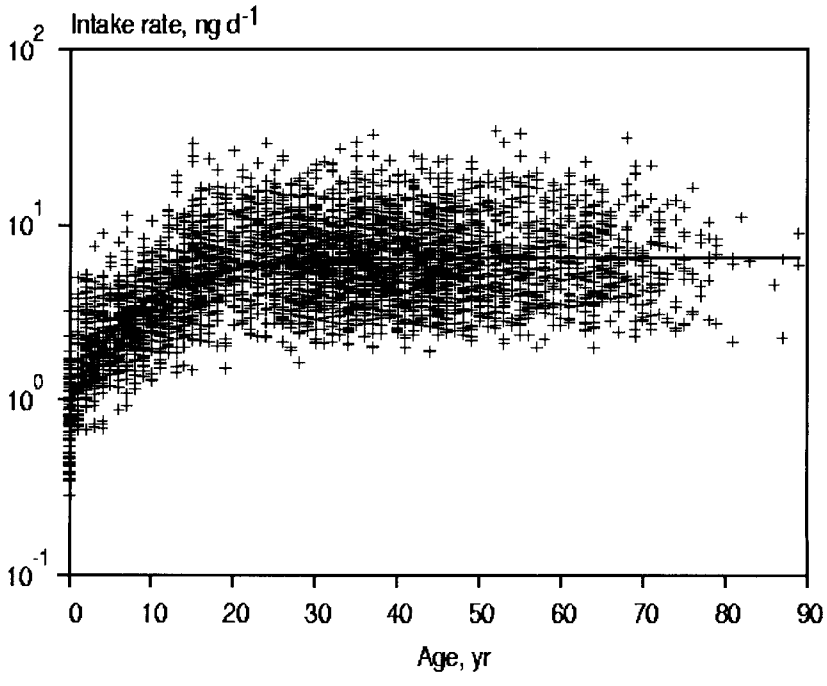

Figure 5. Inhalatory intake rate of B[a]P according to scenario 1 as calculated by Airpex using the B[a]P times series presented in figure 4.

1. Exposure of the total Dutch population;
2. Exposure of the Dutch population living in a industrial urban environment;
3. Exposure of the Dutch population living in an urban environment;
4. Exposure of the Dutch population living in a rural environment;
5. Exposure of the total Dutch population including a low indoor background due to passive smoking;
6. Exposure of the total Dutch population including an average indoor background due to passive smoking.

The intake rate of B[a]P for scenario 1, representing the total Dutch population, is given in figure 5 and amounts to 3-30 ng/day, for a 70 kg person 0.043 to 0.43 ng/kg bw/day. There are no direct measurements for personal exposure to PAHs available at the RIVM to validate these calculated intakes. The other scenarios are calculated likewise, but are not reported here (see Kroese et al. in prep.).

Dermal

Dermal exposure will occur to a variety of matrices containing chemicals. These matrices include soil, aquatic soil, water, dust, and consumer products. Dermal exposure and uptake depends on diffusibility of a chemical within the matrix, volatility of the chemical, concentration gradient of the chemical over the skin and skin permeability (see Hadgraft, 1985; McKone, 1990; ECETOC, 1993; Van Veen, 1995). McKone (1990) identifies volatility and octanol-water partition coefficient as sensitive parameters in dermal uptake. Chemicals with high volatility evaporate before being taken up. Chemicals with a octanol-water coefficient above 10^6 do not pass the watery parts of the skin. In addition, contact parameters like duration of contact and amount of matrix on the skin determine the uptake fraction (Burmaster and Maxwell, 1992; Van Veen, 1996).

Dermal exposure to chemicals in soil is modeled by CSOIL (Van der Berg, 1995). This model takes soil concentration as input, adds assumptions on the contact and uptake rate and calculates uptake. Dermal exposure to chemicals in all kinds of matrices, especially consumer products, is modeled by CONSEXPO (Van Veen, 1997). CONSEXPO models both external exposure and uptake. The 'diffusion in product' model of CONSEXPO includes diffusibility and volatility of the chemical. The diffusional uptake model uses the diffusion gradient over the skin and the skin permeability to estimate uptake.

Dermal exposure to PAHs

Only few studies are available to estimate dermal exposure to PAHs in environmental compartments. Measurement data on PAHs in body suits of wind surfers and urinary excretion of the PAH exposure marker 1-hydroxypyrene show dermal exposure to PAHs in surface water (Van Weerdt, 1990). It is difficult to quantify intake due to this exposure. Skin permeability, duration and frequency of wind surfing will be needed in order to quantify actual exposure to and uptake of specific PAHs via this path.

McKone (1990; McKone and Howd, 1992) presents a model to estimate dermal exposure and uptake by contacting soil. Burmaster and Maxwell (1991) use this model to estimate uptake of benzo[a]pyrene, naphtalene, phenanthrene, fluoranthene, and indeno (1,2,3-cd)pyrene from soil. For naphtalene and phenathrene the predicted fraction taken up is about 10% to 20% of the administered amount. Neither time nor soil loading appear as sensitive parameters. In contrast, predicted uptake fractions of benzo[a]pyrene, fluoranthene, and indeno (1,2,3-cd)pyrene reach 100% in due course of time, and time and soil loading are sensitive parameters for dermal uptake. Measurements for benzo[a]pyrene show a fraction taken up of 1.4% (in vitro, human) to 13.2% (in vitro, rhesus monkey) in 24 hours of exposure (Wester et al., 1990). Addi-

