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0009 Methods For Assessing the Effects of Mixtures of Chemicals

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*Environmental Fate of Mixtures as a  
Background for Human Exposure  
Monitoring*

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**ABSTRACT**

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Numerous compounds are continuously released into the environment during their production and use. The resulting mixtures contaminate the environment and can be a potential threat to organisms including man. Monitoring programmes are designed to assess levels of individual compounds and mixtures in various compartments of the environment. Such levels depend on the release rate and the environmental fate, which in turn is strongly influenced by physicochemical properties and stability. Monitoring can be carried out by chemical, mainly instrumental, analysis (chemical monitoring), analysis of humans and other biological organisms which are representative of exposure (biological monitoring), and observation of biological effects (toxicological monitoring).

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**I INTRODUCTION**

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In the last century, the industrial production of chemicals expanded very fast. The number of compounds of commercial interest grew to over 50 000, production volumes increased considerably, and more than one million tons of several compounds are now produced per year. Approximately 50 substances are produced in amounts of more than 100 000 tons/year, and a few hundred over 10 000 tons/year (SRI, 1980). This enormous chemical production and its continuous growth requires regulation and control of the production, use, and environmental release of potential pollutants.

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Chemical monitoring is part of these regulatory procedures. Other measures are the setting up and standardization of pre-production environmental screening tests for new chemicals (OECD, 1981).

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0290 During the 1970s and 1980s, scientists as well as governments in most technically developed countries became more interested in monitoring programmes for chemicals. Pollution problems on the one hand and accumulating scientific knowledge of environmental processes and toxicological effects on the other, were largely responsible for the progress in the regulatory monitoring of chemicals. Monitoring of chemicals can be divided into two different areas: (a) biological/toxicological monitoring, and (b) chemical monitoring.

0360 In chemical monitoring the basic objective is the registration of concentration changes in time and variations with geographical location. In toxicological monitoring the effects of the concentrations are observed, as they vary in time as well as in geographic distribution. Chemical monitoring of environmental contaminants may be done for a number of reasons. (Holden, 1975): (1) to indicate changes in contamination levels with time; (2) to indicate biological transformations of the pollutant in time; (3) to enable comparison of contamination levels between different areas; (4) to identify highly contaminated areas which can lead to the identification of the pollutant source; (5) to indicate the potential environmental risk to species and ecosystems, especially when used in conjunction with biological (toxicological) monitoring; (6) to indicate the quality of human food, drinking water and air; and (7) to indicate the effectiveness of the control measures used for protection of the environment.

0508 The parallel between the sequence of chemical cycles of compounds produced and the sequence of environmental safety testing and control, of which monitoring is one part, is illustrated in Figure 1.

## 2. EXPOSURE

0540 From the perspective of environmental health chemistry, humans can be exposed to chemicals by different routes (Huglitzinger, 1980). Exposure of individuals is, in

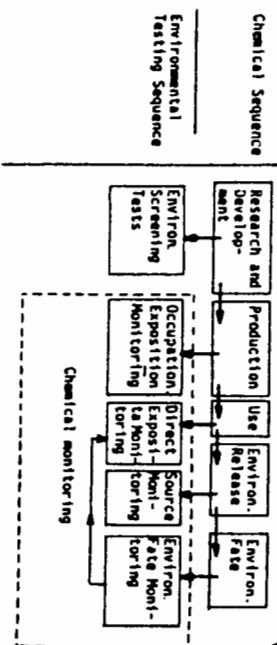


Figure 1 Chemical production and environmental safety testing and control

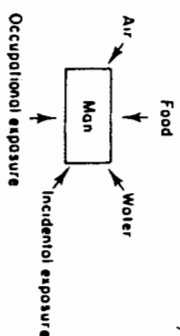


Figure 2 Routes of exposure and origins of chemicals entering the human body

0563 many cases, primarily determined by their behaviour patterns (Figure 2).

0572 Persons working in paint factories, for instance, will be exposed to higher concentrations of organic solvents in air than will others. Similarly, differences in food habits are responsible for disparities of polychlorinated biphenyl (PCB) uptake between fish-eating persons and vegetarians.

