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A set of case studies to illustrate the applicability of DART (Decision Analysis by Ranking Techniques) in the ranking of chemicals

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ABSTRACT

This report provides the results of exploratory research carried out during 2007 and 2008 within the JRC's Institute for Health & Consumer Protection. The research focused on the problem of ranking chemicals according to their environmental and toxicological concern, and aimed to develop a better understanding of how to apply such approaches in the implementation of chemicals legislation, such as REACH and the Water Framework Directive.

A number of limitations were identified in existing approaches for the prioritisation of chemicals. For example, the traditional EU tool, EURAM, was difficult to apply in a consistent way due to the fact that many of the data inputs needed were often missing, which meant that high priority was often given to data-poor chemicals, rather than chemicals that were inherently hazardous or likely to cause a significant risk. This project aimed to address limitations such as this by encoding novel ranking methods into a new user-friendly software tool, and by investigating the applicability of the tool in a number of case studies. The tool developed in this project, called DART (Decision Analysis by Ranking Techniques), is made freely downloadable from the JRC website.

The applicability of DART tool is illustrated through a set of case studies. The first case study aims to summarise and illustrate different ways in which chemometric ranking methods could be used to supplement the use of QSAR methods in the development of chemical categories. The second case study illustrates how ranking methods could be used to supplement the use of QSAR methods in the context of toxicological assessments of potential persistent, bioaccumulative and toxic (PBT) substances. Finally, the third case study, aims to investigate the compatibility of established and novel ranking approaches with the risk assessment paradigm, in which hazard and exposure assessments are integrated into a characterisation of risk. These case studies illustrate some potential applications of ranking techniques in the regulatory assessment of chemicals.

LIST OF ABBREVIATIONS

BCF	Bioconcentration Factor
COMMPS	Combined Monitoring-based and Modelling-based Priority Setting
DART	Decision Analysis by Ranking Techniques
EINECS	European Inventory of Existing Commercial Chemical Substances
EPA	Environmental Protection Agency
ERP	Explorative Research Project
EU	European Union
EURAM	EU Risk rAnking Method
HAR	Hasse Average Ranking
HDT	Hasse Diagram Technique
I_PRIO	Priority Index
I_EXP	Exposure Index
I_EFF	Effect index
LC50	Concentration of the chemical that kills 50% of the test animals in a given time
MCDM	Multicriteria Decision Making Method
OECD	Organisation for Economic Co-operation and Development
QSAR	Quantitative Structure-Activity Relationship
PBT	Persistent, Bioaccumulative and Toxic substances
PCA	Principal Component Analysis
POR	Partial Order Ranking
REACH	Registration, Evaluation, Authorisation and Restriction of Chemicals
SAR	Simple Additive Ranking
SIAM	SIDS Initial Assessment Meeting
SIDS	Screening Information Data Set
SRC	Syracuse Research Corporation
TOR	Total Order Ranking

CONTENTS

1. INTRODUCTION

This report provides the results of exploratory research carried out during 2007 and 2008 within the JRC's Institute for Health & Consumer Protection. The research focused on the problem of ranking chemicals according to their environmental and toxicological concern, and aimed to develop a better understanding of how to apply such approaches in the implementation of chemicals legislation, such as REACH and the Water Framework Directive.

A limited number of ranking methods have been applied for the regulatory assessment of chemicals. In the 2006 ERP a survey of existing approaches suitable for prioritisation identified a number of limitations in existing approaches. As an example, the traditional EU tool, EURAM, was difficult to apply in a consistent way due to the fact that many of the data inputs needed were typically missing in EINECS, which meant that high priority was often given to data-poor chemicals, rather than chemicals that were inherently hazardous or likely to cause a significant risk. In view of the REACH legislation, such limitations needed to be addressed. This was not just a matter of assessing the applicability of existing algorithms to a representative EU dataset, but also depended on the development of new algorithms, and the refinement of existing algorithms, and the subsequent encoding of these novel methods into a user-friendly software tool. This tool, called DART (Decision Analysis by Ranking Techniques), is freely downloadable from the JRC website. The applicability of DART tool is here illustrated on a set of case studies.

The first case study aims to summarise and illustrate different ways in which chemometric ranking methods could be used to supplement the use of QSAR methods in the development of chemical categories. To illustrate possible applications of ranking methods, a data set of phthalate esters was investigated. In the context of developing chemical categories, and more generally in the context of toxicological assessments, chemometric ranking methods can be used to identify trends and different levels of concern (including subcategories), identify different profiles of toxicological behaviour (including subcategories) and select chemicals for strategic testing, in order to generate data supporting the robustness of the category.

The second case study illustrates how ranking methods could be used to supplement the use of QSAR methods in the context of toxicological assessments. As basis for the investigation, a list of "existing" chemicals (put on the market before 1981), screened by a panel of EU scientists as potential persistent, bioaccumulative and toxic (PBT) substances, was analysed for their potential PBT behaviour.

Finally, the third case study, aims to investigate the compatibility of established and novel ranking approaches with the risk assessment paradigm, in which hazard and exposure are assessed and integrated into a characterisation of risk. The so-called Combined Monitoring-based and Modelling-based Priority Setting (COMMPS) scheme, used to establish a first priority setting list within the EU Water Framework Directive, was compared with other priority setting methodologies. As a case study and for demonstration purposes of the potential of these techniques, the comparative analysis was performed on the 85 substances of the monitoring-based list for organic substances in the aquatic environment (European Commission, 1999).

2. BACKGROUD THEORY ON RANKING METHODS

Ranking methods belong to Multicriteria Decision Making (MCDM), a discipline in its own right, which deals with decisions involving the choice of a best alternative from several potential candidates in a decision, subject to several criteria or attribute that may be concrete or vague.