tional experiments (Wester et al., 1993) show 1.4-8.4% (in vitro human) and 9.2 to 13.2% (in vivo, rat) uptake in 24 hours of exposure.
Consumer products with a potential for dermal contact and which contain a significant amount of PAHs on purpose are creosote for wood preservation, coal-tar products for medical use (shampoo, ointment), and roof tiling based on bitumen or asphalt. The latter are hardly used in the Netherlands anymore, removing roof tiling as a significant source of exposure. Mennes et al. (1995b), using CONSEXPO, and Van Rooij (1995), using pyrene as biomarker, report a risk assessment for coal tar shampoo. These shampoos reach a content of 285 mg/kg pyrene and 56 mg/kg B[a]P, and those distributed as pharmaceutical products may have higher concentrations. In a supplement to Mennes et al. (1995), Van Leeuwen (1995) estimates a local exposure concentration between 0.6 and 7.6 ng/cm^2, in accordance with the estimate of 2 ng/cm^2 of Van Rooij (1995). The systemic dose is estimated to be 34 ng/kg bw/day (Van Rooij, 1995) to 60 ng/kg bw/day (Mennes et al., 1995b). Pharmaceutical coal-tar products like ointments are probably even more important sources of PAHs exposure, because these products are for use on damaged skin, which has a higher permeability. No quantitative risk assessment for these products is known.

Oral

Essentially, exposure to chemicals in food can be gathered by two main methods. Firstly, intake can be calculated by merging the concentration of a chemical in every possible food item with the composition of the diet. Slob (1993a; 1993b) developed a statistical method to calcu-

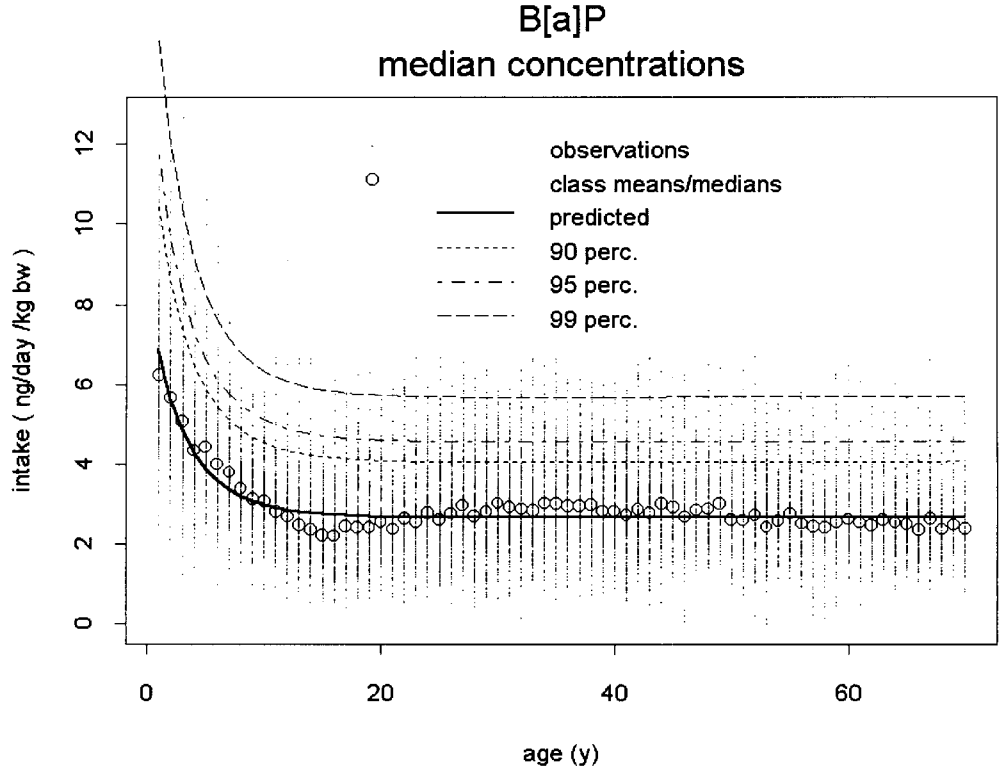

Figure 6. Distribution of dietary intake of benzo[a]pyrene in the general Dutch population, using median concentrations in food.

late food exposure from concentration data and diet composition, which also reveals intra- and interindividual variations. To apply this method, data on food consumption and data on concentrations of chemicals in food are needed. The dietary composition has been investigated by WVC and LNV (1990) and the MORGEN project at the RIVM (see the summary of Heisterkamp and Olling, 1996). With respect to food concentrations, several monitoring programs are running. RIKILT-DLO maintains a database with residues of several chemicals in food and the RIVM performs analysis of food concentrations of contaminants. RIKILT-DLO reports annually, e.g. Van Klaveren (1995).
A second and more direct method to obtain the intake of a chemical is to perform a duplicate diet study, as e.g. reported by Vaessen et al. (1995) for the Netherlands concerning amongst other chemicals nitrate and nitrite, PCB's, several pesticides and migrants from packaging material.
For both methods, the impact of food preparation should be taken into account. For duplicate diet studies, it means that the prepared food should be sampled. For the statistical calculation method, it suggests that concentrations in food should be calculated after preparation.

Oral exposure to PAHs
The intake of PAHs is exemplified by calculations for benzo[a]pyrene and fluoranthene. The data needed to calculate dietary intake are food consumption's patterns and measurements of contaminant levels in food items. Food consumption in the Netherlands is well known by the