0612 In addition to human behaviour, differences between properties of chemicals determine the importance of specific routes to the total human exposure. For example, PCB uptake by air is not important in contrast to the respiratory uptake of carbon monoxide. This means that assessment of environmental and human safety must be influenced by the fate and properties of chemicals. As stated above, at least five types of chemical monitoring programmes can exist: monitoring of (1) occupational exposure concentrations in workrooms; (2) direct exposure concentrations such as food, drinking water, drugs, etc.; (3) pollution sources such as waste water or smoke stacks; (4) environmental concentrations; and (5) environmental fate monitoring.

0726 The first three types of monitoring programmes have existed for years in many countries (SRL, 1981). Government laboratories, for example, have been involved in analysis and quality control of foods for decades to ascertain absence of harmful levels of potentially toxic compounds from materials used for human consumption. At the moment the most advanced monitoring programmes function in this area, for example in drinking water quality control. Source monitoring has been part of the production process control by many industries for years. Originally many plants themselves monitored their waste output into the environment. Recently regulatory agencies started more frequent monitoring programmes in the environs of plants and factories which could release potentially harmful pollutants.

0834 Workroom monitoring for certain industries is regulated by law in many countries. Increasingly stringent requirements for worker safety, as expressed in the lowering of maximum acceptable concentration (MAC) (TLV) values, will demand more and better planned monitoring of actual concentrations in the workplace.

0877 The only type of monitoring that is not used in practice on a large scale is  
0893 environmental fate monitoring. In addition, knowledge of environmental fate  
0902 processes has rarely been used in the other monitoring types in the past. The  
0916 present efforts in environmental fate monitoring have evolved from traditional  
0926 types of programmes. Expansions of the programmes often resulted in useful  
0937 monitoring networks. For example, some sulphur dioxide, PCB, DDT, and  
0947 other pollutant programmes are of high quality and give useful information  
0958 about the environmental distribution of these pollutants. Although these recent  
0968 developments are of interest, they are only the beginning of more fundamental  
0980 fate monitoring which is of importance for human exposure. This is particularly  
0992 true for human exposure to mixtures of chemicals.  
1000 In principle man can be exposed to three types of chemical mixtures, which,  
1013 theoretically, can originate from (a) one production process, (b) coincidental  
1023 presence of components in a sample, and (c) similar chemical and physicochemical  
1035 properties.

1036 (1) The first type of mixture is formed at a certain time and place, and has a  
1052 certain composition. These mixtures may result from chemical factories or  
1062 from incineration processes and are not necessarily composed of compounds  
1072 having comparable chemical structures or properties. For many well-  
1080 controlled processes these mixtures may have relatively stable compositions,  
1089 e.g. cosmetics or artificial food additives. However, many minor com-  
1098 position changes may occur which can be very important toxicologically.  
1108 When the production process varies in time the created mixture can be  
1120 different, which makes comparison difficult.  
1125 (2) The second type of mixture to which biota can be exposed is the coincidental  
1139 mixture. These mixtures are composed of compounds that occur by  
1149 coincidence, at the time and place of sampling in the environment. No  
1161 similarity need exist between the single compounds of the mixture. This  
1172 coincidental presence may be typical of the mixture over long periods or it  
1185 may result from a single release.  
1191 (3) The third type of mixtures are those consisting of compounds with similar  
1203 physical and chemical properties. Because of the similarity in their physico-  
1213 chemical behaviour, many compounds will be present in the same environ-  
1223 mental sample. Because of the various distribution and transformation  
1232 processes of individual compounds, as well as the continuous variation of  
1243 release, the composition of the mixture changes in the environment.

1253 The first two types of mixtures are found not only in environmental samples,  
1266 but also in source, occupational exposure, and direct exposure monitoring.  
1276 Although the latter two types are typical results of fate processes, they are also of  
1291 interest in food and drinking water monitoring.  
1298

### 3 ENVIRONMENTAL FATE PROCESSES

1302 The environmental behaviour of single compounds or mixtures is a combi-  
1313 nation of transformation and distribution processes. These processes not only  
1323 determine the places where compounds will be present, but also the amounts and  
1336 the composition of mixtures which are crucial for monitoring (Figure 3).