Typically, Multicriteria decision making techniques are used for helping people making their decision according to their preferences, in cases where there is more than one conflicting criterion, finding the optimal choice among the alternatives. Making a decision is not just a question of selecting a best alternative. Often the need is to rank all the alternatives for resource allocation, or to combine the strengths of preferences of individuals to form a collective preference.

Mathematics applied to decision making provides methods to quantify or prioritize personal or group judgments that are typically intangible and subjective. Decision making requires comparing different kinds of alternatives by decomposing the preferences into the many properties that the alternatives have, determining their importance, comparing and obtaining the relative preference of alternatives with respect to each property, and synthesizing the results to get the overall preference. Therefore, the strategy consists in breaking a complex problem down into its smaller components, and establishing importance or priority to rank the alternatives in a comprehensive and general way to look at the problem mathematically.

The key starting point of MultiCriteria Decision Making (MCDM) lies in attempting to represent often intangible goals in terms of number of individual criteria. A challenge feature of MCDM methods is the identification of the set of criteria by which alternatives, i.e. substances, are to be compared. The criteria selection is part of the modelling and problem formulation, a significant phase often under-emphasized. A useful general definition of a criterion is the one provided by Bouyssou (Bouyssou, 1990) as a tool allowing comparison of alternatives according to a particular axis or point of view. It is generally assumed that each criterion can be represented by a surrogate measure of performance, represented by some measurable attribute of the consequences arising from the achievement of any particular decision alternative.

In identifying the criteria some thoughts are to be considered: their value relevance, i.e. their link with the decision maker concept of their goals; their understandability and their measurability, i.e. the performance of the alternative against the criteria should be measurable; their not-redundancy in order to avoid that the concept they represent is in attributed greater importance; their judgemental independence, i.e. the preferences with respect to a single criterion should be independent from the level of another; their balancing between completeness and conciseness.

Subjectivity is intrinsic in all decision making and in particular in the choice of the criteria on which the decision is based on and in their relative weight. MCDM does not dissolve subjectivity, but it makes the need for subjective judgements explicit and the whole process by which they are considered is made transparent.

Over the years, several MCDM methods have been proposed (Hobbs and Horn, 1997) in different areas, with different theoretical background and facing different kind of questions and providing different kind of results (Hobbs and Meier, 1994).

Some of these methods have been developed to fulfil the need of specific problems, other methods are more general and have been used in different areas. The different MCDM methods are distinguished from each other in the nature of the model, in the information needed and in how the model is used. They have in common the aim to create a more formalized and better informed decision making process, the need to define alternatives to be considered, the criteria to guide the evaluation and the relative importance of the different criteria.

A detailed review of the theory and application of these methods can be found in Pavan and Todeschini (Pavan and Todeschini, 2008).

2.1 Total order ranking methods

Total order ranking (TOR) methods are scalar techniques that can be used to rank substances on the basis of more than one criterion. The different criteria values are combined into a global ranking index, and substances are ordered sequentially according to the numerical value of the ranking index. Since criteria are not always in agreement, i.e. can be conflicting, there is a need to find an overall optimum that can deviate from the optima of one or more of the single criteria. While a variety of total order ranking methods have been proposed in the literature, three commonly used methods are based on the desirability function, the utility function and the dominance function.

2.1.1 Utility and Desirability

Utility functions and desirability functions are well-known multicriteria decision making methods. The approach is the form most simply and easily understood by decision makers from a variety of backgrounds, since it does not require any stronger restrictions on the preferences structures than the aggregation formula. They are based on the definition of a partial value function, i.e. a transformation function t, for each criterion in order to standardise the partial value functions transforming values of the criteria to the same scale. Typically the best and worst conditions need to be defined for each criterion. This can be done locally, taking simply the best and worst of the available alternatives, or more generally as the best and worst possible conditions in similar contexts. For this purpose, different kinds of functions can be used, the more common ones being linear, sigmoid, logarithmic, exponential, step, normal, parabolic, Laplace, triangular and box. Each criterion is independently transformed into a utility/desirability t_{ij} by an arbitrary function which transforms the actual value f_{ij} of each i-th alternative for the j-th criterion into a value between 0 and 1. Once the kind of function and its trend for each criterion has been defined, the overall Utility/Desirability of each i-th alternative is computed. Utility and desirability functions differ only for the aggregation form of the overall Utility U and Desirability D.

The overall Utility U_i of each i-th alternative is defined, for the unweighted and weighted cases, as arithmetic mean:

$$U_i = \frac{\sum_{j=1}^{p} t_{ij}}{p} \quad U_i = \sum_{j=1}^{p} w_j \cdot t_{ij} \qquad 0 \le U_i \le 1 \tag{1}$$

In the case of the Desirability method, firstly presented by Harrington (Harrington, 1965) and then generalized by Derringer (Derringer and Suich, 1980), the overall Desirability D_i of each i-th alternative is defined, for the unweighted and weighted cases, as geometric mean:

$$D_i = \sqrt[p]{t_{i1} \cdot t_{i2} \cdot \ldots \cdot t_{ip}} \qquad D_i = t_{i1}^{w_1} \cdot t_{i2}^{w_2} \cdot \ldots \cdot t_{ip}^{w_p} \quad 0 \le D_i \le 1 \tag{2}$$

In all the cases, the weight constraint is assumed: $\sum_{j=1}^{p} w_r = 1$.

It can be noticed that the overall desirability is calculated more severely than the utility: in fact, if an element is poor with respect to one criterion, its overall desirability will be poor. If any desirability d_i is equal to 0 the overall desirability D_i will be zero, whereas the D_i will be equal to one only if all the desirabilities have the maximum value of one.

Once the overall utility U_i or desirability D_i for each alternative has been calculated, all the alternatives can be totally ranked according to their U or D values and the element with the highest U or D can be selected as the best one, if its value is considered acceptable.

A Desirability scale, shown in Table 1, was developed by Harrington (Harrington, 1965).

Scale of D	Quality evaluation
1.00	Improvement beyond this point has no preference
1.00 – 0.80	Acceptable and excellent
0.80 – 0.63	Acceptable and good
0.63 – 0.40	Acceptable but poor
0.40 – 0.30	Borderline
0.30 – 0.00	Unacceptable
0.00	Completely unacceptable

Table 1 – Harrington qualitative definition of the Desirability scale.

Both utility and desirability functions are affected by arbitrariness related to the a priori selection of the partial value functions and corresponding upper and lower limits.

2.1.2. Dominance

The dominance function method is based on the comparison of the state of the different criteria for each pair of alternatives. This approach does not require the transformation of each criterion into a quantitative partial value function; it only requires establishing whether the best condition is satisfied by a minimum or maximum value of the selected criterion. For each pair of alternatives (a, b) three sets of criteria are determined:

$P^+(a,b)$ is the set of criteria where a dominates b, i.e. where a is better than b, $P^0(a,b)$ is the one where a and b are equal, and $P^-(a,b)$ is the set of criteria where a is dominated by b.

The dominance function between two alternatives a and b is calculated considering – separately – the weights for the criteria in the P^+ and P^- sets. A $C(a,b)$ value equal to 1 means equivalence of the two alternatives; $C(a,b) > 1$ means that the alternative a is, on the whole, superior to the alternative b, whereas $C(a,b) < 1$ means that the alternative a is, on the whole, inferior to the alternative b. The obtained values can be normalised between 0 and 1.

2.2 Partial order ranking

Partial order ranking (POR) methods are vectorial approaches that recognise that different criteria are not always in agreement, but can be conflicting, which means that not all substances can be directly compared with others.

An example is often used to better clarify what is meant for "conflicts". Let consider a system made up of five, not perfectly correlated, alternatives (a, b, c, d, e), each described by two criteria f_1 and f_2, and the aim is to discover which alternative performs better than the other with respect to all the criteria. The alternatives are sorted, arranging them according to f_1 and f_2 in the permutation diagram (Urrutia, 1987) or by parallel coordinates (Welzl et al., 1998) with a vertical orientation, as shown in Figure 1.

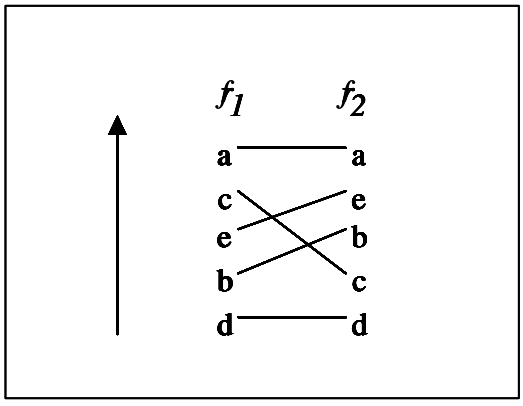

Figure 1 – Alternatives arranged in two sequences according to two different criteria.

This representation highlights the inversions between the two criteria. Alternatives mutually exchange their position according to the criterion used to sort them. The higher the number of criteria, the higher the probability that contradictions in the ranking exist. The partial ranking approach not only ranks alternatives but also identifies contradictions in the criteria used for ranking: some residual order remains when many criteria are considered and this motivates the term partial order. Thus the more known concept of order is the one demanding that all alternatives be comparable i.e. linear or total order, while partial order is the one in which alternatives can be "not comparable". If many alternatives are to be investigated, and especially if many criteria are considered, the parallel coordinates become complex and confusing.

2.2.1 Hasse Diagram Technique (HDT)

The Hasse diagram is a means of illustrating partial order ranking proposed by Hasse in 1952.(Hasse, 1952) It was introduced in environmental sciences by Halfon (Halfon et al., 1952) and refined by Brüggemann (Brüggemann et al., 1999).

The results of the partial order ranking is visualized in a diagram where each alternative is represented by a small circle, within each circle the alternative name, or the equivalence class, is given. Equivalent alternatives are different alternatives that have the same numerical values with respect to a given set of criteria. The equality according to a set of criteria defines an equivalence relation. The diagram is then a kind of dominance diagram, where if an order or cover relation exists then a line between the corresponding pairs of alternatives is drawn, the alternatives belonging to an order relation are "comparable". The diagram has orientation, consequently a sequence of lines can only be read in one direction either upwards or downwards. In case $a \leq b$ and $b \leq c$ then $a \leq c$ according to the transitivity rule; however a line between a and c is not drawn because this connection can be deduced from the lines between a and b and b and c. Incomparable alternatives are not connected by a line and are located at the same geometrical height and as high as possible in the diagram, resulting in a structure of levels. Alternatives belonging to the same level are incomparable.

However, that a location of alternatives at different levels does not imply comparability. According to the Hasse diagram terminology, the alternatives at the top of the diagram are called maximals while those alternatives which have no alternatives below are called minimals and they do not cover any further alternative. In the environmental field, where the Hasse technique was first applied, the criteria describe the alternatives in terms of environmental hazard. The main assumption is that the lower the numerical value the lower the hazard. If a high numerical value of a criterion corresponds to low hazard the criterion values must be multiplied by -1 to invert their order. Therefore, by this convention, the maximal alternatives are the most hazardous, and are selected to form the set of priority alternatives. Alternatives that are not comparable with any other alternative are called isolated alternatives, and can be seen as maximals and minimals at once: according to the caution principle they are located at the top of diagram within those elements that require priority attention. A typical Hasse diagram is illustrated in Figure 2.

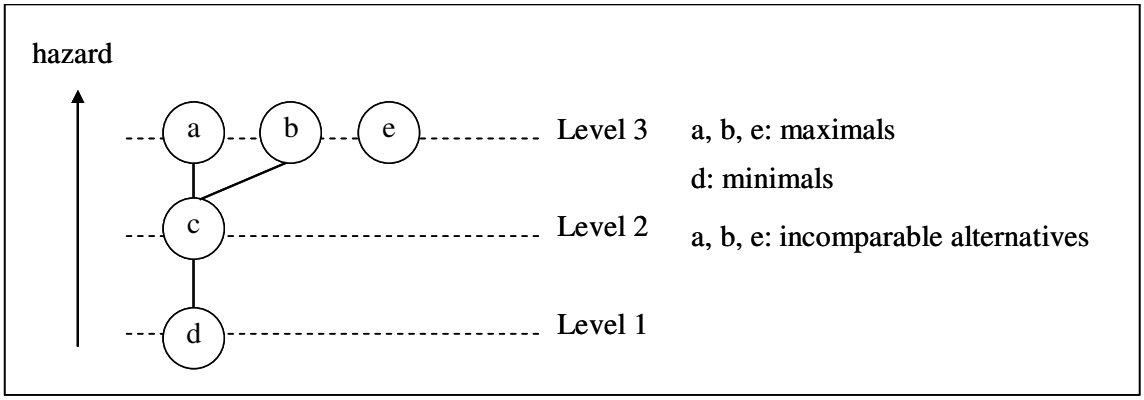

Figure 2 – Typical Hasse diagram.

In recent years the Hasse diagram technique (HDT) has been widely applied for different purposes in several fields: evaluation of aquatic toxicological tests (Brüggemann, et al., 1995, Brüggemann, et al., 1997); analysis of waste disposal sites (Halfon, 1989); ranking chemicals for environmental hazard (Halfon, 1986, Newman, 1995); comparison among ecosystems (Brüggemann, et al., 1994, Pudenz et al., 1999, Pudenz et al., 2000, Munzer et al., 1994, Brüggemann et al, 1999); chemicals priorization (Brüggemann et al, 1999).

3. DART (DECISION ANALYSIS BY RANKING TECHNIQUES)

Common to different types of chemicals legislation (including REACH) is the intention that the risks resulting from the manufacture, use and disposal of chemicals should be assessed and their use regulated if necessary. However, when large numbers of chemicals require a risk assessment, to ensure effectiveness and efficiency in the risk assessment process, it is necessary to establish a suitable priority setting procedure as a preliminary step before undertaking detailed risk assessments. However, the most effective approach to priority setting is a matter of scientific and regulatory debate, since the process rapidly becomes more complex as more criteria (properties of concern) are taken into account. From the scientific perspective, a rational approach is to rely on the integrated use of multiple tools based on chemometric and decision analysis methods.

To provide a research tool for investigating the application of such methods, the ECB commissioned the development of DART (Decision Analysis by Ranking Techniques). This software tool is designed to support the ranking of chemicals according to their environmental and toxicological concern and is based on the most recent ranking theories. Different kinds of order ranking methods, roughly classified as total and partial-order ranking methods are implemented. DART encodes several techniques for Multi-Criteria Decision Making (MCDM) analysis, which can be used to facilitate and make more transparent the cost-benefit analyses that underlie decision-making (such as the decision not to test but to rely on non-animal data, such as QSARs or in vitro tests).

DART (Decision Analysis by Ranking Techniques) was developed by Talete srl (Milan, Italy) under the terms of a JRC contract. It is made available as a free download (DART, 2008). It implements several total ranking methods and a partial ranking method (the Hasse Diagram Technique). Besides applying ranking methods, DART also allows performing several pre-processing analysis; which can be fundamental to allow the processing of big datasets, characterized by huge numbers of substances and described by several criteria. Cluster analysis by k-Means, Principal Component Analysis are the best known pre-processing methods implemented in DART, together with less known methods, like the bins partition and the reduction of significant digit.

These pre-processing methods should be applied to the dataset before proceeding to the ranking analysis. Their purpose is to produce a better dataset without any relevant information loss. The concept of “better dataset” is strictly related to the type of the desired ranking analysis and to the peculiarities of the dataset itself. For example, PCA is a good solution to reduce the number of variables; clustering is instead a good way to reduce the number of elements; rounding or partitioning into bins can help to reduce incomparable objects in the Hasse diagram. The pre-processing menu can be accessed once a dataset is imported or loaded. The methods are divided into two categories: methods working on variables and methods working on objects.

Seven total ranking techniques, named Desirability, Utility, Dominance, Concordance, SAR (Simple Additive Ranking), HAR (Hasse Average Ranking) and Absolute Reference Ranking, are implemented in DART, together with several charts and statistics that help the user to better understand the results obtained.

The Hasse diagram partial ranking technique is also implemented in DART. Several indices are provided to evaluate the analysis performed. The theory of these indices is described in (Pavan and Todeschini, 2004). The Hasse diagram chart provided in DART can be exported to the clipboard, or saved as a jpeg image. An example of a DART output, including a Hasse diagram, is provided in Figure 3.