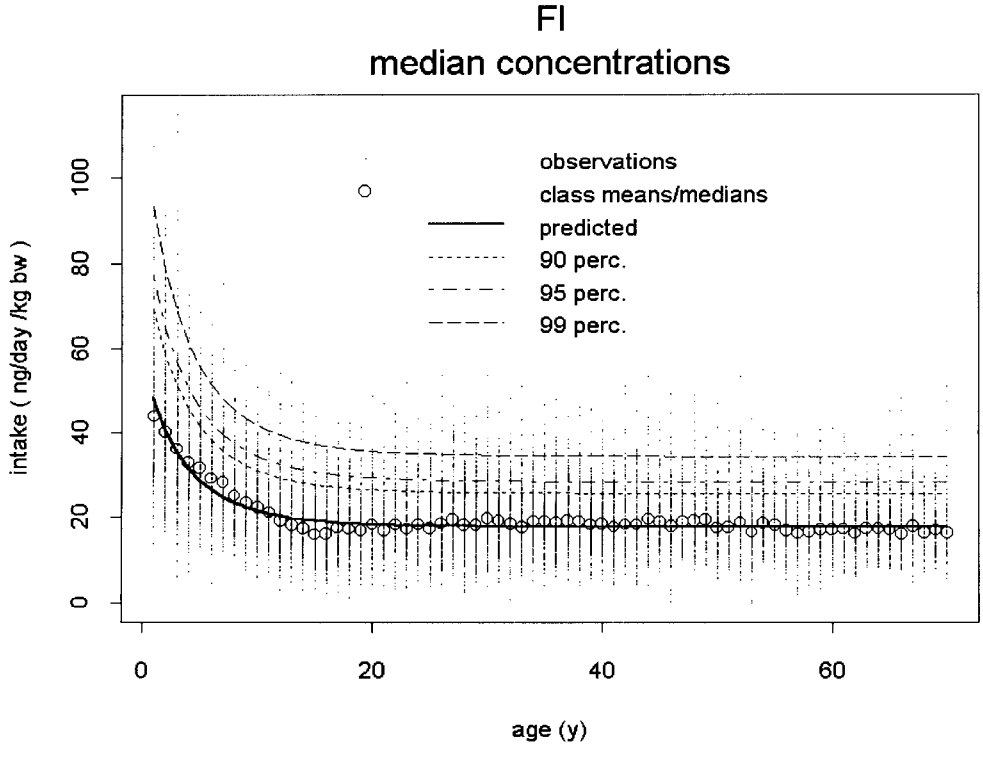

Figure 7. Distribution of dietary intake of fluoranthene in the general Dutch population using median concentrations in food.

national food consumption survey (WVC and LNV, 1990), although consumption of people keen on specific products might be underestimated by this survey. The food consumption survey does not take breast feeding and bottle milk into account, and is thus useful from 1 year of age. Measurement of PAH-levels is a bottleneck, because not all PAHs are being measured in a sufficient number of food items. De Vos et al. (1990) review PAH levels in food items. Additionally, PAHs were detected in seafood (Vaessen en van der Kamp, 1988); in baked or grilled meat (Vaessen et al., 1988); in cooking oil (Vaessen en Wilbers, 1989); in cabbage from home gardens (Vaessen et al., 1989) and in dried subtropical fruits (Vaessen et al., 1991). A calculation of the intake of benzo[a]pyrene (fig. 6) and fluoranthene (fig. 7) is reported by Heisterkamp en Van Veen (1997). Because per capita calculations are made, intra- and interindividual variances are retained in the study. In addition, age is included as a co-variable. As a result, a distribution of intakes as a function of age is calculated, allowing percentiles of intake to be estimated. Both figure 6 and 7 show that PAH intake of children at the age of 1-2 years, standardized to body weight, doubles that of adults. This is due to partly a larger intake of food per kilogram body weight, and partly the lower body weight itself. From the age of 15 onwards, PAH intake is a stable figure.
Not all PAHs can be extracted from their matrix once they arrive in the gastrointestinal tract. Unpublished research at RIVM/LBO (Sips, pers.comm.) using an *in vitro* digestion model shows that only 15-22% of the benzo[a]pyrene in contaminated soil becomes available in the gastrointestinal tract. The experiments make use of an *in vitro* digestion model which determines the fraction of a chemical that is expected to be released from its matrix in the gastrointestinal tract. The model simulates the tract by three treatments, the first simulating saliva, the second simulating the stomach, and the third simulating the intestine (Bruil et al., 1997). The digestion model predicts only gastrointestinal release, but neither uptake nor bioavailability following release in the gastrointestinal tract.

3.6 From external to internal dose: toxicokinetics

The events following external exposure to a compound can be divided into two phases, a *pharmacokinetic* (or *toxicokinetic*) phase, in which the adjustable elements of dose, dosage form, frequency, and route of administration (= dose regimen) are related to the concentrations of the compound in the body, and a *pharmacodynamic* phase, in which the concentration of a compound at the site(s) of action is related to the magnitude of the effect(s) produced (Rowland and Tozer, 1995). Pharmacokinetics comprises processes like absorption, metabolism, distribution and excretion.The difference between the terms pharmacokinetics and toxicokinetics is not clear, although the term toxicokinetics is mainly applied for pharmacokinetics of a compound in toxicology studies.
The main benefit of taking pharmacokinetics into account in risk assessment is the ability to predict 1) sites of action and 2) concentrations at those sites on the basis of doseregimen (= external exposure) and on the basis of physical-chemical properties of the compound. Since the concentration at the site of action determines the extent of effect, pharmacokinetics form an important tool in predicting effects.
Physiologically Based PharmacoKinetic (PBPK) models are compartmental models that simplify the body to a number of physiologically relevant compartments. Those compartments typically include blood, body fat, liver, slowly perfused organs, and richly perfused organs. Blood has a special role, because it transports chemicals and distributes them over the body. Because PBPK models are based on physiologically relevant compartments, exchange between compartments can be modeled by blood flow between compartments. All routes of

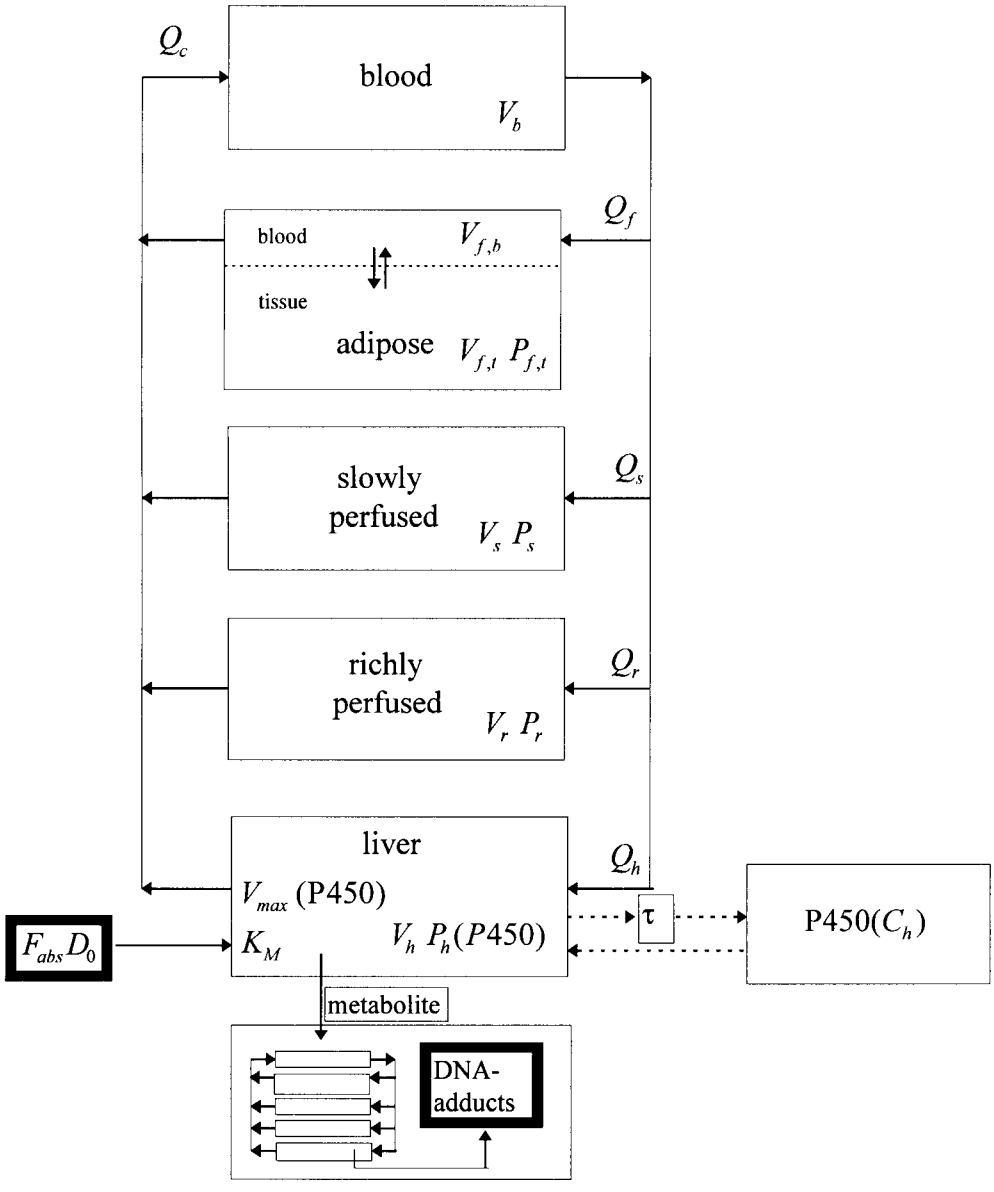

Figure 8. Physiologically Based PharmacoKinetic (PBPK) model for B[a]P: model scheme for the rat.

entry can be included in the model, such as skin permeation, oral uptake, or inhalatory uptake. Elimination of the chemical occurs by metabolism (e.g. by the liver) or renal clearance. PBPK models can be applied to calculate internal dose from external dose, to integrate doses from various routes of entry, to predict internal dose resulting from repeated dosing, to calculate residues in meat and milk, &c. Knowledge of pharmacokinetics and insight by PBPKmodels is necessary for route-to-route extrapolation and for animal-to-human extrapolation.

From external to internal dose: Oral exposure to B[a]P and DNA adduct formation
In Zeilmaker and *et al.* (1997a,1997b,1997c) a cellular model for the accumulation of lipophilic chemicals in the mammalian cell was developed. This model is based on the interaction of lipophilic chemicals with the Ah-receptor and its result, the induction of P450 enzymes. The cellular model was incorporated into a PBPK model and used to describe the toxicokinetics of TCDD and B[a]P in the rat after oral exposure (Zeilmaker *et al.*, 1997a,1997b,1997c), see figure 6 for the structure of the B[a]P PBPK model. In the rat liver the model simulates an essentially non-linear relationship between the external exposure, i.e. the amount of B[a]P administered per kg body weight, and the internal exposure in the liver, i.e. the concentration of B[a]P and B[a]P metabolites and number of DNA adducts. At relative low dose levels this relationship became approximately linear. After the scaling to man the PBPK model was used to study the formation of DNA adducts in the human liver as a function of the amount of B[a]P administered. It was found that, at equal external exposure, the human liver accumulates substantially more DNA adducts than the rat liver (factor 10 to 200). This suggests that a risk assessment on the basis of external oral exposure to rats may underestimate the genotoxic activity of B[a]P in the human liver.

3.7 Human health effects

Human health effects are the last part of the source/emission-effect chain. Only in case effects have been observed in the exposure situation under review or in case they are reasonably anticipated there is a need to specify actual risks and to analyse the whole chain to seek for exposure reduction. If, on the other hand, actual exposures are below limit-values and there are no indications for health effects from epidemiological studies, there is no need to fully identify relevant sources and emissions. As such, one could state that the effect part drives the need for further exploration of the whole chain. Unfortunately, the health effects part has a lot of intrinsic uncertainties. The estimation of health risks preferentially is based on observations in humans, but in most instances has to rely on effects observed in animals as a surrogate.
Epidemiology is hampered by a shortage of sensitivity. Only in case of well designed studies such as case-controls with interventions, for large populations or when humans have been exposed to very high concentrations of the substance, causal relationships may be established. A new development is developed to overcome these limitations, the so-called meta-analyses.
Most cases risk assessors have to rely on animal data for their estimation of human health risks, which is hampered by shortage of specificity. Clearly, there are many differences between humans and animals typically used for this purpose, i.e. rodents. These differences are of anatomical, fysiological as well as behavioral nature, to just mention some. Also, in animal experiments one typically has to interpret effects observed at high doses for their relevance to the much lower doses normally encountered by humans.
Traditionally, two types of effects are discerned: chemicals that have an effect threshold below which no effects appear and chemicals that have no such threshold. These two effect types can be characterized as follows.

Chemicals considered to have an effect threshold:
Non-carcinogenic chemicals and non-genotoxic carcinogens are supposed to have an effect threshold, i.e. in an organism (e.g. animals or humans) harmful effects will not occur below a certain exposure level: the so-called No-(Adverse)-Effect Level (N(A)EL). In certain cases human data will be available to determine such a NOAEL. After application of a safety fac-

tor, an acceptable level of exposure is obtained and is referred to as the so-called Acceptable Daily Intake (ADI; for food additives or pesticides residues), Total Daily Intake (TDI; for food contaminants) or Tolerable Concentration in Air (TCA; for inhalation). As stated, however, in most cases acceptable epidemiological data are not available and safe exposure levels have to be derived from animal experiments. In translating this figure into a limit value for humans two extrapolation steps are envisaged. First, the dose metric used for the conversion of a dose for animals into one for humans is in case of oral exposure on a daily weight basis per kilogram bodyweight, and in case of inhalation exposure on a mean weight basis per cubic meter. A second extrapolation step accounts for (possible) differences in sensitivity between animals on the one side and sensitive humans on the other. For both these latter extrapolations default uncertainty factors are applied with the size of 10 each.
This NOAEL approach has received a lot of criticism. It is inaccurate as an estimate for the "true" NAEL, doesn't provide any information on its confidence limits, and does not offer guidance to assessments of risk in case of exceedences of limits. An alternative was recently suggested with the probabilistic method called 'PROAST' (Slob and Pieters, 1997). It first calculates the uncertainty distribution for a so-called critical effect dose (CED; in animals) that is associated with the critical effect size (CES). In PROAST the extrapolation steps from animals to sensitive human subpopulations are then described, not as single extrapolation values but as distributions of uncertainty.

Chemicals considered to have no effect threshold:
Genotoxic carcinogens are not considered safe, irrespective of the level of exposure. Thus, any dose is assumed to pose a risk of DNA damage that may ultimately lead to cancer. Therefore, a limit value here represents an exposure level with an 'acceptable' risk, i.e. a health policy determined risk level considered as negligible. As adequate human data are very rare, most Human Limit Values (HLVs) stem from chronic animal carcinogenicity studies (Janssen et al., 1998). In the latter case the lowest dose with a significant increase in tumour incidence is taken as point of departure for linear extrapolation downwards to a dose representing the acceptable risk. In case duration of exposure or of observation were not chronic, i.e. not covering at least 90% of the lifespan of the animal, proportional corrections are made. Contrary to the procedure with chemicals considered to have an effect threshold, no corrections are applied for either interspecies or intraspecies differences in sensitivity. The dose metric used for the conversion of a dose for animals into one for humans is similar to that described for chemicals considered to have an effect threshold.

Dose measures
A dose measure reflects aspects of site of action and time scale, in contrast to exposure which is merely a concentration at the outside. With respect to site of action, four kinds of dose measure may be derived from exposure (fig. 9), being specific local effects for the inhalatory, dermal and oral routes and systemic effects once uptake into the body has taken place. Local effects are highly specific for the exposure route and depend on local concentration of chemical. Systemic effects are in principle not dependent on route of exposure, although effects requiring metabolism (e.g. bioactivation) attain route specificity. For example, all blood from the intestine will pass the liver via the portal system and is subject to metabolism, while chemicals entering by the dermal route only partially pass the liver. Depending on the characteristics of the chemical, local, systemic or both effects may occur.

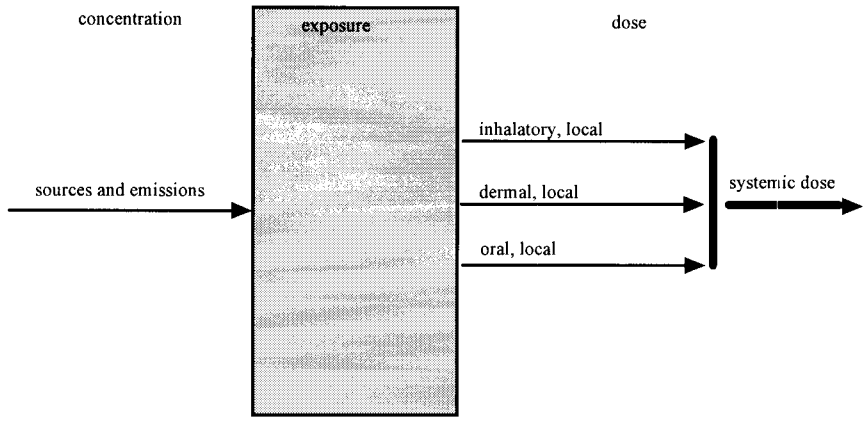

Figure 9. Exposure-to-dose translation.

The time scale of dose depends on the dominant time scale for effects to evolve. If exposures cause acute effects, an acute dosis has to be derived, for example the maximum concentration in air or the uptake during the period of use. If exposures cause (semi)chronic effects, the dose measure will reflect a longer time scale, for example a year or life time average dose. The US-EPA refers to the latter as the Lifetime Average Daily Dose (LADD).

Human health effects of PAHs and human limit values

PAH mixtures as encountered in environmental media are considered probably carcinogenic to humans by all routes of exposure, acting via a genotoxic mechanism (IARC, 1986). This is based on both human studies involving exposure to PAH mixtures (e.g. coke-oven industries) as well as numerous studies with experimental studies with PAH or individual PAH compounds. The carcinogenic effects observed were predominantly local, i.e. at the site of contact. In humans inhalation exposure is associated with lungcancer, whereas animal studies show skin tumours upon dermal exposure, and tumors of the upper digestive tract, liver and the hematopoietic system after oral exposure. From experimental studies it is apparent that the carcinogenic activity of PAH mainly resides in the high molecular weight fraction, i.e. PAH with at least three (non-straight ordered) phenyl rings.

As stated above, any exposure of humans to this kind of chemicals is assumed to pose a certain risk for cancer. Therefore, in the Netherlands HLV's (i.e. exposure levels representing an acceptable risk of one-in-a-million for lifetime exposure; a risk level regarded 'negligible') are calculated using linear extrapolation to zero dose from the tumour incidences observed either in exposed humans or experimental animals (Health Council of the Netherlands, 1994).

With PAH, adequate human dose-response data for risk assessment purposes are available for inhalation exposure only. For the oral exposure route one had to rely on chronic animal carcinogenicity studies with B[a]P of rather poor quality (Slooff, 1989). Recently, fortunately, the results of experimental studies with rats and mice exposed to B[a]P and coal tar of good quality have become available (Culp *et al.*, 1998; Kroese et al., in preparation). Risks associated with dermal exposures were considered relatively unimportant for the general population by Slooff in 1989, and no official HLV was established. Risks associated with incidental high dermal exposures have been estimated ad hoc using observations from animal experiments (Brinkman *et al.*, 1989; Mennes *et al.*, 1995b).

For establishing the actual risks at exposures higher than the HLV's, the same linear dose response curve is used that was applied for deriving HLV's (unless, of course, better dose-response data or data on interspecies differences etc have become available meanwhile).

Inhalation exposure: For inhalation exposure the HLV was derived by taking the mean of the risk assessments from three epidemiological studies, two dealing with work-associated exposures (a gas work and a coke-oven industry), and one with exposures at home (Chinese women cooking on smoky coal). The increases in lungcancer observed in all these individual studies were considered due to solely PAH; PAH were monitored by measuring B[a]P (i.e. B[a]P was taken as indicator for carcinogenic PAH). The dose-response data in each study were fit with different (low dose) linear models. The calculated slope values were averaged to arrive at the Dutch HLV (Slooff, 1989); for this, also (simple proportional) corrections were made to arrive at an average daily dose or concentration (i.e. from exposure conditions as encountered in the human studies).
The HLV for inhalation exposure, i.e. exposure level representing an acceptable risk of one-in-a-million for lifetime exposure, was calculated to be 0.01 ng B[a]P/m^3 (Slooff, 1989). Expressed in a different way, this equals a risk factor of 0.1 per µg B[a]P/m^3 for lifetime.

Oral exposure: There is no official HLV for oral exposure to PAH. An advisory value was proposed in the Integrated Criteria Document PAH (ICD; Slooff, 1989), which was derived from two drinking water studies performed in the sixties in which experimental animals were exposed to B[a]P: those of Horie *et al.* (1965) and Chouroulinkov *et al.* (1967) (see Slooff, 1989). In these studies B[a]P was found to induce upper digestive tract, and forestomach tumors, respectively. From these dose-response data linear extrapolation to zero dose yielded risk factors of 2.5-5 x 10^{-5} for lifetime exposure to 1 µg B[a]P /kg bw,daily, i.e. for experimental animals as well as for man (without evidence to the contrary). Clearly, for PAH this figure will be higher, i.e. when B[a]P is taken as PAH indicator. In the ICD PAH (Slooff, 1989) scaling factors of 4 - 8 for the 10 PAH discussed are put forward, and Kramers and Van der Heyden (1988) speculate on a factor of 10 - 25 if B[a]P is taken as indicator of all carcinogenic PAH. If one would take 10 as a mean of these scaling factors this would result in risk factors of 2.5-5 x 10^{-4} for lifetime exposure to 1 µg B[a]P/kg bw,daily.
Recently, studies in rats and mice were performed that may result in some higher risk factors for B[a]P (Culp *et al.*, 1998; Kroese et al., in preparation). Besides B[a]P, mice were also exposed to coal tar mixtures and the relative potency of this 'PAH mixture' appeared less than 5 times as potent when based on the amount of B[a]P present; although different from the PAH profile humans are exposed to via the diet, the PAH profile of the coal tar mixtures tested had a relative potency below expectations. These studies also show systemic tumors, both after B[a]P (in rats) as well as after coal tar (in mice; Culp *et al.*, 1998; Kroese et al., in preparation).

Dermal exposure: In their report on the cancer risks from dermal exposure to PAH at the polluted Laura area in Kerkrade, Brinkman *et al.*. (1989) calculate a one-on-a-million risk for lifetime exposure to 0.003 ng/cm^2 skinsurface, using animal experiments (Holland and Frome, 1983) and linear extrapolation. Expressed in a different way, this equals a risk factor of 0.33 per µg B[a]P/cm^2 for lifetime. If one takes B[a]P as PAH indicator, a higher risk factor will

Table 3. Risk factors associated with exposure to PAH

route	source species	lifetime risk factor
inhalation	humans	0.1 per µg B[a]P/m^3
oral	mice	2.5-5 x 10^{-4} per µg B[a]P/kg bw,daily.
dermal	mice	?

have to be taken; in their analysis Brinkman *et al.* mention 2-5 for the PAH found at this specific location.
In case exposure takes place via different routes the question raises as to whether this may result in accumulation of internal dosis and, herewith, effects. be a piling up. Interspecies conversion is on bodyweight basis for oral exposure and on air concentration for inhalation exposure. Thus, both intake, uptake, distribution, metabolism and excretion, as well as all toxicodynamic processes are assumed to be equally scaled among experimental species and humans, as long as data demonstrating the opposite are absent.

4. DISCUSSION

The central question of the report remains: is the source-to-effect chain a suitable model to describe fate and health effects of chemicals and can it be described with available models and data ? That question is elaborated using PAHs as lead, to explore available data and model sources. In the following, the approach is discussed starting with a review of the PAH example in light of information needed for the source-to-effect chain. That part is concluded with a comparison with other PAH studies that include the full chain. Subsequently, the use of the approach in risk assessment and management are discussed. Finally, the importance of contacts with high concentrations of chemicals for total exposure is discussed.

It can be concluded that enough information and models are present to make a risk assessment for PAHs applicable to the scale of 'The Netherlands', but a detailed discussion of PAHs is postponed to the evaluation document (Kroese et al. et al., in prep.). The available information is represented by predicted air concentrations in section 3.3, and inhalatory, dermal and oral exposures in section 3.5. Due to the steep increase in data needs, it is not possible to describe exposure and risk in more detail than the national scale. Only for the inhalatory route, a division between rural and urban areas is made. The exposure estimates for the inhalatory and oral route give insight into the large variability of exposures.
From the exposures, dose measures are calculated that can be compared to the human limit values presented in section 3.7. The concentration in urban air regularly exceeds the tolerable concentrations for air. Further high inhalatory exposures are caused by smoking and indoor fire places (Slooff et al. 1989). Dermal exposure estimates, mainly originating from consumer products, pharmaceuticals and soil, show that if dermal exposure occurs, human limit values may quickly be reached. Although oral intake makes up most exposure, tentitative oral limit values are exceeded only occasionally.
Most information appeared to be available for only few chemicals, notably benz[a]pyrene and fluoranthene. Two composite measures, the 10 of VROM and the 6 of Borneff, are available as indicator for total PAH emissions and environmental load. We expect to encounter this situation for other mixtures too: an assessment of the group will in fact be an assessment of a few members. Does that alter a risk assessment ? Emission table 2 suggests it might, because emission patterns are not uniform. Emmision patterns of the10 of VROM and fluoranthene differ considerable from that of benzo[a]pyrene. Subsequent distribution and exposure may also differ, in part because physico-chemical properties will differ: some PAHs are volatile (naphtalene), others are hardly so (benzo[a]pyrene) resulting in different distribution and routes of exposure. A simplifying factor is that B[a]P is the most toxic PAH, and B[a]P exposures will dominate PAH risk assessment.

Emission, distribution and exposure of benzo[a]pyrene has also been studied by Mennes et al. (1995a), Teeuwisse and Van Hout (1996) and Vissenberg and Swartjes (1996). Comparing the present exercise with the first two, USES based, approaches, excluding intake by consumer and pharmaceutical products, shows that intakes predicted by Mennes et al (1995) and Teewisse and Van den Hout (1996) are an order of magnitude higher than the intakes pre-

dicted here (fig. 5, 6 and 7). Their conclusion that food is the main route of intake is substanciated by our analysis although the relative importance differs. In our approach too, food delivers over 90% of total intake. The CSOIL based approach of Vissenberg and Swartjes (1996) shows a thousandfold larger intake of benzo[a]pyrene than our estimate, based on continuous presence on polluted soil at the human toxicological limit value of 1110 mg/kg dry matter. Their analysis indicates that, for polluted soils, ingestion of soil will dominate daily intake of benzo[a]pyrene, far exceeding intake by food. Mennes et al. (1995) and Teeuwisse and Van den Hout (1996) do not consider soil, consumer products and pharmaceutical products. Vissenberg and Swartjes (1996) and our study show that contact with high concentrations of chemicals, such as PAHs, in these matrices will dominate exposure and should be included in studies describing the source-to-effect chain.

Risk assessment is traditionally limited to the last part of the source-effect chain, taking environmental, product and food levels as input, and integrates this information into exposure and effect assessments. If environmental, product and food levels are not known in sufficient detail, exposure assessment will be hampered. In the present case, there was no complete set of air quality, soil, and surface water data, but for air a time series could be constructed. The data on soil and surface water levels do no permit a comprehensive analysis of exposure, althrough data concerning exposure of surfers on fresh water (Van Weerdt, 1990) indicate that no significant exposure though surface water is expected. For food and consumer products, relativily adequate data sources where found. However, these data sources comprise only a few publications, for food but a single (Vos et al., 1990).
When spatial and temporal differentiation is needed, data become even more scarce and model approaches will be limited by available data. For air quality, for example, several studies needed to be combined to generate a time series with sufficient time resolution for exposure assessment. In addition, some models do not include a spatial component. Where current approaches fail to include spatial and temporal variability, they will fail to predict the distribution of exposures over the general population.

The translation of exposure to dose imposes difficulties in using dose-effect data. These difficulties arise at least at four points. Firstly, dosage as used in toxicological experiments does regularly not match the actual exposure with regard to timing, frequency, intensity, and nature. Especially with nonlinear kinetics or dose-effect relations, the calculation of dose from actual exposure becomes a tedious exercise. And without a thorough actual dose, it is difficult to make a thorough risk assessment.
Secondly, exposure measures should be expressed in time scales (hours, days, years, lifetime) appropriate to the effect. For example acute effects will generally be linked to exposure on the time scale of hours or even minutes (maximum concentration), while carcinogenicity will generally be linked to exposures on a scale of years (life time averaged exposure). Often, information is lacking to establish a match between exposure measure and effect.
Thirdly, different subpopulations may significantly differ in their contact to a chemical, thereby differing in exposure. Dose should be represented as a measure differentiated towards subpopulations with their own lifestyle and ways of contact..
Fourth, uptake is hardly considered but may become important, especially where route-to-route extrapolation is necessary. Uptake can be estimated by models, but estimates keep a

substantial amount of uncertainty, which easily reaches an order of magnitude (see Wilschut et al., 1995). Measured uptake data are hardly available.

If risk management becomes necessary, measures can be taken i) to reduce emissions into the environment and ii) to directly reduce exposures. In order to select important emissions to reduce, emission sources need to be characterized in sufficient detail and the impact of each major source on environmental concentrations should be known (Van Kampen et al., 1991; Wesselink and Bovenkamp, 1997). The presented emission data allow for an overview of the various sources that emit to air, water and soil, although the emissions to soil are not known in detail. Equilibrium partitioning of the chemicals between air, water and soil is then used as a first step to estimate environmental concentrations. It appears problematic to estimate the impact of the various emissions on the concentrations in air, water and soil if more precise estimates are needed. One of the causes is that geographical variation in emission is neglected in the emission data. Even diffuse sources will be concentrated, for instance road traffic concentrates on the main roads and consumer emissions in the larger agglomerations. Another cause might be that also temporal variations are not taken into account in the emission data. As a result, intensive emission peaks at particular sites remain hidden in the emission data.
It appears to be difficult to estimate food levels from environmental concentrations. As above, the lack of knowledge about geographical variation in environmental concentrations is one of the main causes of these difficulties. Another is lack of knowledge about uptake and distribution in plants and animals. A pilot study regarding cattle concluded that the lack of partition coefficients hampers use of mathematical models to estimate body concentrations from environmental concentrations (Van Eijkeren et al., 1998).
Direct reduction of exposure can be used to reduce risks due to consumer and pharmaceutical products. Several options are possible, for instance setting a limit to chemical concentrations, design of containers that release a predefined amount of product, or to limit the period that someone uses the product. These measures can be quite effective in reducing human risk due to direct exposures to chemicals. Reducing exposures which connect to lifestyle, such as smoking, may significantly lower exposure but they are difficult to achieve.

Where exposures differ significantly through the population, two questions emerge. The first question is which part of the population is in (regular) contact with high concentrations of chemicals, the second which concentrations are contacted if contact takes place. The first question is raised because it appeared that levels of PAH far exceeding background levels are present at specific sites or in specific products, and only that part of the population entering that site or using those products has a potential for high exposures. A problem is that it is often unclear which sites or which products contain PAHs. For example, products with high PAH-levels are removed from the market once identified, but other products with elevated PAH-levels keep appearing. Because not everybody will contact high concentrations of PAH, the probability of contact is an essential part of an exposure assessment and is needed to calculate population exposure. There is, unfortunately, not much insight in this probability. For contact with multiple media containing PAH the situation is worse, no data about correlations in product use and life style are available. The latter poses the question if we can assess the risks of contacting multiple media at the moment.
With respect to PAHs, the group at elevated exposure appears to be those parts of the population that live on PAH-polluted sites, use products with elevated PAH-levels, have a fire place

and do smoke. For example, people regularly using certain anti-dandruff shampoos with coal-tar may get benz[a]pyrene exposures that do not exclude adverse health effects (Van Koten-Vermeulen et al., 1995).
Studies that only account for environmental emissions and equilibrium partitioning among environmental compartments easily neglect high exposures and risks due to localized sources or specific product use. This is clearly demonstrated by the millionfold difference of benzo[a]pyrene intake in a local and a regional scenario (Mennes et al., 1995a). In addition, intake of benzo[a]pyrene on polluted soil increases thousandfold in comparison to the regional scale estimate of USES, due to ingestion of soil (Vissenberg and Swartjes, 1997). Risks assessments and risk reduction measures should therefore take these localized sources and specific products into account in order to complete their assessments.

The question that remains is whether the approach as discussed here by the example of PAHs is also applicable to other chemicals. This question can be answered confirmative if the exercise provided insight beyond the specific case of PAHs. These insights exist. Firstly, it appeared that individual exposure to consumer products or polluted soil may cause exposures that are high compared to background exposure. It makes clear that lifestyle is an important factor underlying exposure and risk. It is expected that this issue will hold for many chemicals. Secondly, it is concluded that spatiotemporale patterns in PAH-emission should be known before being able to assess location specific exposures and effects. Finally, the present exercise provided insight in the variability of exposure, where possible as a function of age. This proves to be valuable to discern groups at high exposure.

5. CONCLUSION

In conclusion, the source-to-effect-chain appears to be a good vehicle to describe fate and risk of chemicals. Screening analysis along the chain can be conducted rather quickly by USES or EUSES. Refined analysis as described in the underlying report will take much more work and data, but provides insight into the variability of exposures and the presence of groups with high exposures. As a result, upper tail exposure and risk estimates and population exposures and risks become feasible. Unfortunately, data limitations prohibit a good description of spatiotemporal patterns and variability of exposure over the general population.

It can be concluded that enough information and models are present to make a risk assessment for B[a]P as indicator for total PAH. A detailed discussion of the risk assessment is postponed to the evaluation document (Kroese et al., in prep.). Oral intake of food accounts for about half of total B[a]P intake, but oral intakes are around the level of the tentative human limit value. In contrast, B[a]P concentrations in urban air regularly exceeds the tolerable concentrations for air. Dermal exposures, mainly originating from consumer products, pharmaceuticals and soil, show that if contact occurs, human limit values may quickly be reached.

The study revealed insights that are more general than the PAH example. Firstly, it appeared that individual exposures to consumer products or polluted soil may cause exposures that are high compared to background exposure. Secondly, it is concluded that spatiotemporal patterns in emission should be known before being able to assess location specific exposures and effects. Finally, the present exercise provided insight in the variability of exposure, where possible as a function of age. This proves to be valuable to discern groups at high exposure.

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