1346 Variation of the chemical composition of mixtures after production and  
1356 environmental release is a continuous process. Many distribution processes that  
1366 influence those changes in composition are governed by the physicochemical  
1376 properties of the substances. Hydrophobicity, volatility, solubility in water,  
1385 presence of polar groups, and other properties are of interest for the distribution  
1398 behaviour. Final disposition of chemicals is also influenced by transformations  
1408 for which, for example, biochemical and thermal stability are important  
1418 properties (Hutzinger and Verkamp, 1981).

1423 Although some of these fate processes are properly understood at the  
1434 laboratory level, most of the relations between environmental behaviour and  
1444 chemical structure variables are oversimplified. Scientific knowledge is increas-  
1452 ing rapidly in this area, and in many cases it is sufficient to use it as a background  
1470 for environmental fate monitoring programmes (Huck-van der Plas and Huck,  
1480 1979).

#### 3.1 Environmental Simulation Models and Monitoring

1487 Simulation models of transformation and distribution processes in nature at  
1497 different levels are available. Some of them are concerned with only small parts of  
1511 the total environment (microlevel), for example at certain small ponds or rivers.  
1523 Other focus on the global environment (macrolevel). Proper simulation at the  
1534 mesolevel (e.g. Rhine River in combination with North Sea) do not exist at the  
1548 moment.

1549 The potential of simulation models in the creation of monitoring programmes  
1560 is at present restricted. For the macrolevel environment, quasi-thermodynamic  
1569 equilibrium assumptions are made most of the time (Haque and Freed, 1974,  
1581 Mackay, 1982). This includes assumptions that global mixing is sufficient by

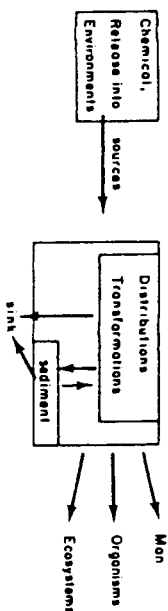


Figure 3 Environmental fate of chemicals

1593 convenient distance transport systems, and that transitions between  
1601 environments, phases are well described in terms of mass-flow relationships. To  
1612 some extent transformation processes can be incorporated in these models  
1622 (Mackay, 1987). The central problem in these models results from the fact that  
1633 equilibrium or steady-state levels for many environmental compartments can be  
1645 calculated, but they will never be reached. This is partly due to the insufficient  
1659 descriptions of transition processes used in the models. Another fundamental  
1669 problem is the description of the kinetic rates of most processes. Although both  
1682 of the above problems will restrict the use of models to set up monitoring  
1696 programmes, these fate models will provide an important background to the  
1707 monitoring of global pollutants which include persistent chlorinated aromatic  
1716 compounds such as PCBs, sulphur dioxide, nitrogen oxides, and some heavy  
1727 metals. At the environmental microlevel, quasi-thermodynamic fate models are of  
1737 little value for monitoring for at least two reasons. First of all, the environmental  
1751 microsystem in question is not isolated and is strongly influenced by its  
1763 surrounding systems. These interactions between microsystems are intensive,  
1771 which means that variations in neighbouring systems directly influence the  
1782 behaviour of compounds in the system under investigation. Expansion of the  
1793 proposed monitoring programme to a larger area is not possible because the  
1805 modelling problems at the mesolevel are even more complex. The second type of  
1818 problem at the microlevel is the dependence of the usefulness of a model on the  
1833 type of pollutant source. In global monitoring the source type is not relevant, but  
1847 at the microlevel this is of major importance for the type of monitoring that must  
1862 be used. For example, the release of lead or nitrogen oxides from automobile fuel  
1876 is very dispersed at microlevels whereas the release of effluent from a chemical  
1889 plant into a pond is geographically concentrated. Both these extremes need  
1900 different types of fate monitoring. Although many problems arise at the macro-  
1912 as well as the microlevel, there are existing models which can be used for  
1926 monitoring at these levels. At the mesolevel even more complex problems arise. A  
1939 quasi-thermodynamic description cannot be used for several reasons and, in  
1949 addition, interactions between different types of pollutant sources create other  
1960 problems.

### 1962 3.1.1 Some Problems of Models and Chemical Monitoring at the Mesolevel.

1972 *An Example: Monitoring of Pollutants in the Aquatic Environment.*  
1981  
1990 Transformation and distribution processes of pollutants in the aquatic environ-  
2002 ment and in other natural compartments are largely determined by the structural  
2013 properties of the compounds. Also, the composition of that particular aquatic  
2026 area is of importance to the behaviour of the substances. For example, the  
2036 persistence of compounds capable of undergoing hydrolysis will be determined  
2050 by the pH of the water, and rate of degradation by microorganisms of the  
2050 compounds will be influenced by the water temperature and other factors. One

2062 of the c processes in the aquatic environment is adsorption of pollutants on  
2075 sediment, particulates. Adsorption/desorption processes are generally  
2082 described by the adsorption isotherm given by Langmuir or Freundlich.  
0010 For the majority of non-ionized organic compounds of current industrial and  
0021 environmental interest, the adsorption process is strongly influenced by the  
0031 organic matter content of the adsorbent. This means that after the release of a  
0045 certain amount of pollutant the percentage adsorbed will depend on the  
0056 composition of the adsorbent. Thus, the release of chlorobenzenes in a sand,  
0068 area will result in a different environmental distribution than release into a peat  
0081 area.  
0082 Adsorption is not only of interest in itself but it also determines to a large  
0097 extent, other processes. The mobility of chemicals is strongly reduced after  
0108 adsorption. Particulates in the hydrosphere, like rivers, are transported man  
0118 times more slowly than the streaming water and dissolved compounds. Even  
0129 between particulates, differences in transport rates exist; the lighter particulate  
0139 move faster and the heavier move very slowly because of rapid sedimentation. At  
0152 these aspects are of interest for the environmental behaviour of the pollutants.  
0164 No adsorption means transportation is as fast as the streaming of the water.  
0177 Adsorption to heavy particulates means rapid sedimentation at the dumpin  
0187 place. Besides the total adsorption potential, which is described by the Langmuir  
0199 and Freundlich isotherm, the rates of adsorption and desorption are also  
0210 important for the determination of fate. Rapid adsorption means fast removal of  
0222 the pollutant from the major transport system. On the other hand, slow  
0234 desorption from the sediment results in a continuous release of pollutants into  
0246 the environment. This can result in a persisting pollution concentration long  
0257 after industrial production and release have been stopped (Figure 4).  
0266 Adsorption is closely related to other fate processes in the aquatic environ-  
0277 ment. Bioaccumulation of hydrophobic chemicals by fish, for example, is much  
0288 faster by direct uptake from water than by internal uptake from the intestine.  
0301 tract. Rapid adsorption in this case means reduction of the bioavailability of the  
0314 compounds. The reverse can be true for organisms that live in the sediment  
0327 because of the sedimentation of heavy particulates, pollutants will be available  
0338 for filter feeders (mussels, etc.) if the adsorption is a reversible partition process.  
0351 Also, in volatilization, biodegradation, and other transformation and distri-  
0359 bution processes, adsorption plays a major role. This knowledge ideally should  
0370 influence the set-up of the aquatic monitoring programmes, for example  
0381 separation of the sample into dissolved compounds and particulates. Partition  
0392 the pollutant in the different sample fractions gives information about the  
0403 potential transport rate, the mean residence time, availability to biota, and other  
0415 environmental processes (Figure 5).  
0418 In addition to fish and other biota, sediment and water have to be analysed  
0433 well. The particulates fraction, in particular the size and weight distribution,  
0445 important in assessing the mean transport rates and the potential bioavailability.

- Dumping of three compounds
- I Rapid adsorption, slow desorption
  - II Slow adsorption, rapid desorption
  - III No adsorption

Dumping time =  $t_0$

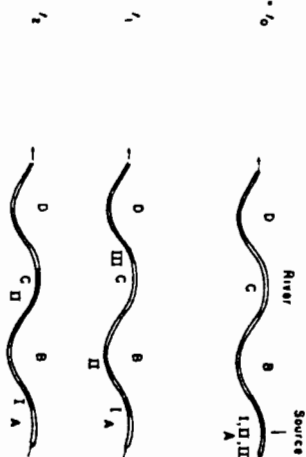


Figure 4 ' Dumping of three compounds. Compound I: rapid adsorption, slow desorption. Compound II: slow adsorption, rapid desorption. Compound III: no adsorption. Dumping time =  $t_0$ . Because of the rapid adsorption of I, this compound creates a local, highly concentrated pollution at position A, which is not significantly available to biota. Dumping of compound II results in a long-lasting pollution of low concentration at all positions A-D, which is more bioavailable. Compound III gives rise to a short, intense exposure of biota at all positions

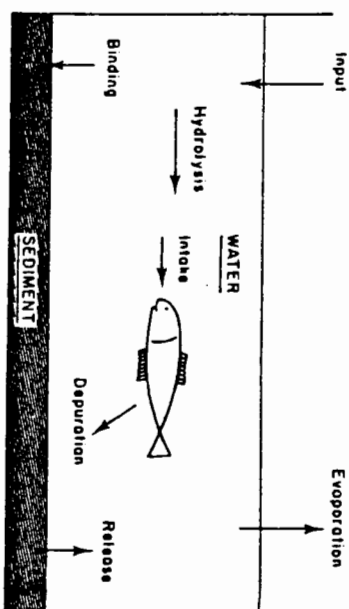


Figure 5 Fate processes in aquatic environments

0456 of adsorbed pollutants. Analysis of sampled waters without separating the  
0466 particulate fraction can mean that the detected amount of pollutant was  
0477 adsorbed to floating particulates. The potential reduction of bioavailability after  
0487 adsorption probably says nothing about the potential environmental risk. This is  
0498 not only of interest for biota living in water that will be used for human  
0513 consumption (fish), but also for the use of this water as a source of drinking water  
0529 (Figure 6) (Mivecos, 1982).

0532  
0533

#### 4 MONITORING OF MIXTURES

0536 Aside from the intensive interrelation between released chemicals and natural  
0546 environment, disposition of mixtures creates another dimension of complex  
0555 problems for monitoring. These problems have, to some extent, a toxicologi-  
0566 cal/biological background. As mentioned above, mixtures in the environment  
0575 can be divided into at least three different types: often combinations of chemicals  
0588 cause potentially higher risks for biological damage to organisms of ecosystems  
0599 than occurs with single compounds. This is a result of the potential synergistic  
0612 toxicological action of the combined exposure. Of course the reverse (antagonis-  
0622 tic effects) can also take place. This new uncertainty is an inherent problem with  
0636 mixtures. Interpretation of monitoring results is for this reason a totally different  
0648 task than for single compounds. Many interactions of substances are known at  
0660 the moment. Also, interrelations between chemicals and particulates, fog, or  
0670 other natural conditions are often described. These interrelations resulting from

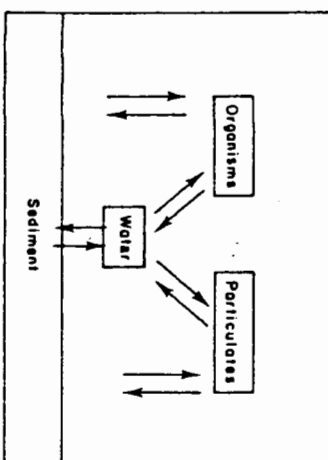


Figure 6 Important compartment of the aquatic environment that should be analysed in an environmental fate monitoring programme together with the relevant fate processes

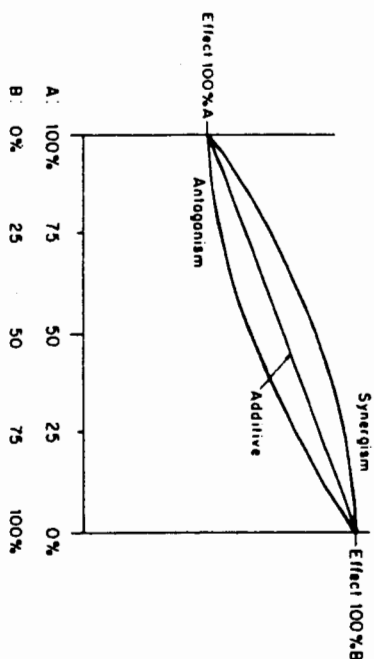


Figure 7 Joint action of two chemicals A and B

0680 the environmental behaviour of substances and mixtures must be used in  
 0691 chemical monitoring. Monitoring of nitrogen oxides and related smog com-  
 0700 pounds, for example, must be intensified on sunny days in heavy traffic areas  
 0713 because the potential pollution load on these days is greater.  
 0723 Because many distribution and transformation processes influence the  
 0731 environmental behaviour of the single compounds of a mixture, the mixture  
 0742 composition is changing continuously. After release from a mixture based on the  
 0754 production process, the unstable and degradable compounds may disappear  
 0763 after some time. The more stable components of the mixtures persist. The  
 0773 persisting compounds may have different distributional behaviours which results  
 0784 in further separation of the original mixture. For example, from an industrial  
 0797 PCB mixture the lower chlorinated biphenyls are degraded by microorganisms,  
 0807 but the higher chlorinated compounds persist. Depending on the differences in  
 0818 hydrophobicity, molecular configuration, and potential to metabolize, these  
 0826 compounds will adsorb to sediment or accumulate in organisms. As an overall  
 0838 result, the composition of PCB mixtures in organisms and sediments is  
 0849 completely different from the PCB mixtures originally released.  
 0857 This means that the analytical composition of the recovered mixture depends  
 0868 on the amount of sampling and the location in which the mixture is sampled.  
 0882 Interpreting the relation of the analysed composition to the original mixture  
 0893 composition at the time of release is generally impossible.

Aside from the transformations and distributions that are of importance  
 for released mixtures, fate processes also determine the disposition of other

0923 pollutants. results in the creation of new mixtures in environmental samples  
 0935 with components from different origins. Many mixture combinations are a result  
 0946 of the similarity of physical and chemical properties of the constituent  
 0957 compounds. Combinations of PCBs, DDT, toxaphenes, and other persistent  
 0966 organic chemicals are examples of these newly created mixtures. Also, totally  
 0977 different pollutant compounds can be present in environmental samples as, for  
 0988 example, mercury and PCBs in fish. In this instance coincidental occurrence is  
 1000 not based on comparable fate behaviour.

1006 The potential risks from the environmental health safety point of view cannot  
 1018 be estimated in most of these cases. Toxicological interrelations of different types  
 1030 of compounds are scarcely known, and even the biological availability of  
 1041 individual compounds in the presence of others can vary. Due to the continuous  
 1054 variation of the chemical compositions of mixtures, standardization of sampling,  
 1064 preparation, and final analysis are problematic.

1070

#### 1071 4.1 Chemical Monitoring with Biota

1075

1086 When studying the environmental fate of chemicals or pollutants, or assessing  
 1097 the exposure of organisms or man to pollutants, biological information can  
 1097 support the physicochemical method of pollution monitoring. In many cases,  
 1107 organisms are used as indicators of the presence of pollution. The biological or  
 1120 toxicological impact of single compounds and mixtures cannot be adequately  
 1141 estimated by chemical analysis alone, even if the analysis is straightforward.  
 1141 Alternatively, measuring only biological responses or changes in ecosystem  
 1150 characteristics, without knowing pollutant concentrations, is also insufficient in  
 1159 environmental fate monitoring. Therefore, adequate information of dose-  
 1166 response curves must include an array of information about (a) the concentration  
 1178 of the chemicals or other pollutants being tested, (b) ecosystem quality and  
 1190 exposure conditions, and (c) the observed species. Biological evidence, however,  
 1200 can find useful applications in correlating exposure concentrations and bio-  
 1209 logical response to estimate the potential health risk for human exposed to  
 1221 environmental pollutants.

1223 Active use of biota in monitoring can be divided into two types: (a) active  
 1237 toxicological monitoring, and (b) active biological monitoring. The first type of  
 1248 monitoring with biota is used to prevent release of high levels of harmful  
 1261 contaminants. Many indicator species of ecosystems can be used to warn against  
 1273 too high pollution levels. This use of biota for toxicological monitoring is  
 1285 possible in many different situations (Cairns and Van der Schift, 1980) and can  
 1298 vary from early warning systems with fish in waste effluents, to damage of trees  
 1312 due to acid rain. The other potential use of biota in monitoring has no  
 1326 toxicological implications. The organisms act solely as a pollutant indicator by  
 1337 means of the pollution content which is assumed to be an index of the average

- 1352 availability of pollutants to biota at the collection site and its close surroundings  
 1365 (Philips, 1978).  
 1367 Most of the developed biota monitoring programmes are conducted in the  
 1378 aquatic environment and are based on or concerned with, for example, the  
 1390 environmental fate of organochlorine compounds such as PCBs, radionuclides,  
 1399 or heavy metals. The species used for these programmes are normally fish,  
 1411 mussels, oysters and algae.  
 1415 The major advantages of the use of biological indicators over the usual  
 1427 physicochemical methods for monitoring are: (1) direct measurement of the  
 1437 biologically available amount of the total pollutant, which cannot be determined  
 1448 from studies of water or sediment; (2) time integration of the ambient pollution  
 1461 concentration at the site of a collection, which can only be elucidated from water  
 1475 analysis by the study of a large number of samples; (3) the high concentrations of  
 1490 pollutants obtained in comparison with the surrounding environment which can  
 1500 reduce detection problems; (4) the relatively low cost; and (5) the possibility to  
 1513 monitor a large variety of pollutants at one time.  
 1522 However, the net uptake of pollutants such as heavy metals or organochlorine  
 1534 compounds by indicator organisms is subject to a variety of biological, physical,  
 1546 and physiological variables. The effects of natural or sampling variables may  
 1557 interfere with the correct interpretation of results from indicator surveys for  
 1568 pollutants. Variables that must be considered in indicator surveys are: (1) the  
 1581 choice of the indicator organism; (2) body lipid content; (3) physiological factors  
 1593 such as age, size, weight, sexual cycle, reproduction, shell deposition, etc.; (4)  
 1605 effects of season; (5) salinity; (6) temperature; (7) geophysical differences (at  
 1616 various collection sites); (8) interactions between individual chemicals; and (9)  
 1626 toxicity of chemical compounds. Indicator surveys provide valuable methods for  
 1636 monitoring the exposure to chemical mixtures in specific environmental  
 1645 compartments. This is due to their ability to accumulate various substances at  
 1657 certain places during a certain period. These typical biota properties make  
 1668 biological monitoring a very useful support to physicochemical detection  
 1677 methods of pollutants in the environment.  
 1683  
 1684

## 5 CONCLUSIONS

- 1685 To develop more sophisticated monitoring programmes to assess and control  
 1695 exposure of man to mixtures of chemicals, some modifications in the approaches  
 1708 of many programmes are needed. In exposure monitoring in the workplace,  
 1719 present intake models for man are generally sufficient. These models, in  
 1730 combination with monitoring data, result in useful estimates for the average  
 1741 exposure in those situations. In food, water, and other types of direct exposure  
 1754 monitoring, the same developments exist and can be used in practice at the  
 1767 moment. Traditionally 'source monitoring' programmes had defined ap-  
 1774 proaches. Monitoring the environmental fate of single compounds and mixtures

- 1784 to monitor the exposure of man requires totally different philosophies; the  
 1795 pathways and nature of the contaminants must have a central place. The  
 1807 continuous variation of absolute concentrations of compound mixtures and also  
 1817 the composition changes make the modelling of potential exposure very difficult.  
 1828 This is not only of interest for the design of monitoring programmes and for  
 1842 the installation of data collection network, but also for simulation models to  
 1854 interpret these data. Further developments in environmental fate monitoring  
 1863 must be influenced by knowledge of transformation and distribution processes.  
 1873 Although at the moment knowledge of typical fate problems is not always  
 1885 sufficient, neglecting them may result in inefficient monitoring programmes and a  
 1896 waste of money and scientific manpower. Biologically active forms of the  
 1907 contaminants present must also be considered. The same is true for the potential  
 1920 transition from one chemical form to another, and for the transfer from one  
 1933 environmental compartment to another.  
 1937  
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