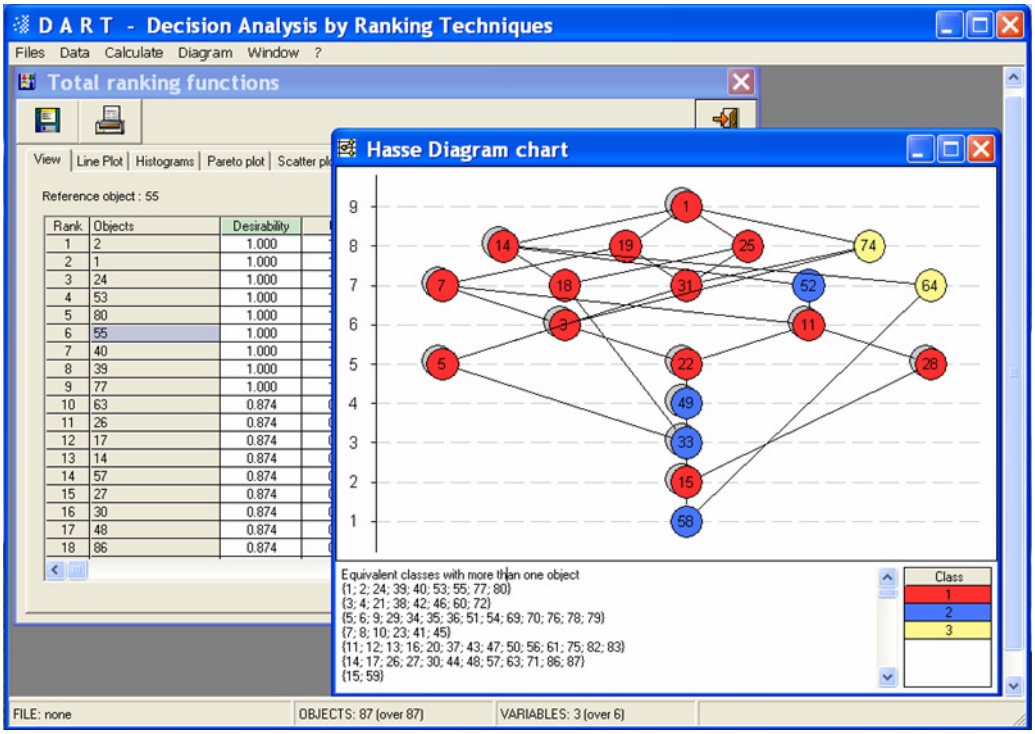

Figure 3. Example of DART output.

The applicability of DART is illustrated in the following paragraphs.

4. APPLICATION OF RANKING METHODS TO ORGANIC CHEMICALS

4.1 Introduction

This study aims to summarize and illustrate different ways in which chemometric ranking methods could be used to supplement the use of QSAR methods in the development of chemical categories. To illustrate possible applications of ranking methods, a data set of phthalate esters was investigated.

In the context of developing chemical categories, and more generally in the context of toxicological assessments, chemometric ranking methods can be used to:

a) identify trends and different levels of concern (including subcategories)
b) identify different profiles of toxicological behaviour (including subcategories)
c) select chemicals for strategic testing, in order to generate data supporting the robustness of the category

Different levels of confidence could be assigned to the results of chemometric ranking, depending on whether experimental or estimated data are used for the input variables. In this study, ranking methods were applied to estimated data generated by QSARs, which reflects the worse-case scenario that no suitable experimental data is available. It is proposed that this approach, combining the use of QSAR and ranking methods, could be used to develop an initial category hypothesis (or proposal), which is subsequently refined by using experimental data.

It is emphasised that the general purpose of this investigation was to explore and illustrate how ranking methods could be used in the formation of chemical categories, using a dataset of phthalate esters as an example of a category of organic chemicals. It was *not* the purpose to re-evaluate any substance-specific data or conclusions made in the regulatory assessments of specific phthalate esters.

For completeness and for background information, it is noted that various regulatory assessments have been conducted on phthalate esters:

a) an OECD SIAM category on a more restricted set of seven high-molecular weight phthalates has been developed (OECD, 2005)
b) EU risk assessments have been completed for two higher molecular weight esters (EC, 2003)
c) EU harmonised classifications have been agreed for seven phthalate esters (ECB CLASSLAB database)
d) A total of 14 phthalate esters were considered during an initial screening exercise by the EU PBT Working Group. However, as a result of further evaluation, none of these was considered as potential PBTs (ECB, 2002).

4.2 Identifying trends and different levels of concern

In this investigation, a chemically diverse set of 323 phthalate esters, including the seven members of SIAM category on high molecular-weight phthalates esters, were investigated and ranked according to their predicted PBT behaviour. Total and partial ranking methods were applied to three main properties determining the PBT behaviour: persistence, the bioconcentration factor (BCF) and acute aquatic toxicity (96h fathead minnow), as calculated with BIOWIN, BCFWIN and ECOSAR, respectively. To simplify this illustration, additional types of toxic effect, such as chronic aquatic toxicity, chronic mammalian toxicity, carcinogenicity, mutagenicity and reproductive toxicity, were not taken into account.[1]

The predictions generated by each model were coded into a scale of 1 to 4, corresponding to low (score=1), low/moderate (score=2), moderate/high (score=3) and high concern (score=4), as shown in Table 2. In the case of acute aquatic toxicity, the lowest level of concern was based not only the predicted LC50 values, but also on the predicted aqueous solubility. If the aqueous solubility of a substance was estimated by WSKOWWIN to be less than 0.001 mg/L, the substance was considered to be of no concern due to insufficient concentration in the aqueous phase.[2] The estimated value of 0.001 mg/L corresponds with an experimental solubility limit of 0.01 mg/L (it was found that for this data set, the WSSKOWIN predictions tend to be lower than the experimental values by a factor of 10).

Ultimate persistence prediction	BCF	Toxicity (LC50 (mg/L))[1]	Concern score
$P \leq 2$	$BCF > 2000$	$LC50 \leq 1$	4
$2 < P \leq 3$	$1000 < BCF \leq 2000$	$1 < LC50 \leq 10$	3
$3 < P \leq 3.5$	$1000 < BCF \leq 2000$	$10 < LC50 \leq 100$	2
$P > 3.5$	$BCF \leq 1000$	$LC50 > 100$	1

Table 2. Conversion of P, B and T predictions in different levels of concern. [1]The toxicity bands are equivalent to the EU R-phrases R50 (LC50≤1), R51 (1<LC50≤10), R52 (10<LC50≤100) and unclassified (LC50>100).

4.3 Total order ranking of phthalates based on the desirability function

Since the "best" condition for each property (P, B and T) is related to the minimum score, each property was independently transformed into a desirability (and utility) by an inverse linear transformation, as illustrated in Figure 4.

[1] In a regulatory framework, such as EU PBT assessment strategy, evidence of such effects would also be considered when deciding whether a substance meets the "T" criteria.

[2] This is a simplification, because in principle, chronic toxicity could still arise even in the case of insoluble substances, and even acute toxicity could arise through the uptake of particles to which the insoluble chemical is adsorbed.

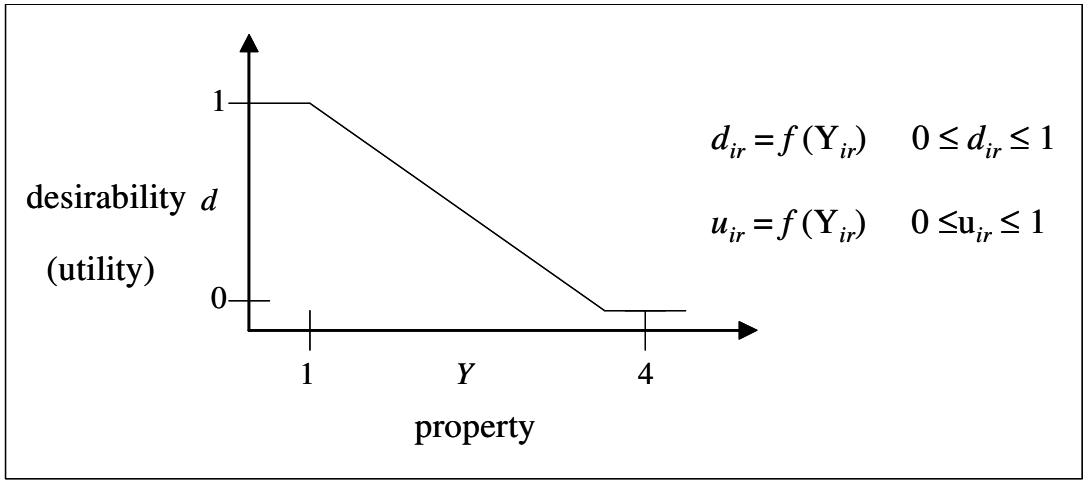

Figure 4. Inverse relationship between the ranking score for a property and its desirability or utility.

Thus, the best condition, corresponding to the chemicals predicted to be safest, has a desirability equal to 1, whereas the worst condition, corresponding to the chemicals predicted to be the most hazardous, has a desirability of 0.

The three properties were equally weighted in the ranking procedure and for each chemical the PBT hazard score was calculated as 1 – *Di* (*Ui*), where *Di* (*Ui*) is the overall desirability *Di* (or utility *Ui*) of the chemicals. Thus, the PBT hazard score ranges from 0, for chemicals with the least PBT concern, to a maximum of 1 for chemicals with the highest PBT concern (Figure 3).

The ranking based on the desirability function is severe: it gave a PBT hazard score of 1 if *any of the three* properties (P, B and T) had a score of 4, and only gave a PBT hazard score of 0 if *all of the three* properties had scores of 0. As shown in Figure 5, one of the SIAM members (CAS 68515-47-9) received the maximal score of 1, whereas four of seven SIAM phthalates had a lower PBT hazard score (score of 0.306), and two others had an even lower ranking (score of 0.126).

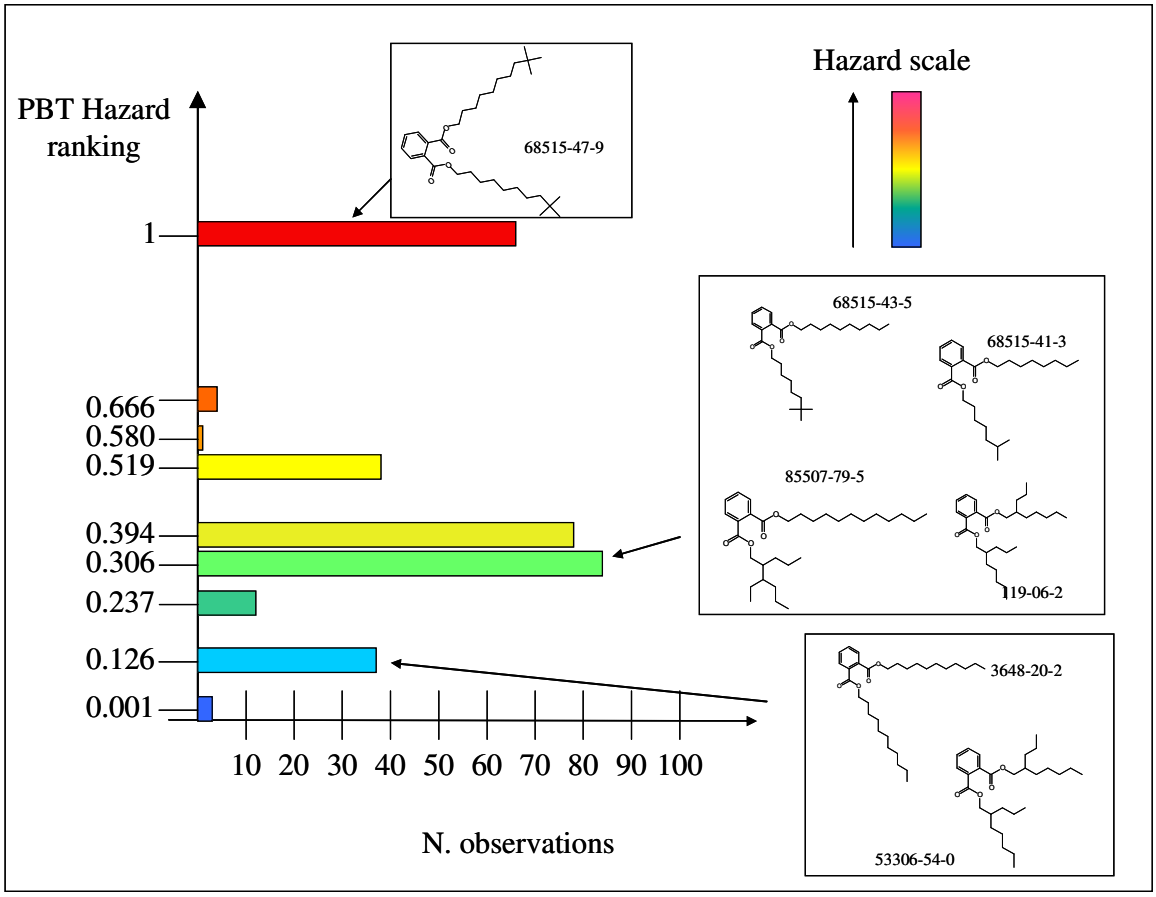

Figure 5. Total order ranking of phthalates based on the desirability function.

4.4 Total order ranking of phthalates based on the utility function

The application of the desirability function resulted in a large number of phthalate analogues appearing to be of high concern, which was considered unrealistic in view of the known properties of some of these chemicals. Therefore, the utility function was applied to rank the chemicals in a less severe manner.

The ranking based on the utility function allows better discrimination between chemicals based on their overall PBT profile (Figure 6). It can be seen that four the seven SIAM phthalates are considered to have the same PBT hazard score (score of 0.223), whereas one of the SIAM members has a higher ranking (score of 0.334), and two have a lower ranking (score of 0.112). Thus, the utility function produced the same relative order between the SIAM phthalates as the desirability function, but the absolute differences were less exaggerated.

The ranking based on the utility function gave a PBT hazard score of 1 if (and only if) *all three* properties (P, B and T) had a score of 4. This result was obtained for only two of the 323 chemicals: dipropyl 3,4,5,6-tetrachlorophthalate and tris(2-chloroethyl) 4,5,6-trichloro-1,2,3-benzenetricarboxylate. Because the utility function assigns the highest ranking only when all three hazard scores have maximal values, it could in

principle be exploited in the identification of potential PBTs.[3] However, in the case of the phthalates dataset, the two chemicals with the highest PBT hazard ranking of 1 (mentioned above) failed to meet EU criteria for PBT assignment. In fact, the chemical with the lowest predicted LC50 value in the dataset was dipropyl 3,4,5,6-tetrachlorophthalate (LC50=0.45 mg/L), which is above the EU criterion for T assignment of 0.1 mg/L.

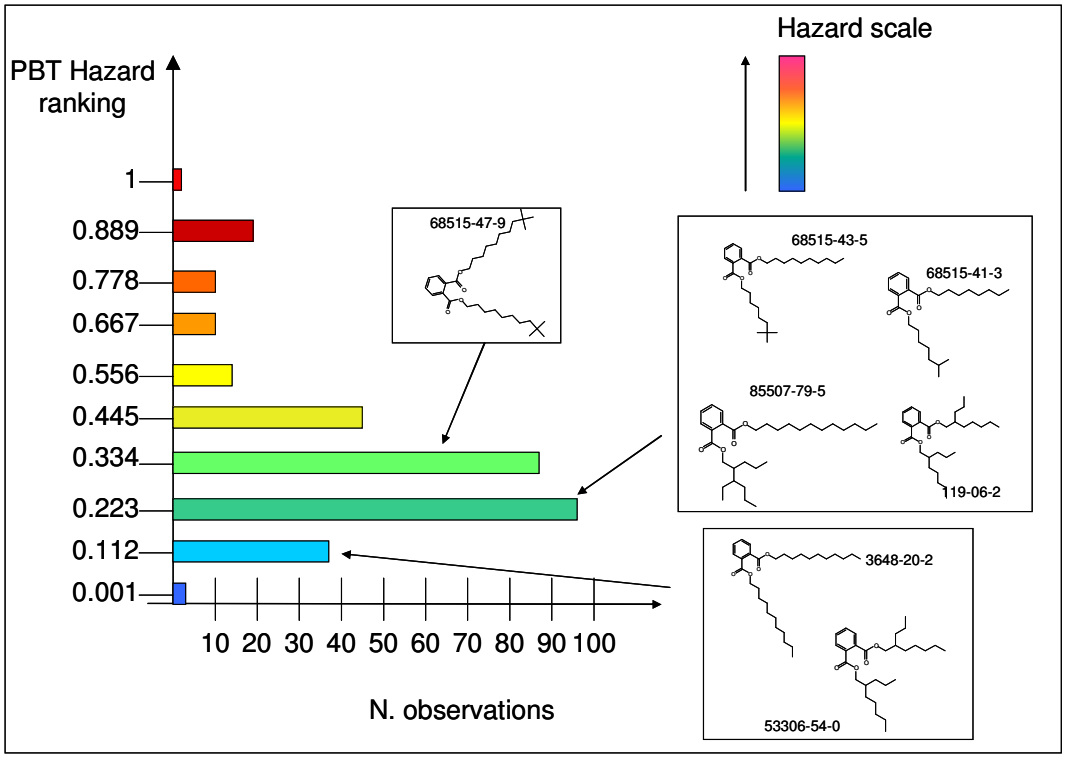

Figure 6. Total order ranking of phthalates based on the utility function

The utility function does not resolve whether the concern results from P, B or T. For example, if one of the three properties has a score of 4 (high concern for a single property), and the other two properties have scores of 1 (low concern), the PBT hazard score is the same, irrespective of whether the high concern results from P, B or T (Table 3). Thus, this type of ranking could be used to identify subcategories if it is sufficient to distinguish between chemicals based on their "average" behaviour across several properties.

Ultimate persistence concern score	BCF concern score	Toxicity concern score	PBT Hazard score
4	1	1	0.334
1	1	4	0.334

Table 3. Generation of a PBT hazard score by using the utility function.

[3] According to the EU PBT criteria, a substance is identified as a PBT if it meets all three criteria for P, B and T.

4.5 Identifying different profiles of toxicological behaviour

4.5.1 Total order ranking of phthalates based on the dominance function

To obtain a full discrimination between chemicals based on their individual P, B and T properties, i.e. to identify different profiles of PBT behaviour, total order ranking based on the dominance function can be used. Thus, if three chemicals have two properties with a score of 3, and one property with a score of 4, there are three possible combinations of the scores (Table 4). By applying the dominance function, each combination is distinguished by a different PBT hazard score (Table 4).

Ultimate persistence concern score	BCF concern score	Toxicity concern score	PBT Hazard score
3	4	3	0.870
3	3	4	0.897
4	3	3	0.917

Table 4. Generation of a PBT hazard score by using the dominance function.

As illustrated in Figure 7, the use of the dominance function enables qualitative differences between the phthalates to be detected, resulting in the identification of 25 different PBT profiles. The different profiles could be regarded as different subcategories within the larger category of 323 phthalates.

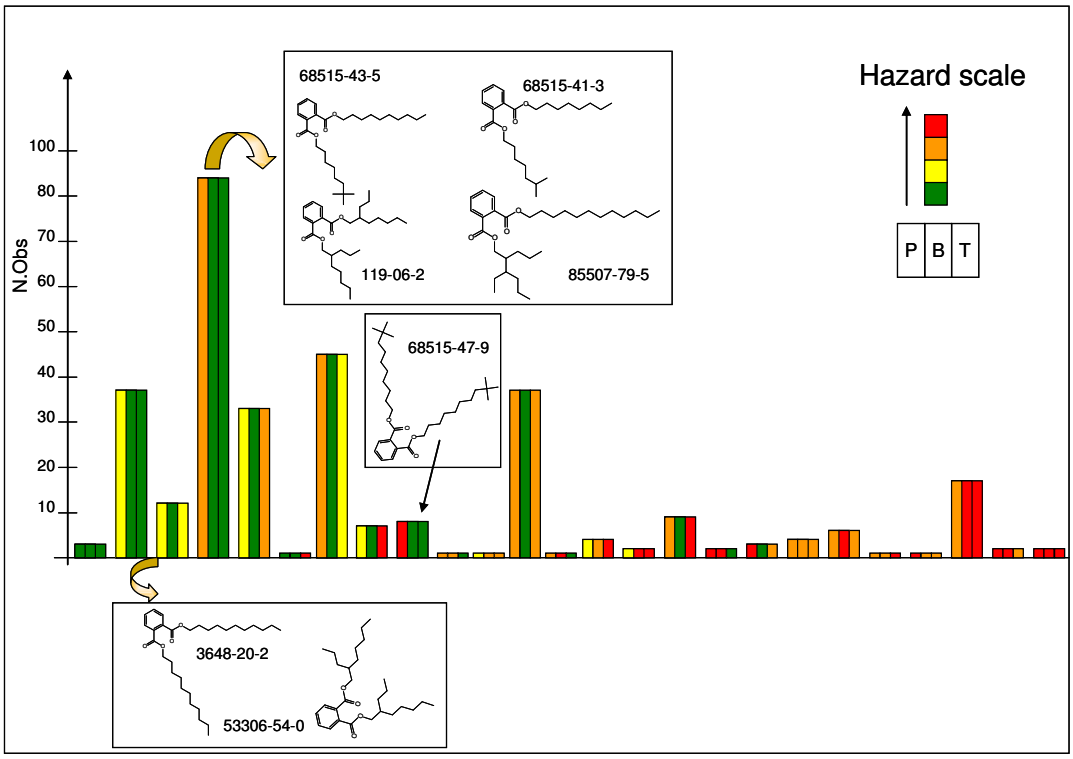

Figure 7. Total order ranking of phthalates based on the dominance function.

4.5.2 Partial order ranking of phthalates

Partial order ranking overcomes the main limitation of total order ranking methods that information on conflicting properties is lost. