

Special Report

No 2

**Existing Chemicals
Recommendations for Priority Setting**

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SPECIAL REPORT

No. 2

EXISTING CHEMICALS

Recommendations for Priority Setting

Contents

A. Introduction	1
B. General Principles	3
B.1 Establishment of a Starting List	3
B.2 Identification Step	4
B.3 Hazard Assessment Step	4
C. EEC Proposal for a Council Directive on the Evaluation and the Control of the Environmental Risk of Existing Substances	5
D. Approaches to the Identification of Priority Chemicals	6
D.1 General	6
D.2 Principles of Scoring Systems	7
D.3 Comments on Scoring Systems	7
D.4 Conclusions	9
E. ECETOC Recommendation for Priority Setting	10
E.1 The Identification of Priority Chemicals in the Screening Stage	10
E.2 Guidance for Assigning Chemicals to Hazard Categories.....	13
E.3 Combining of Biological Effects and Exposure	15
E.4 Priority Setting	16
Figure 1 - Flow Chart of the ECETOC Screening Process	20
Figure 2 - Matrix of Possible Combinations of the Ratings for Exposure, Toxicity and Ecotoxicity	21
Example 1 - 1,4 Dichloro-2-nitrobenzene	22
Example 2 - Isophorone	24
Annex	
Criteria for Classification of Chemicals by Ecotoxicological Effects	26
Acute Aquatic Toxicity	26

ECETOC Special Report

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Existing Chemicals: Recommendations for Priority Setting Report

A. Introduction

The chemical industry and national and international organisations have undertaken evaluation of environmental and toxicological risk on many of the chemical products produced and marketed over past years. It is recognised however, that there is need to undertake a systematic examination of all existing chemicals to identify those with the greatest hazard potential and to undertake risk assessments when necessary. Recently, international and national authorities have been devoting effort to identify such "priority chemicals".

The magnitude of the task is great since large numbers of chemicals are involved. There are over 60,000 on the US-TSCA list and more than 100,000 on the EEC inventory (although fewer are of commercial importance). Moreover, the information needed to set priorities for many of these chemicals is either not available or difficult to obtain. Therefore the chemical industry and the EEC require a system which is economical in the use of time and resources and yet identifies those chemicals with the greatest potential risk to man or the environment for more detailed assessments.

Initial attempts at priority setting are based upon arbitrary selection of certain groups of chemicals rather than upon a systematic evaluation of all existing chemicals. To improve upon this the OECD (1986) reviewed possible approaches to priority setting and developed guidelines.

More recently the EEC Commission has made a proposal for an EEC Council Regulation on the evaluation and control of environmental risks of existing chemicals. However, although this proposal describes how data will be collected, it does not specify how the data will be used to select the priority chemicals for further risk evaluation.

Degradability	26
Bioaccumulation	28
Guidance for Ecotoxicological Hazard Classification	28
Appendix I Scoring Systems: Description and Evaluation	29
Bibliography	57
Appendix II Members of the Task Force	58
Appendix III Members of the ECETOC Scientific Committee	59

In order to clarify how priority chemicals can be identified ECETOC has reviewed the principles involved and put forward ideas and proposals for a systematic step by step process.

This report

- discusses the principles underlying priority setting
- describes the EEC Commission Proposal
- makes recommendations for a priority setting process for existing chemicals.

B. General Principles

The ultimate aim of priority setting for existing chemicals is the identification of chemicals which have a potential for significant risk to man or environment and which require further evaluation.

Because of the large number of existing chemicals any procedure will necessarily consist of a number of steps, as described in the following sections.

B.1 Initial Selection : Starting List

The first step is to select from the chemicals on the inventory lists a starting list of chemicals of particular interest. Selection should be based on data which are easily obtainable.

Those selected would be :

- chemicals for which a significant exposure potential can be assumed from the quantities produced and/or their use pattern;
- chemicals for which a health and/or environmental hazard potential can be assumed from their chemical structure;
- chemicals identified by analysis in the work place and/or in the environment.

The aim of this initial step is to produce a manageable list of chemicals on which, given available resources, more extensive data can be collected for priority setting. The particular basis of initial selection will depend on the objective of the priority setting process. Thus if chemicals are to be identified which might be hazardous to the environment it will be advisable to start with a list of chemicals likely to produce high environmental exposure. On the other hand, chemicals expected to have a high toxic potential should be listed if the aim is to identify chemicals likely to be hazardous in the workplace.

B.2 Identification Step

In the identification step, chemicals on the starting list are screened to identify those which have priority for further consideration because there is evidence of hazard or, alternatively, because there is insufficient evidence to assess hazard. For the majority of chemicals only a limited amount of data is expected to be available within a reasonable time period and a compromise has to be found between the need to collect the maximum possible data relevant to hazard assessment and the availability of resources necessary for the collection of all information on a chemical.

After collation, the data are evaluated to identify those chemicals which may merit risk assessment either because available information suggests a high hazard potential or because data inadequacies suggest an urgent need for hazard assessment.

B.3 Hazard Assessment Step

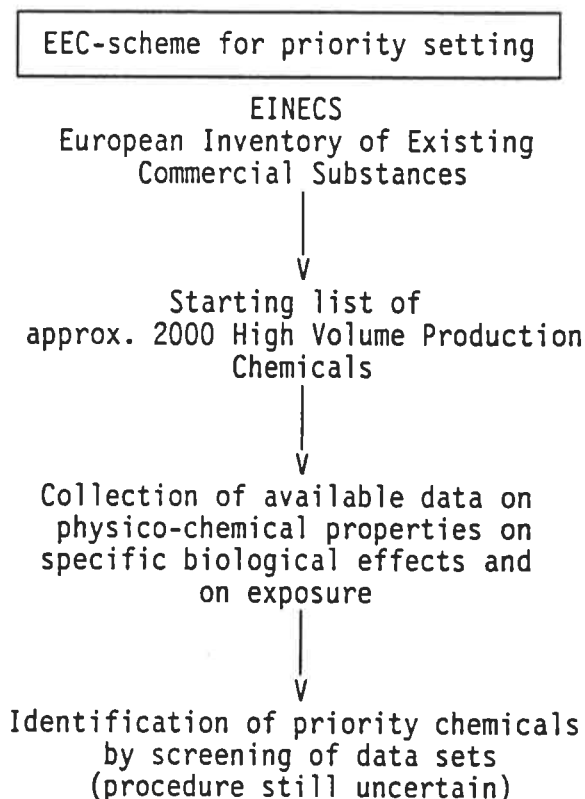
In the hazard assessment step the available data are reviewed in order to determine the nature and extent of any risks to man or environment and measures necessary for the control of risks associated with production and use of the chemicals.

For those chemicals for which available data are insufficient even for a preliminary assessment of hazard potential, the additional data required for risk assessment to man or the environment will need to be defined.

C. Proposal for a Council Regulation (EEC) on the Evaluation and the Control of Environmental Risks of Existing Substances (see Official Journal of the European Communities C 276 from 5.11.90 ISSN - 0378-6986)

The general concept of this proposed regulation requires that certain information concerning chemicals produced or imported in quantities of more than 1,000 tonnes per year will have to be reported. The primary information requirements are: chemical identity, quantities produced or imported, use-pattern, specific physico-chemical data, chemical fate, ecotoxicological and toxicological data. On the basis of this information and national lists of priority chemicals, the Commission in consultation with Member States, will regularly draw up lists of priority chemicals or groups of chemicals requiring special attention because of the possible effects they may pose to man or the environment. Therefore, a systematic stepwise approach is to be adopted as shown below.

The proposed Regulation does not describe how these priority chemicals will be selected.



D. Approaches to the Identification of Priority Chemicals

D.1 General

One of the most difficult aspects in all priority setting systems is how to assess the data collected in the screening phase (use pattern, toxicology ecotoxicology, etc) and present it in a clear and comparative format.

This will require methods that are a balance between scientific accuracy and regulatory requirements. An apparently easy method would be to allocate numerical scores to the chemicals on the basis of their respective hazard potential and to sort them according to the magnitude of a combination of scores.

There are occasions when it is useful to assign a numerical value to a combination of biological effects produced by a chemical and then use the value obtained as a standard against which to measure the effectiveness of control procedures. Hygiene standards (TLV'S, MAKs, etc) are the best example of this concept and the process of their derivation has acceptance throughout the world. Even so, the assigned numbers should not be used without expert knowledge on the significance of the biological test results on which they are based. The numbers themselves merely represent a value in specific units that provide adequate levels of protection. It is inappropriate to rank chemicals in terms of their hygiene standards because they are set to control different types of adverse effects. One chemical is not necessarily considered a higher priority (or greater risk) than another with a standard twice as high. For example phosgene has an MAK value of 0.4 mg/m^3 , whereas hydrogen cyanide has a value of 11.0 mg/m^3 . The numbers do not simply mean that hydrogen cyanide is 27.5 times less hazardous than phosgene - rather that knowledge is necessary to recognise the very different toxicological hazards that each represents.

Nevertheless numerical scoring systems have been proposed for priority setting purposes.

D.2 Scoring Systems

These systems rely on condensing, the information (sometimes complex) gained from physico-chemical properties, toxicological and ecotoxicological effects into simple numerical scores for each chemical and for each property.

For the purpose of ranking, other scores are necessary e.g. estimates of concentrations in the environment, during domestic use or in the work place.

Finally all the scores are combined by arbitrary mathematical equations which differ according to the system used to produce one or more final score(s) for priority setting for each chemical.

D.3 Comments on Scoring Systems

Many scoring systems for priority setting have been developed e.g. Sampaolo and Binetti (1985, 1989); Weiss et al (1988), Koenemann and Visser (1988) and more recently by the UK-Department of Environment (DoE 1991). (A detailed description and critique of these systems are given in the Appendix I of this report).

Although these four scoring systems differ from one another, all are based on the principles described above. They have the advantage of being clear because decisions can be reached easily and they can be adapted to computerised systems.

Usually the available toxicological and ecotoxicological data are incomplete and thus no direct comparison between the chemicals is possible. For unavailable data estimated scores are used based either on related properties from which data are available or on structure activity relationships or simply by inserting "default" scores which assume certain properties for the chemical for the purpose of priority setting.

The systems combine in various ways the scores for different properties by mathematical treatment, e.g. for estimating the possible concentration of a

chemical in the environment, scores for release rates are integrated with those for biodegradation, atmospheric half life etc. The main drawback with this method is that if scores allocated to biological end points are combined with each other or with surrogate scores on exposure, this leads to scientifically meaningless figures with an unjustifiable degree of accuracy.

For example the scoring system of Sampao and Binetti (1985, 1989) collates scores for biological effects with exposure surrogate data in mathematical equations even though these scores have different meanings and therefore are not equivalent.

The UK "DoE (1991) Priority Setting Scheme" is quick and simple, but it is based on only few data and ignores more complex aspects such as chronic toxicity for which data may be available. It uses "worst-case" default values if information is unavailable. The mathematical calculations combining the scores to produce priority figures are entirely arbitrary.

The system of Weiss et al (1988) also combines all data on biological effects into a single score, although it discriminates between the three compartments air, soil and water. It is based on standardised data suitable for computer evaluation thus rendering it difficult to include any non-standardised additional information which may be of great value in priority setting. Additionally it does not take into account the important field of human exposure via consumer products.

The scoring method used in the system of Koenemann and Visser (1988) is also based on rough assumptions and arbitrary score ratios but discriminates between different exposure/effect combinations. Scoring requires expert judgement. The "scoring profile", consisting of 10 different end scores, could be used to score a number of chemicals in different ways according to anticipated hazards, but it does not allow allocation of an overall priority ranking.

D.4 Conclusion

Ranking chemicals according to a numerical value which is solely and directly related to one property only, can be an acceptable procedure. Such a procedure could lead to a valid list of chemicals ranked for example, according to their eye irritancy. It is wholly inappropriate to compare a dose (or concentration level) with another, obtained in a different laboratory with a different chemical and end-point in order to claim that one chemical has a higher priority for hazard assessment than another. For example, the sub-acute toxicity of chemicals may be ranked by comparing the highest dosage levels which produce no adverse biological responses in animal studies (i.e. by comparing the no-effect levels). Nevertheless expert judgement is needed to assess the relative significance of the effects produced by each chemical on man or the environment when deciding which of the chemical constitutes the greatest potential human health or environmental hazard.

The principle of assigning scores to each and every physical property and biological test result and totalling the scores to set relative priorities is scientifically unsound. It is impossible to reduce the multivariate human and environmental responses to one or even a single numerical values. A further criticism of all systems discussed is the use of surrogates for exposure in calculating numerical values for priority setting.

As a result of these deficiencies it is recommended that scoring systems should not be used for priority setting.

E. ECETOC Recommendation for Priority Setting

Bearing in mind the considerations and principles formulated in chapters B and D, a proposal is made for a priority setting system which is more sound from scientific basis and is manageable for screening a significant number of chemicals.

By analysing the data given in the EEC data sets [Annex II of the EEC Proposal of a Council Regulation (EEC) in Off. J. C276, vol 33, 5.11.1990]*, chemicals can be screened according to exposure and possible hazard potential to man and environment in order to assign them to different priority groups.

The ECETOC recommendation for priority setting does not use numerical scores but relies upon case by case evaluation using expert judgement. This expert judgement should be supported by a short written explanation.

E.1 The Identification of Priority Chemicals at the Screening-Stage

To screen chemicals according to exposure and possible hazard potential the following sequence of steps for priority setting are proposed:

First step: Exposure potential

should be expressed in practical terms relevant to a few use pattern categories rather than on the basis of scores allocated to estimates of emission quantities and physico-chemical data.

Chemicals should first be prioritised according to their use patterns* and hence exposure as follows:

- High exposure corresponds to wide-dispersive use,
- Medium exposure corresponds to non-dispersive use,
- Low exposure corresponds to uses in closed systems and/or inclusion on or into matrices.

* See ECETOC (1991) "Guidance for Completion of the EEC Data Set" Special Report N°. 1.

Information on environmental compartments to which a chemical is discharged and in which it will accumulate is also of use in priority setting. This can be derived from knowledge of physico-chemical properties (ECETOC, 1988). This information is included in the process, as given in the Examples 1 and Example 2.

Chemicals which have low exposure are set aside. Chemicals for which available information on exposure is insufficient for a decision to be made are considered to have high exposure potential.

Second Step: Toxicological or ecotoxicological data

should be used to evaluate the potential hazard to man or the environment. Since multiple biological observations should not be expressed as a simple numerical score, toxicological or ecotoxicological data should be summarised by short descriptions suitable for subsequent expert evaluation. It is recommended, for comparability and clarity, that the effects are grouped as follows:

- acute effects,
- subacute/subchronic and chronic effects (including effects on reproductive organs),
- genotoxic/carcinogenic effects,
- teratogenic effects,
- ecotoxic effects.

Such data should be evaluated and the chemical placed into one of the 3 following hazard categories using the guidance given in Section E.2.

- confirmed hazard,
- no clear decision possible,
- low hazard.

Third Step: Gaps in information

should be clearly identified. If, on the basis of scientific judgement certain types of data seems unnecessary, this should be stated and justified briefly.

Fourth Step: The selection of priority chemicals

should proceed by correlating the exposure assessment (first step) with the biological data (second and third step) and allocating them to one of the following 3 Main Priority Groups by using the matrix described on page 15.

Group I

Chemicals for which, on the basis of their exposure potential and biological properties, a confirmed hazard potential exists for man and/or the environment. These are candidates for hazard assessment.

Group II

Chemicals for which available data do not allow a clear decision to be made about their hazard potential. In these cases either additional tests will have to be conducted or additional information on use patterns will have to be collected.

It should be possible to re-assign these chemicals to Groups I or III, when the additional data have been collected or developed.

Group III

Chemicals with a low exposure potential, low biological hazard or both are considered to have low priority for risk assessment. This group of chemicals is set aside.

Chemicals placed in Group I or Group II may be further subdivided into different Priority Ranges by ranking exposure and/or toxic potential as described in Section E.4 and summarised in the flow chart of the ECETOC screening process (Fig 1).

E.2 Guidance for Assigning Chemicals to Hazard Categories

When assigning chemicals to one of the 3 hazard categories (see under E.1, second step) the following criteria should be used:

Toxicological Effects

Confirmed Hazard

Include all chemicals for which data demonstrate one or more of the following effects:

Acute mammalian effects:

Chemicals which are very toxic, toxic, corrosive or sensitising as defined by the EEC 7th amendment.

Subacute, subchronic, chronic mammalian effects:

Substances labelled with R48 as defined by criteria in the EEC 6th amendment.

Genotoxic / Carcinogenic effects:

Substances which show positive results in relevant mutagenicity screening tests or in relevant long term studies.

Teratogenic effects:

Substances which show teratogenic effects if administered in dosages not producing maternal toxic effects (ECETOC 1986a).

No Clear Decision Possible

Include all chemicals for which there is insufficient data for one or more parameters listed above to allow evaluation of toxicological effects.

Low Hazard

To be assigned to chemicals which the data do not meet the criteria to be classified as "Hazard Confirmed" for the following effects:

- Acute mammalian effects,
- Subacute, subchronic, chronic mammalian effects,
- Genotoxic/carcinogenic effects,
- Teratogenic effects.

Ecotoxicological Effects

Using the definitions given in the Annex to Acute Aquatic Toxicity, Degradation and Bioaccumulation, chemicals are assigned to:

Confirmed Hazard

Include all chemicals which data demonstrate the following effects:

Very toxic or have a combination of the following properties,
toxic + inherently degradable + bioaccumulative,
toxic + poorly degradable,
toxic + bioaccumulative, or
harmful + bioaccumulative.

No Clear Decision Possible

All chemicals for which data are insufficient to allow evaluation of ecotoxicological effects.

Low Hazard

To be assigned to chemicals which the data do not meet the criteria to be classified as "Hazard Confirmed" for the following effects:

Harmful + readily degradable, or
Toxic + readily degradable.

E.3 Combining Biological Effects and Exposure

The process for applying the ECETOC procedure requires the use of a matrix.

Chemicals are classified according to hazard categories for the biological effects by allocation to the corresponding fields in the matrix presented below. An overview which includes the exposure potential is used to assign chemicals to their Main Priority Group and Priority Range. A short statement should support this decision e.g. Examples 1 and Example 2.

Matrix for Categorisation of the Hazard Potential of a Chemical in the ECETOC Priority Setting Process

Chemical Name:
CAS N° :

Biological Effects	Confirmed Hazard	No decision possible	Low Hazard
Acute Toxicity			
Subchronic/ Chronic Toxicity (incl. Reprod. organs)			
Genotoxicity/ Carcinogenicity			
Teratogenicity			
Ecotoxicity			

Exposure (described by Use-Pattern):

Main Priority Group:

Priority Range:

Environmental compartment to which chemical will be discharged:

Environmental compartment in which chemical is likely to remain:

Justification:

E.4. Priority Setting

Chemicals assigned to Group III (low exposure or low biological effects) are of low priority and no immediate action will be necessary.

Setting the priorities of chemicals in Group I or Group II requires careful consideration. For those chemicals presenting a readily recognised hazard for man or environment a more detailed and quantified consideration of actual risk involved may be needed urgently. For many of such cases, risk control measures may have been adopted already. For others a more detailed assessment, especially of exposure, may lead to the conclusion that the risk is not as high as was at first suspected on the basis of the limited initial data. Consequently, gathering more information on exposure or filling data gaps by additional testing of chemicals in Group II to confirm a suspected hazard may be just as important as the assessment of hazard for chemicals in Group I. It is therefore recommended that chemicals in Group I and Group II are assessed in parallel.

It may be necessary to apply a further priority setting step in order to produce manageable numbers of chemicals for expert assessment. Chemicals placed into Group I and Group II can be subsequently assigned in each group to further 3 Priority Ranges described below (see also Figure 1).

All chemicals within each Priority Range are basically considered to have the same priority level.

Criteria to be applied on chemicals in Group I and Group II for assigning to Priority Ranges:

Group I Chemicals where the exposure levels are either high or medium and a confirmed biological hazard has been identified (These chemicals are candidates for Hazard Assessment).

1st Priority Range : Chemicals with High Exposure and Confirmed Toxicological and Ecotoxicological Hazard.

2nd Priority Range : Chemicals with High Exposure and Confirmed Toxicological and Low Ecotoxicological Hazard.

: Chemicals with High Exposure and Low Toxicological Hazard and Confirmed Ecotoxicological Hazard.

: Chemicals with Medium Exposure and Confirmed Toxicological and Ecotoxicological Hazard.

3rd Priority Range : Chemicals with Medium Exposure and Confirmed Toxicological Hazard and Low Ecotoxicological Hazard.

: Chemicals with Medium Exposure and Low Toxicological Hazard and Confirmed Ecotoxicological Hazard.

Group II Chemicals where exposure levels are either high or medium, or where exposure cannot be identified and the biological data do not allow a clear decision (Candidates for further data gathering or testing).

1st Priority Range : Chemicals with High Exposure
or Not Identified Exposure and
insufficient Biological data are available
for assigning hazard category.

2nd Priority Range : Chemicals with Medium Exposure and
no Biological data are available.

: Chemicals with Medium Exposure and
biological data indicate
a Confirmed Hazard in
Toxicology or in Ecotoxicology.

3rd Priority Range : Chemicals with Medium Exposure and
Biological data indicate
a Low Hazard in Toxicology
or in Ecotoxicology.

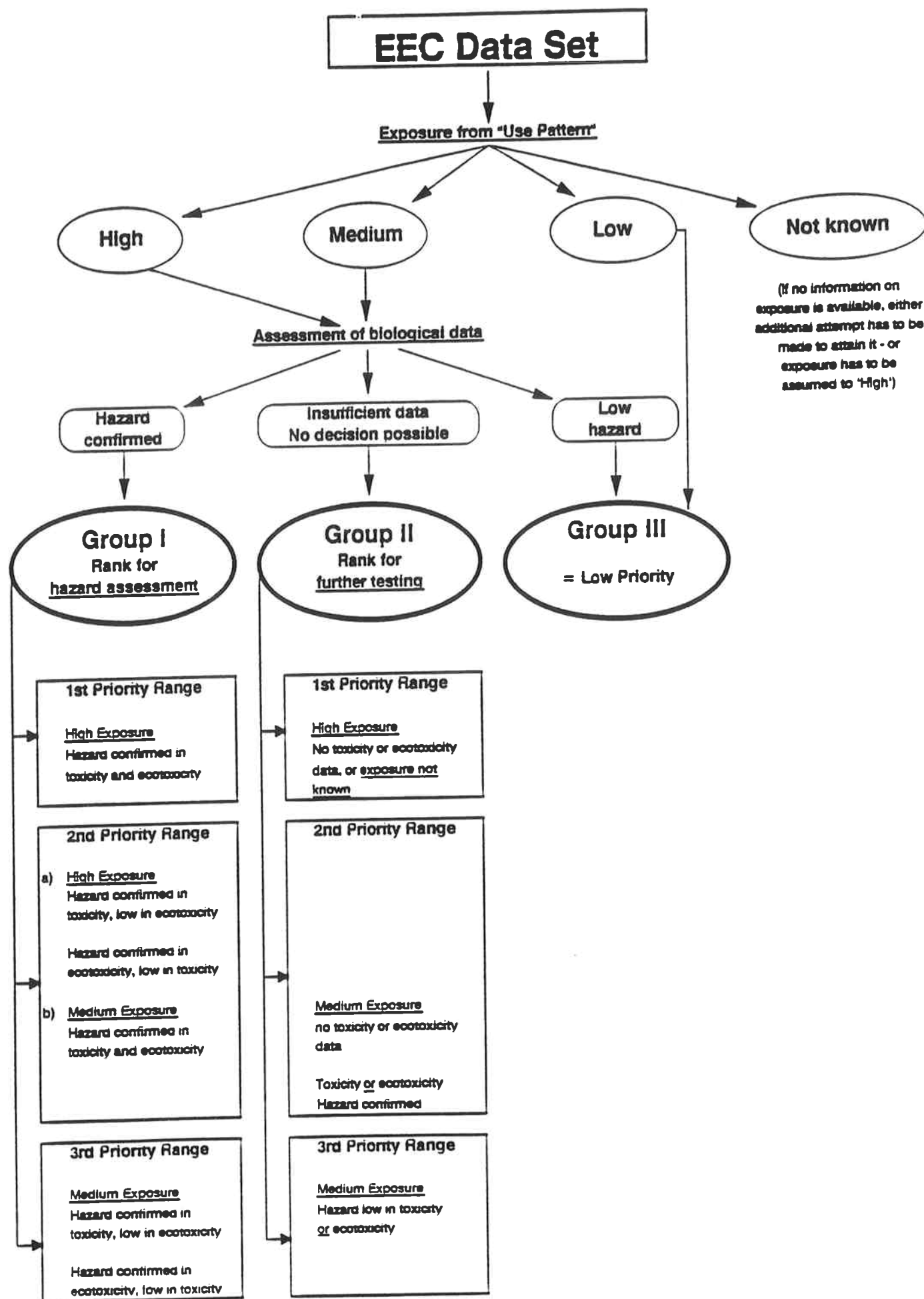
Additional information obtained on the chemicals is then used to
re-assign them to either Group I or Group III.

Group III Chemicals identified to be of low priority and therefore to be
set aside.

At some later stage it may be desirable to introduce priorities
within this group based on the principles described previously
for Groups I or II.

Based on the flow chart of the ECETOC screening process (Fig.1) all possible combinations of the ratings for EXPOSURE, TOXICITY and ECOTOXICITY are given in Fig.2.

The two examples, 1,4-Dichloro-2-nitrobenzene (Example 1) and Isophorone (Example 2) will serve to illustrate how criteria can be used to assign chemicals to the priority groups. The proposed ECETOC procedure, does not represent an arbitrary scoring system which requires little or no expert judgement. It recognises that there is no credible, scientific substitute for involving appropriate expertise.



Matrix for assigning chemicals into the main Priority Groups I - III and all possible combinations of the ratings for Exposure, Toxicity and Ecotoxicity

[illegible]

EXAMPLE 1.

Categorisation of the Hazard Potential of
1,4 Dichloro-2-nitrobenzene
in the ECETOC Priority Setting Process

Chemical Name: 1,4-Dichloro-2-nitrobenzene
CAS N° : 89-61-2

Biological Effects	Confirmed Hazard	No decision possible	Low Hazard
Acute Toxicity	X		
Subchronic/ Chronic Toxicity (incl. Reprod. organs)	X		
Genotoxicity/ Carcinogenicity	X		
Teratogenicity		X	
Ecotoxicity	X		

Exposure (described by Use-Pattern): Low (closed systems)

Main Priority Group: III

Priority Range: -

Environmental compartment to which chemical will be discharged: water, air

Environmental compartment in which chemical likely will remain: water

Justification:

1,4-Dichloro-2-nitrobenzene is classified as acutely toxic because of acute oral and dermal toxicity and the risk of methaemoglobin formation. The chemical is not a sensitiser in the Maximisation Test. A decrease of erythrocyte count and haemoglobin content occurred in subacute toxicity tests, no effect levels were not specified.

The chemical is mutagenic in the Ames test without S9 mix. Data on teratogenicity are not available.

1,4-Dichloro-2-nitrobenzene is toxic to fish, less toxic to bacteria. It is poorly biodegradable (static test = modified OECD test 302 B; modified MITI test); log Pow is 3.09 (calculated).

Due to the acute toxicity effects the chemical is handled only under strictly controlled conditions. The exposure potential to the environment is low (discharge by effluents and vents together is less than 50 kg/y - mostly to the atmosphere - at one production site).

Despite of its toxicity and ecotoxicity the chemical has a low priority because its exposure potential is low.

EXAMPLE 2.

Categorisation of the Hazard Potential of Isophorone in
the ECETOC Priority Setting Process

Chemical Name: Isophorone
CAS N° : 78-59-1

Biological Effects	Confirmed Hazard	No decision possible	Low Hazard
Acute Toxicity			X
Subchronic/ Chronic Toxicity (incl. Reprod. organs)			X
Genotoxicity/ Carcinogenicity		X	
Teratogenicity			X
Ecotoxicity			X

Exposure (described by Use-Pattern): High (non dispersive use, wide dispersive use)

Main Priority Group: II

Priority Range: 1st Range

Environmental compartment to which chemical will be discharged: water, soil

Environmental compartment in which chemical likely will remain: water, soil

Justification:

The acute toxicity of isophorone is low with LD₅₀ values around 2000 mg/kg and a LC₅₀ > 7000 ppm. Repeated dose toxicity does not show significant effects below doses of 100 - 150 mg/kg after oral application and 25 ppm after inhalation.

The chemical is negative in several in vitro gene-mutations tests and has no mutagenic activity in vivo. There is some evidence of carcinogenicity

in male mice. No selective toxicity to the embryo or foetus has been found. Toxicity to aquatic organisms is low.

Isophorone is rapidly photodegraded in air; the situation for water biodegradation is not clear.

During production and use the chemical will be discharged in limited quantities into water and soil, from where it will evaporate into air.

Limited discharge of the chemical into the environment and low toxicity to aquatic organisms indicates a small hazard potential for the environment. When used as a solvent man may be exposed.

Unclear evidence of carcinogenicity requires further assessment and additional information on exposure is needed.

ANNEX

Criteria for classification of Chemicals by Ecotoxicological Effects:

A generally accepted classification scheme for ecotoxicity does not exist. Therefore it is recommended that the criteria for labelling chemicals "Dangerous for the Environment" are adopted (7th Amendment of Directive 67/548 EEC in preparation).

Acute aquatic toxicity

Taken for the most sensitive species:

LC ₅₀ /EC ₅₀	≤ 1 mg/l	very toxic
LC ₅₀ /EC ₅₀	1 - 10 mg/l	toxic
LC ₅₀ /EC ₅₀	10 - 100 mg/l	less toxic (harmful)

Degradability

Degradability is a key criterion for exposure estimation when a chemical is released into the environment. It may be due to one or more of the following processes: biological transformation, hydrolysis, photolysis, photochemical or other chemical reactions. Two aspects are important:

- the extent of molecular breakdown,
- the kinetics of the transformation reaction.

A chemical would be regarded favourably, either if it degraded ultimately to inorganic compounds or partially to products which are known to break down easily.

Regarding the duration of such processes, some classification of biological degradation data has been widely accepted. For example the data derived from standard aerobic aquatic tests are grouped into the following categories:

readily biodegradable,
inherently biodegradable,
poorly biodegradable.

Criteria for the categories are given in the relevant OECD and ISO test methods.

For biodegradation in soil and sediments a different time scale has to be applied and a rigid categorisation cannot be given. The estimation of a half-life for biodegradation of chemicals in these compartments is not suitable since the processes are rather complex and cannot be described by "zero" or "first order" kinetics. It is concluded that a consideration of all these factors together is required and this in turn relies on expert judgement.

Abiotic degradation kinetics are evaluated according to the compartment where they are most likely to occur. Since such reactions usually obey "zero" or "first order" kinetics degradation time may be calculated in terms of half-life. Abiotic degradation should be extended additionally to include the breakdown products.

A reasonable approach for differentiating between stable and unstable compounds is the comparison of half-life and spatial dissipation in the environment. For example, the time taken for a full circulation cycle of the the air in one hemisphere is approximately one month, for the hydrosphere - open oceanic water - about a year. Exchange processes in soil, especially long distance transport of groundwater, may take periods from weeks to decades. In order to avoid accumulation, the stability of a chemical which is constantly emitted into the environment should be less than the period needed for dispersion in the relevant compartment. Therefore in these situations a generally accepted time scale does not exist, nor should one be given since the overall evaluation of a chemical has to include its toxicological potential.

The physico-chemical properties of a chemical are important in the determination of its migration from one environmental compartment to another, and therefore all degradation process (abiotic and biotic) must be considered

in air, soil and water. The evaporation of chemicals from surface waters to atmosphere should also be taken into account.

Bioaccumulation

Chemicals that show a concentration factor of >100 times in higher aquatic organisms above that of the surrounding water or with a log P_{ow} of >3 are considered to be bioaccumulative.

Guidance for Ecotoxicological Hazard Classification

Using these definitions chemicals can be classified in hazard categories using combinations of acute toxicity, degradability and bioaccumulation as described in Section E.2.

APPENDIX I

SCORING SYSTEMS

Description and Evaluation

Contents

1. Description of Various Scoring Systems	30
1.1 Scoring System of Sampaolo and Binetti (1986; 1989)	30
1.2 The UK DoE Priority Setting Scheme (1991)	31
1.3 Scoring System of Weiss et al (1988)	32
1.4 Scoring System of Koenemann and Visser (1988)	34
2. Evaluation of the Scoring Systems.....	36
Tables and Figures	40

1. Description of Various Scoring Systems

1.1. Scoring System of Sampaolo and Binetti (1986; 1989)

Scores are developed for physico-chemical, toxicological and ecotoxicological properties both for data which exist and which are deficient. Where data are absent, the score is estimated from data on related chemicals or from structure-activity relationship (SAR). Detailed guidelines on how to estimate scores in the absence of data are provided. The scores are added for each of the 3 properties and the sums are used for subsequent calculations.

Additional estimates known as "multiplier parameters" are made. These relate to

- quantity of chemical in the market,
- routes of direct exposure (personal/domestic/occupational),
- environmental spread,
- persistence,
- bioconcentration,
- size of risk population.

A "General Risk Index" (GRI) is calculated from the scores and the multiplier parameters using an equation (Table 1). The GRI is expressed as a percentage of the maximum possible score number; the higher the GRI, the higher the anticipated risk from environmental, domestic and/or occupational exposure.

Similar mathematical equation have been developed to emphasise the importance of various end points so that risk indices can be calculated in relation to personal exposure, environmental exposure or irreversible effects.

Details of the criteria used and the range of scores are given in Table 2, which also contains examples of the method applied to 3 chemicals.

No distinction is made between scores based on available or non-available data in the risk index calculation. The calculation of a "priority index" (PI) from the "risk index" (RI), however, discriminates between the two groups of scores. In the equation

$$PI = R \times RI$$

the "priority coefficient" (R) is defined as the ratio of the number of estimated scores to the total number of scores. Thus R varies between 0 (= all data available) and 1 (= no data available). It is concluded that the higher the priority index the higher the necessity for further testing.

In the ranking of priorities, the top group will consist of chemicals with high anticipated risk but few data, the middle group with high anticipated risk and more data or of lower anticipated risk but few data, and the bottom group of lower anticipated risk and more data (see examples given in Table 2).

1.2. The UK DoE Priority Setting Scheme (1991)

This scheme, many details of which are still unpublished, is intended for priority ranking of chemicals with regard to their possible effects on man and the environment. It is based on the following 5 parameters.

- Annual tonnage: the log value is used as a score.
- Toxicity: Mammalian and aquatic toxicity, are scored separately in a range between 1 and 6. For mammalian toxicity a score is derived from only acute and sub-acute data. For aquatic toxicity, chronic

data are used where available. Whichever of these two scores is the greater is used as the final toxicity score.

- Bioaccumulation: Bioconcentration factors or, where not available, $\log P_{ow}$ values are scored at 5 intervals between 1 and 2.
- Degradation: 3 scores are established: between 1 and 3 for ready biodegradability, between 1 and 4 for inherent biodegradability and for half-life in the atmosphere. The worst-case score is used.
- Use-pattern: In a 4 point scheme, chemicals are scored on the likelihood of their release to the environment during normal use.

The final score is obtained by multiplying the scores of the 5 parameters together. Toxicity is the most important parameter, followed by use pattern, persistence, tonnage and bioaccumulation. The higher the score, the higher the priority.

1.3. Scoring System of Weiss et al (1988)

This system is also intended for priority ranking of chemicals with regard to their possible effects on the environment. Priority ranking is carried out separately for the 3 compartments air, soil and water.

The system is based on all accessible data defined in levels 0, I and II of the Directive 79/831/EEC. The minimal data set required consists of production volume and use type for exposure estimation, and acute toxicity and ecotoxicity data for effects. It is suggested that important but missing data are estimated from structure-activity relationship (SAR) (Klein et al, 1988). Chemicals of extremely high toxicity, with emissions of > 1 t/y, are immediately categorised as of high priority ("black box").

Exposure is estimated separately for the compartments air, soil and water, from the quantity released into the environment, biodegradation,

photolysis and accumulation potential. The "Quantity in Environment" is calculated from production volume (t/a) and use pattern where it is assumed that the release into the environment is 3 % for intermediates, 10 % for chemicals used in "processing" and 100 % for end use products. The quantity in the different compartments is estimated firstly at "Initial Partitioning" and secondly, after equilibration, using level 1 of Mackay's fugacity model (Paterson and Mackay, 1985). Biodegradation and photolysis half life contribute negatively, whereas accumulation is rated positively because of enhanced presence of the chemical in organisms (Table 3). The data are recorded in the form of an "exposure fingerprint" (Fig. 1). The quality of the data used (experimentally determined, calculated or extrapolated) should be stated.

The individual effect end-points are grouped together and scored as follows: mutagenicity/carcinogenicity (max.score 6), long-term toxicity (max. 4), reproductive toxicity (max. 3), acute toxicity (max. 2) and skin effects (max. 1) (Table 4). The data are recorded as an "effects fingerprint" which contains 2 threshold lines separating 3 hazard ranges (Table 5).

Final scoring is then performed in the following way: if the bar for a criterion in a fingerprint graph exceeds the second threshold line, all available scores for this criterion are given. If the bar reaches a level between the two threshold lines, half of the maximum scores for a criterion are given. If the bar does not reach the first line, no scores are given, indicating a low contribution of the respective criterion to the overall hazard of a chemical.

The scores thus generated may not be of equivalent importance for all three environmental compartments and are, therefore, multiplied with the relative "weights" for air, soil and water as indicated in Table 3 and 4. For comparability, the scores for all criteria of exposure are summed, with the maximum sum obtainable set at 100%. The effects criteria are processed in the same way. The actual scores are expressed as percentages of the possible scores.

As a result of this procedure three pairs of scores are generated for each of the three environmental compartments. These are plotted in two-dimensional graphs in which the contributions of the various criteria are represented by arrows, resulting in "image points" for each chemical in each compartment (Fig 2.).

Priority ranking can be done graphically by inserting the "image points" of all chemicals under consideration into one graph for each compartment. Lines of constant priority can be drawn in these diagrams separating different priority classes. (Fig. 3 and Table 8).

A computer programme (written in Turbo-Pascal) is available for the necessary calculations, attribution of scores and plotting of image points.

1.4. Scoring System of Koenemann and Visser (1988)

In this system, exposure to organisms by chemicals in the environment and by consumer products is taken into consideration, but not human occupational exposure. It is not intended to produce a single priority figure. The end product is a "scoring profile" which leaves room for discussions about final priority setting and allows sorting of a number of chemicals according to 10 different criteria. The system follows the lines of the OECD (1984) Report. Practical experience led to an adjustment for scoring the parameters "mutagenicity" and "carcinogenicity" (Timmer et al, 1988).

The system is based on comparison of the estimated exposure of target organisms with the level of exposure above which effects may occur (NOEL). The ratio of these levels is a "safety factor", which is different for different target organisms and for different exposure scenarios.

The parameters listed in the headings 1-5c of Table 9 are used in the scoring system. Scores are allocated to each parameter as outlined in the Table. If information is not available figures have to be estimated.

Four different exposure scenarios are scored (see Table 10),

Finally the exposure and effects are integrated in the following combinations:

Exposure	Effects	Abbreviations	max. scores
air	general toxicity for mammals	A and 1	6 + 3 = 9
"	mutagenicity	A and 2a	6 + 3 = 9
"	carcinogenicity	A and 2b	6 + 3 = 9
soil/water	toxicity for aquatic organisms	B and 3	6 + 3 = 9
water	general toxicity for mammals	C and 1	8 + 3 = 11
"	mutagenicity	C and 2a	8 + 3 = 11
"	carcinogenicity	C and 2b	8 + 3 = 11
products	general toxicity for mammals	D and 1	8 + 3 = 11
"	mutagenicity	D and 2a	8 + 3 = 11
"	carcinogenicity	D and 2b	8 + 3 = 11

Each score is subtracted from the maximum value which can be reached for that combination. Thus a series of 10 endscores is achieved which represent the scoring profile.

The endscores reflect the magnitude of the "safety margin" between "scored hazard" and "maximum hazard" for each of the combinations. Since the individual scores are on a logarithmic scale (Table 9), an endscore of 1 represents a safety factor of 10, 2 of 100, etc.

Chemicals with high toxicity, high persistence or very high exposure are separated ("black box") and checked to see if they could be hazardous in special circumstances.

2. Evaluation of the Scoring Systems

Sampaolo and Binetti provide guidance on how to deal with missing data in a simple way. Its advantages are:

- decisions can be reached easily;
- it clearly distinguishes between scores based on actual or estimated data;
- it combines anticipated risk and completeness of the data base in assessing the priorities for further testing;
- it is adaptable to the EEC questionnaire and does not require much expertise in fixing scores.

The disadvantages are:

- there is a mathematical treatment of the scores, leading to one single arbitrary priority figure;
- the maximum number of scores for physico-chemical, toxicological and ecotoxicological properties is 1:2:1 which suggests that the ratio was selected arbitrarily;
- the weighting of the various scores within a group is also arbitrary and would need more careful consideration; some parameters cannot be used due to lack of data, e.g. "toxicity for higher plants";
- most estimated scores are based on structure-activity relationships (SAR) for broad groups of chemicals usually characterised by just 1 functional group (Sampaolo and Binetti, 1986; Astill, 1983); even for closely related chemicals SAR is not sufficiently developed to provide reliable results (ECETOC, 1986b).

- identical scores are given for parameters of a totally different nature; thus scores for physico-chemical properties may be given the same weighting as biological data e.g. low molecular weight is scored the same as sensitising properties:
- only one factor is ascribed for environmental diffusion so that there is discrimination between the different environmental compartments; persistence is based mainly on biotic degradation in water and the "quantity on the market", even if known, is a doubtfully valid surrogate for the level of exposure.

The UK "DoE Priority Setting Scheme" has the advantage that it is quick and simple. It uses few data, ignoring more detailed data which may be available. It uses default values if data are unavailable. The mathematical calculation of the priority figures is arbitrary.

In the Scoring System of Weiss et al data gaps are filled by estimates made from structure-activity relationships. Only few data are used in the system, resulting in wide margins of uncertainty.

Its advantages are:

- decisions can be reached easily,
- it is adaptable to the EEC questionnaire,
- it is computer-supported and once installed can be operated easily,
- it classifies chemicals of very high toxicity into a "black box" category thus preventing "dilution" of a particularly dangerous property with favourable scores from other end-points.

The disadvantages are:

- scoring is based on a limited data set, thus chemicals are ranked even though a decision is not possible without further data;

- estimates of the "Quantity in Environment" are made from crude assumptions;
- the weighting of the various scores is arbitrary;
- the environmental distribution (calculated according to Mackay level 1) is not valid for chemicals which degrade in the environment;
- SAR is not sufficiently developed to provide reliable estimates (ECETOC, 1986b);
- scoring by computer would necessarily neglect the non-standardised contents of the "Summary" sections of the EEC questionnaire;
- the system does not take into account occupational and domestic exposure;
- it is not clear how the 3 priority figures obtained for each of the compartments (air, soil and water) would influence the overall priority setting.

In the Koenemann and Visser System a set of parameters is defined, on which scoring is performed schematically. The authors recognise, that experts are required for setting scores, so that information additional to base set data is taken into account. This is a disadvantage with regard to shortage of professional manpower but an advantage regarding the viability of scoring.

Other advantages of the system are:

- decisions can be reached easily;
- it is adaptable to the EEC questionnaire;

- it classifies chemicals with high toxicity, persistence or high exposure into a special category for peer-checking by experts ("black box");
- the resulting "scoring profile" allows a quick overview of the way a chemical may present a hazard.

The disadvantages are:

- no detailed instructions are given on how SAR should be applied and how estimates should be made in the absence of data;
- the final scoring profile does not reflect the quality of the data;
- estimates of the quantity in the environment are made on crude assumptions;
- the environmental distribution (estimated according to Mackay level 1) is not valid for chemicals which degrade in the environment.

Table 1

Scoring System of Sampaolo and Binetti

Equations Used for Calculation of Various Risk and Priority Indices
(Abbreviations see next page)

1. General Risk Index

$$GRI = \frac{(PCP + TP + ETP) \times Q \times BC \times (PDE + ED \times P) \times RP}{6300} \times 100$$

2. General Priority Index

GPI = R" x GRI, where R" is the ratio of the sub-sum of scores estimated to the sum of all scores

3. Risk Index for Direct Personal Exposure

$$RI = \frac{(PCP + TP) \times Q \times PDE \times BC \times RP}{2025} \times 100$$

4. Risk Index for Environmental Exposure

$$RI = \frac{(PCP + TP + ETP) \times Q \times BC \times ED \times P \times RP}{3600} \times 100$$

5. Risk Index for Irreversible Effects due to Professional Exposure

$$RI = \frac{TP(CMT) \times Q \times PRE \times BC \times RP}{315} \times 100$$

Table 1 cont.

Scoring System of Sampaolo and Binetti

List of Abbreviations used

BC	=	bioconcentration score
DE	=	domestic exposure score
DPE	=	direct personal exposure score
ED	=	environmental diffusion score
EE	=	environmental exposure score
ETP	=	ecotoxicological properties score
GPI	=	general priority index
P	=	persistence score
PCP	=	physico-chemical properties score
PDE	=	plurality of direct exposure (PE + DE + PRE) score
PE	=	personal exposure score
PI	=	priority index
PRE	=	professional exposure score
Q	=	quantity on the market score
R	=	priority coefficient
R '	=	coefficient of priority as to PCP + TP
R "	=	coefficient of priority as to PCP + TP + ETP
GRI	=	general risk index
RI	=	risk index
RP	=	size of risk population score
TP	=	toxicological properties score

Table 2

Application of Scoring System of Sampaolo and Binetti to 1,2-Dibromoethane (DBE), Isophorone (ISO) and Dichloronitrobenzene (DCNB)

Parameter	Range	DBE		ISO		DCNB	
		a.*	n.a.**	a.*	n.a.**	a.*	n.a.**
Physical and chemical properties (PCP)							
Molecular weight***	0-2	2	-	2	-	2	-
Melting point	0-2	2	-	2	-	1	-
Boiling point	0-2	1	-	0	-	0	-
Relative density***	0-2	0	-	1	-	-	1
Vapour pressure	0-2	2	-	1	-	1	-
Surface tension***	0-2	-	2	-	2	-	1
Water solubility	0-3	2	-	2	-	1	-
Fat solubility	0-3	-	3	3	-	-	3
Flammability	0-3	0	-	0	-	0	-
Explosivity	0-2	0	-	2	-	2	-
Oxidising properties***	0-2	0	-	-	0	-	1
Sub-sum:		9	5	13	2	7	6
Sum: max.25		13		15		13	
Toxicological properties (TP)							
Acute toxicity	0-5	3	-	0	-	1	-
Irritation	0-3	2	-	2	-	0	-
Sensation	0-2	0	-	0	-	0	-
Long term tox.	0-5	3	-	5	-	2	-
Mutagenesis	0-10	-	10	0	-	-	10
Carcinogenesis	0-15	15	-	-	2	-	10
Teratogenesis	0-10	-	5	0	-	-	2
Sub-sum:		23	15	7	2	3	22
Sum: max.50		38		9		25	
Ecotoxicological properties (ETP)							
Acute tox. fish	0-5	3	-	1	-	5	-
Tox. daphnia magna	0-5	-	5	3	-	-	1
Tox. birds***	0-5	3	-	-	3	-	1
Tox. higher plants***	0-5	5	-	0	-	-	5
Tox. algae	0-5	-	5	3	-	-	1
Sub-sum:		11	10	7	3	5	8
Sum: max.25		21		10		13	
Multiplier parameters							
Quantity on the market	0-3	3	-	2.5	-	2	-
Personal exposure	0-1	0.5	-	0	-	0	-
Domestic exposure	0-1	0.5	-	0	-	0	-
Occupational exposure	0-1	1	-	1	-	0.5	-
Environmental spread	0.5-2	1	-	1	-	0.5	-
Persistence	0.5-2	2	-	-	1.5	2	-
Bioconcentration	0.5-1.5	-	1.5	1	-	1.5	-
Size of risk population	0.5-2	1.5	-	1	-	0.5	-

(* datum available, ** datum not available)

(*** parameter not included in EEC-questionnaire)

Table 2 cont.

Scoring System of Sampaolo and Binetti

Risk Indices and Priority Indices

Index	DBE		ISO		DCNB	
	RI	PI	RI	PI	RI	PI
General (GRI)	31.3	12.8	3.4	0.71	1.82	1.29
(Rank)*	(9)*	(10)*	(50)*	(60)*	(58)*	(52)*
Environmental exposure	27.4	11.2	3.5	0.74	2.13	1.51
Personal exposure	34.7	13.3	3.0	0.49	1.41	1.04
Irreversible effects/ profess. exposure	85.7	42.9	3.17	3.17	21.0	21.0

* Rank within a group of 82 compounds, 80 of which (including DBE) are given as examples by Sampaolo and Binetti (1989).

Priority Coefficients

(to be used for calculation of Priority Indices
from Risk Indices)

	DBE	ISO	DCNB
R' (personal exposure)	0.38	0.17	0.74
R'' (environ./general exp.)	0.41	0.21	0.71
R''' (irreversible effects)	0.50	1.00	1.00

Table 3

Scoring System of Weiss et al

Threshold values for exposure and the respective scores. Weight factors to be applied for the different compartments.

Criterion	Scale of exposure scores			Weight		
				Air	Soil	Water
Quantity in compartment (tons/annum)	<10 0.0	10-100 2.0	≥100 4.0	1.0	1.0	1.0
Initial partitioning (tons/annum)	<10 0.0	10-100 1.0	≥100 2.0	1.0	1.0	1.0
Biodegradation	Ready -2.0	Inherent -1.0	None/no data 0.0	0.0	1.0	1.0
Photolysis half-life (d)	<1 -2.0	1-10 -1.0	≥10/no data 0.0	1.0	0.0	0.0
Accumulation (log P_{ow})	<2 0.0	2-4 0.5	≥4 1.0	0.0	1.0	1.0

Figure 1

Scoring System of Weiss et al

Exposure "fingerprint" for 2-propenenitrile (acrylonitrile). The characters on the right of the single bar charts indicate the quality of the data (0, experimentally determined; 1, calculated by QSAR; 2, extrapolated beyond the range of the experiment). t/a = tons per annum.

(|||||) independent of compartment; (▨) air; (▩) soil; (▧) water.

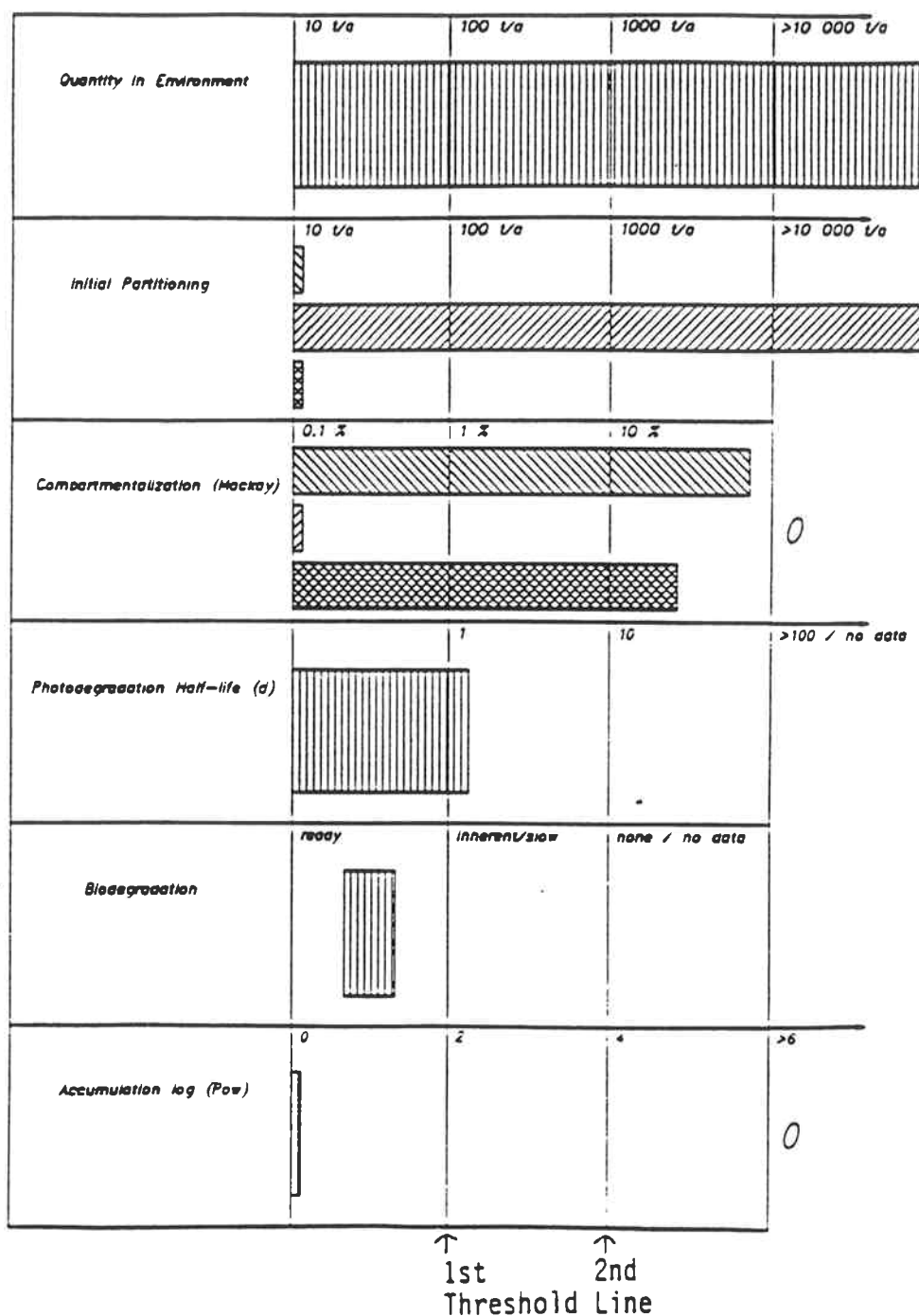


Table 4

Scoring System of Weiss et al

Threshold values for effects and the respective scores. Weight factors to be applied for the different compartments.

	No scores	Half scores	Full scores	"Black box"	Weight		
					Air	Soil	Water
1. Carcinogenicity/mutagenicity: maximum 6 scores							
Mutagenicity	Both tests negative	At least one in vitro test positive	In vivo positive	In vivo and in vitro positive	1.0	1.0	1.0
Carcinogenicity			Confirmed in vivo		1.0	1.0	1.0
2. Prolonged toxicity: maximum 4 scores							
Chronic toxicity (2 years)							
Oral/dermal	>5	5-1	≤1	≤0.01	0.5	1.0	0.0
OR				(oral only)			
Inhalative	>0.04	0.04-0.01	≤0.01	≤0.0001	1.0	0.5	0.0
OR							
Subchronic/subacute toxicity (90 d/28 d)							
Oral/dermal	>25	25-5	≤5	≤0.05	0.5	1.0	0.0
				(oral only)			
Inhalative	>0.2	0.2-0.05	≤0.05	≤0.001	1.0	0.5	0.0
Prolonged aquatic toxicity (fish, <i>Daphnia</i> ; worst case)							
	>1	1-0.1	≤0.1	≤0.001	0.0	0.0	1.0
Plant growth	>250	250-10	≤10	≤1	1.0	1.0	1.0
Algae	>50	50-1	≤1		0.0	0.5	1.0
If no long-term toxicity test available, then							
Bioaccumulation	<100	100-1,000	≥1,000		0.0	1.0	1.0
OR							
log <i>P</i> _{ow}	<2	2-4	≥4		0.0	1.0	1.0
3. Teratogenicity/fertility: maximum 3 scores							
Teratogenicity	No	—	Positive		1.0	1.0	1.0
Fertility							
Terrestrial	No	—	Positive		1.0	1.0	0.0
Aquatic	No	—	Positive		0.0	0.0	1.0
Plants	No	—	Positive		0.0	1.0	0.0
4. Acute toxicity: maximum 2 scores							
Acute toxicity							
Rat, oral	>2000	2,000-200	≤200	≤2	0.5	1.0	0.0
Rat, dermal	>2000	2,000-400	≤400		0.5	1.0	0.0
Rat, inhalative	>50	50-5	≤5	≤0.05	1.0	0.5	0.0
Birds, oral	>2000	2,000-200	≤200		1.0	1.0	0.0
Earthworm	>500	500-10	≤10		0.0	1.0	0.0
Acute aquatic toxicity (fish, <i>Daphnia</i> ; worst case)							
	>10	10-1	≤1	≤0.01	0.0	0.0	1.0
5. Skin effects: maximum 1 score							
Skin irritation	None	Mild-severe	Corrosive		1.0	1.0	0.0
Skin sensitization	None	—	Positive		1.0	1.0	1.0

Table 5

Scoring System of Weiss et al

Effects "fingerprint" for 2-propenenitrile (acrylonitrile). The characters on the right of the single bar charts indicate the quality of the data (0, experimentally determined; 1, calculated by QSAR; 2, extrapolated beyond the range of the experiment).

Carcinogenesis Rat	none	confirmed in vivo	0
Mutagenesis Ames	negative	in vitro positive	0
Teratogenesis Rat	negative	positive	0
Fertility (Mammals / Birds) Rat	negative	positive	0
Fertility (Higher Plants)	negative	positive	n
Fertility (Aquatic)	negative	positive	n
Skin Sensitization Guinea pig	none	positive	0
Skin Irritation Rabbit, skin	none	mild to severe	0
Acute Tox. LD50 oral Mouse	2000 mg/kg	200 mg/kg	<2 mg/kg
Acute Tox. LD50 dermal Guinea pig	2000 mg/kg	400 mg/kg	n
Acute Tox. LC50 inhal. Mouse, m	50 mg/l	5 mg/l	<0.05 mg/l
Subacute Tox. NOEL oral	25 mg/(kg d)	5 mg/(kg d)	<0.05 mg/(kg d)
Subacute Tox. NOEL dermal	25 mg/(kg d)	5 mg/(kg d)	n
Subacute Tox. NOEL inhalative	0.2 mg/l	0.05 mg/l	<0.001 mg/l
Subchron. Tox. NOEL oral	25 mg/(kg d)	5 mg/(kg d)	<0.05 mg/(kg d)
Subchron. Tox. NOEL dermal	25 mg/(kg d)	5 mg/(kg d)	n
Chronic Tox. NOEL oral	5 mg/(kg d)	1 mg/(kg d)	<0.01 mg/(kg d)
Chronic Tox. NOEL dermal	5 mg/(kg d)	1 mg/(kg d)	n
Subchron. Tox. NOEL inhalative Rat	0.2 mg/l	0.05 mg/l	<0.001 mg/(kg d)
Chronic Tox. NOEL inhalative Rat	0.04 mg/l	0.01 mg/l	<0.0001 mg/l
Acute Birds Tox. LD50 oral	2000 mg/kg	200 mg/kg	n
Acute Earthworm Tox. LC50	500 mg/kg	10 mg/kg	n
Plant Growth EC50	250 mg/kg	10 mg/kg	<1 mg/kg
Acute Aquatic Tox. EC50/LC50 <i>Lebomis macrochirus</i>	10 mg/l	1 mg/l	<0.01 mg/l
Subacute Aquatic Tox. NOEC	1 mg/l	0.1 mg/l	<0.001 mg/l
Algae Reproduction EC50	50 mg/l	1 mg/l	n
Fish Accumulation	100	1000	n
Accumulation (Eise)	100	1000	n

↑ 1st
↑ 2nd
Threshold Line

Scoring System of Weiss et al

Water

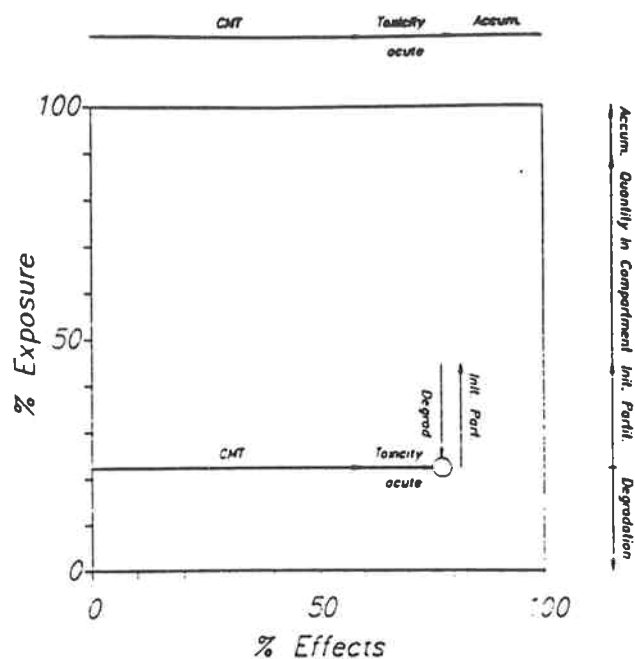
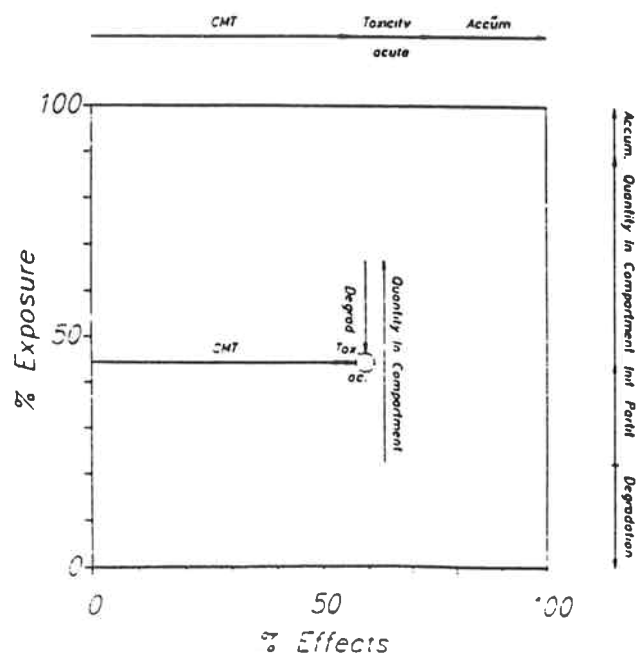
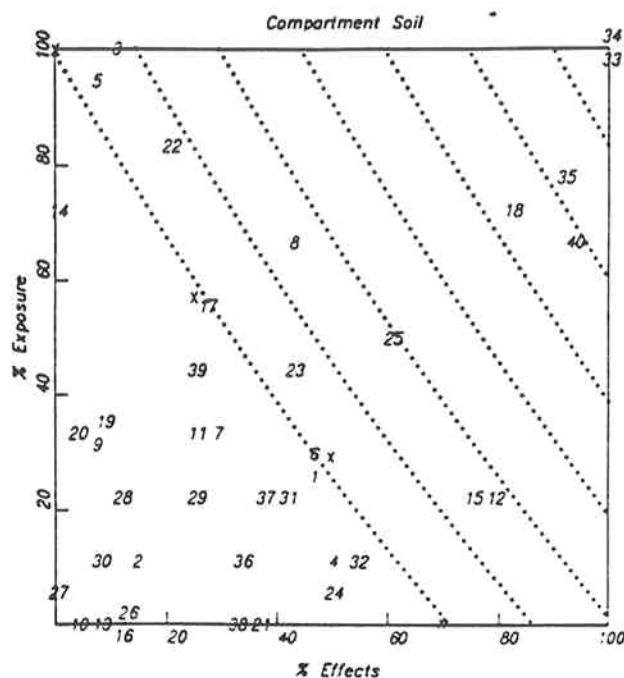
Soil

Figure 3

Scoring System of Weiss et al

a) : Image Points for 40 Chemicals and Lines of Constant Priority for
Compartment: Soil



b) : Image Points for 40 Chemicals for Compartment: Water

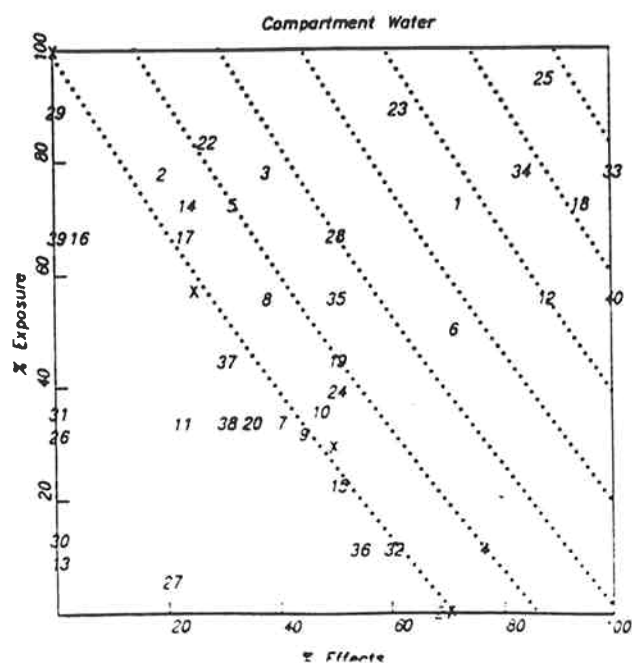


Table 8

Scoring System of Weiss et al

Ranking of 40 Substances for which Image Points are Included in Fig. 3a and b

N°.Chemical Name	Ranks for Soil	Compartment Water
1 Benzene	15	8
2 4-Nitrophenol	33	20
3 Pentachlorophenol	11	11
4 4-Chloroaniline	18	14
5 Atrazine	-	15
6 Trichloroethene	13	9
7 1,2,4-Trichlorobenzene	22	27
8 Hexachlorobenzene	8	18
9 Fluoranthene	30	24
10 2-Nitrophenol	39	21
11 Perylene	24	35
12 Benzidine	7	6
13 (Z)-2-Methyl-2-Butenenitrile	37	40
14 2,6-Dichlorobenzonitrile	21	19
15 1,1-Dichloroethene	9	26
16 Dimethyl(C10-C16 Alkyl)amine N-oxides (mixture)	36	36
17 3,4-Dichlorobenzotrifluoride	14	22
18 gamma Hexachlorocyclohexane (Lindane)	5	3
19 2-Benzyl-4-Chlorophenol	28	16
20 n-Octane	32	31
21 Styrene Oxide	27	25
22 Bisphenol A	10	13
23 Thiourea	12	7
24 2,4,6-Trichlorophenol	23	17
25 Tris(2,3-Dibromopropyl)Phosphate	6	2
26 m-Phenylenediamine	35	37
27 Bromobenzene	38	38
28 Aniline	31	10
29 2,4-Dichlorophenoxyacetic Acid	25	30
30 Nitroethane	34	39
31 Nitromethane	17	36
32 1,1-Difluoroethane	16	23
33 1,1,1-Trichloro-2,2-bis-(4-Chlorophenyl)Ethane (DDT)	2	1
34 1,1-Dichloro-2,2-bis-(4-Chlorophenyl)Ethane (DDD)	1	4
35 1,1-Dichloro-2,2-bis-(4-Chlorophenyl)Ethene (DDE)	3	12
36 Phthalic Acid, Butoxycarbonylmethyl Butyl Ester	26	28
37 1,1-Difluoroethane	20	29
38 Phosphoric Acid Triethyl Ester	29	32
39 2,4,5-Trichlorophenoxy Acetic Acid	19	34
40 Polychlorinated Diphenyls (mixture)	4	5

Table 9

Scoring System of Koenemann and Visser

Scoring Criteria

1. General mammalian toxicity

Score	Route ^a	Tests longer than 1 month ^b	Tests one month and shorter ^b	Acute toxicity ^c
3	oral/dermal inhalation	NEL < 0,5 NEL < 1	NEL < 2,5 NEL < 5	LD50 < 25 LC50 < 50
2	oral/dermal inhalation	NEL 0,5-5 NEL 1-10	NEL 2,5-25 NEL 5-50	LD50 25-250 LC50 50-500
1	oral/dermal inhalation	NEL 5-50 NEL 10-100	NEL 25-250 NEL 50-500	LD50 250-2500 LC50 500-5000
0	oral/dermal inhalation	NEL > 50 NEL > 100	NEL > 250 NEL > 500	LD50 > 2500 LC50 > 5000

Notes :

- No difference is made between the scales for oral and dermal administration, in line with the minor differences which are found in classification systems such as in Annex VI of the EEC directive 79/831/EEC.
- NEL in mg/kg/day for oral/dermal exposure and in mg/m³ for inhalatory exposure.
- LD50 in mg/kg, LC50 in mg/m³
- Information on sensitisation and teratogenicity is also collected and scoring is performed by an expert in the field when information was available. For these end points no estimates were asked from the scoring experts.

2a. Mutagenicity

Score	Criteria
3	Positive in at least 2 types of short term mutagenicity tests
0	Negative in at least 2 types of short term mutagenicity tests and no positive test result
1*	Negative in short term mutagenicity test and no positive test result
2*	No (clear) or insufficient data available; ambiguous results
3*	At least one short term mutagenicity test positive and/or suspect (e.g. based on structure-activity relations).

2b. Carcinogenicity

Score	Criteria
3	Proven carcinogen in humans or in one or more <u>in vivo</u> animal experiments
0	Negative in <u>in vivo</u> animal experiments with at least two species, no positive results
1*	Negative in at least one <u>in vivo</u> animal experiment and not sufficient other information to decide to a 0 score
2*	No (clear) or insufficient data of <u>in vivo</u> animal experiments available : ambiguous results
3*	No (sufficient) data of <u>in vivo</u> animal experiments and positive in at least 2 types of short term genotoxicity tests.

* Under EC50 is understood: the EC50 (immobilisation) for Daphnia (24 or 48 hr), the LC50 (48 or 96 hr), for fish or comparable data.

Table 9 cont.

3. Toxicity for aquatic organisms

<u>Criteria</u>		
Score	Chronic toxicity	Acute toxicity
3	NOEC 10 < ug/l	EC50 < 1 mg/l
2	NOEC 10-100 ug/l	EC50 1-10 mg/l
1	NOEC 100-1000 ug/l	EC50 10-100 mg/l
0	NOEC > 1 mg/l	EC50 > 100 mg/l

4. Environmental exposure

4a. Use volume

<u>Score</u>	<u>Criteria</u>	
5	Use volume	$>10^4$ ton/year
4	Use volume	10^3-10^4 ton/year
3	Use volume	10^2-10^3 ton/year
2	Use volume	$10-10^2$ ton/year
1	Use volume	1-10 ton/year
0	Use volume	<1 ton/year

Note:

When it is known or estimated that more than 30 % of the production or processing of the total amount of the compound takes place at one location, one extra point has to be added to the score by the scorer.

4b. Percentage release to the environment

<u>Score</u>	<u>Criteria</u>	<u>Indication</u>
3	Use in chemical industry in closed systems	< 0,3 %
2	Use in chemical industry in open system; use in general industry	0,3-3 %
1	Some disperse use, by a number of specific consumer categories	3-30 %
0	Largely disperse use; widely spread use by consumers	> 30 %

4c. Degradation in air

<u>Score</u>	<u>Criteria</u>
3	halflife < 1 week
1	halflife 1 week - 1 year
0	halflife > 1 year

Note:

Information on (bio)degradation in soil/water is often only semi-quantitative in nature. Frequently occurring classifications are "readily biodegradable" and "inherently biodegradable". The first class is assumed to have half-lives of less than 1 week, the second one between 1 week and 1 year. Due to the greater uncertainty in the latter class there is a difference of 2.

Table 9 cont.

4d. Distribution in air (d1) and soil/water (d2)

<u>Score</u>	<u>Criteria</u>
3	In compartment considered <0,3 % of the total quantity of the compound
2	" " " 0,3-3% " " " "
1	" " " 3-30% " " " "
0	" " " > 30% " " " "

Two scores are given : d1-score for compartment air
d2-score for compartment soil/water

Note:

The distribution is calculated according to ref. 3.

4e. Bioconcentration

<u>Score</u>	<u>Criteria</u>	<u>Inorganic compounds and organometals</u>
	<u>Organic compounds</u>	
2	log P > 4	log BCF > 3
1	2 < log P < 4	1,5 < log BCF < 3
0	log P < 2	log BCF < 1.5

Note:

If significant dissociation occurs (pK < 7 for acids or > 7 for bases) lower score can be assigned to take into account the diminishing influence of dissociation on bioconcentration.

5. Exposure via products

5a. Use pattern

<u>Score</u>	<u>Criteria</u>	<u>Examples</u>
3	Compounds in products generally used in household, buildings, vehicles, etc.	Clothes, furniture, upholstering, detergents, cleaning agents, frequently used types of dyes, disinfectants, plastisizers, synthetic materials, motor fuels, packing materials, etc
2	Compounds in products less generally used	Hobby and do-it-yourself materials, special types of dyes, glues, inks, tools, etc.
1	Compounds in products not frequently used	Photographic materials, maintenance material for pieces of apparatus, etc
0	Compounds in products which are rarely used not occupationally	Industrial raw materials, solvents, additives, etc.

Table 9 cont.

5b. Exposure frequency

<u>Score</u>	<u>Criteria</u>	<u>Examples</u>
3	Exposure frequency > once per week	Clothes, furniture, upholstering, household products like detergents and cleaning agents, printing ink, paints, pigments, etc.
2	Exposure frequency: once per week - once per month	Hobby-materials, household products like shoe polish, polishing agents, motor fuel etc.
1	Exposure frequency: once per month - once per year	Solvents, maintenance materials for furniture and cars, specific cleaning agents, gardening chemicals etc
0	Exposure frequency < once per year	Solvents in paints, maintenance materials for house or floor-covering etc.

5c. Intensity of exposure

<u>Score</u>	<u>Criteria</u>	<u>Examples</u>
2	High	Solvents used indoors, sprays, fluids, which are frequently used and come in contact with the skin, dusts etc.
1	Moderate	Solvents used outdoors, textiles additives, compounds in solutions in low concentrations, not volatile fluids etc.
0	Low	Polymers, including the monomers and plasticisers contained, metal products etc.

Note to 5a, b, c: parameter 5a is reflecting the number of people potentially exposed, 5b indicates the frequency of exposure and parameters 5c the degree of exposure to a chemical. These three parameters are considered to be independent variables indicating the total exposure of man to consumer products.

Table 10

Scoring system of Koenemann and Visser

Scoring of the various exposure scenarios

A. Exposure via air

When exposure via air occurs, the following scores can be integrated:

- use volume (4a, maximum 6)
- percentage release (4b, maximum 3)
- degradation in air (4c1, maximum 3)
- relative occurrence in air (4d1, maximum 3)

The integration can be described as:

$$A = 4a - 4b - 4c1 - 4d1 \text{ (maximum 6)}$$

B. Exposure via soil/water

When exposure via soil/water occurs, the following scores can be integrated:

- production volume (4a, maximum 6)
- percentage release (4b, maximum 3)
- degradation in soil/water (4c2, maximum 3)
- relative occurrence in soil/water (4d2, maximum 3)

The integration can be described as:

$$B = 4a - 4b - 4c2 - 4d2 \text{ (maximum 6)}$$

C. Indirect exposure of terrestrial organisms via water

For the exposure of terrestrial organisms (including man) indirectly via water (with prediction), the following scores can be integrated:

- production volume (4a, maximum 6)
- percentage release (4b, maximum 3)
- degradation in soil/water (4c2, maximum 3)
- relative occurrence in soil/water (4d2, maximum 3)
- bioconcentration (4e, maximum 2)

The integration can be described as:

$$C = 4a - 4b - 4c^2 - 4d^2 + 4e \text{ (maximum 8)}$$

D. Exposure via products

When exposure via products occurs, the following scores can be integrated:

- use pattern (5a, maximum 3)
- exposure frequency (5b, maximum 3)
- intensity of exposure (5c, maximum 2)

The integration can be described as:

$$D = 5a + 5b + 5c \text{ (maximum 8)}$$

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APPENDIX II

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No.3	Risk Assessment of Occupational Chemical Carcinogens
No.4	Hepatocarcinogenesis in Laboratory Rodents : Relevance for Man
No.5	Identification and Assessment of the Effects of Chemicals on Reproduction and Development (Reproductive Toxicology)
No.6	Acute Toxicity Tests, LD ₅₀ (LC ₅₀) Determinations and Alternatives
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No.9	Assessment of Mutagenicity of Industrial and Plant Protection Chemicals
No.10	Identification of Immunotoxic Effects of Chemicals and Assessment of their Relevance to Man
No.11	Eye Irritation Testing
No.12	Alternative Approaches for the Assessment of Reproductive Toxicity (with emphasis on embryotoxicity/teratogenicity)
No.13	DNA and Protein Adducts: Evaluation of their Use in exposure Monitoring and Risk Assessment
No.14	Skin Sensitisation Testing
No.15	Skin Irritation
No.16	Mutation Research, Special Issue: Early Indicators of Non-Genotoxic Carcinogenesis

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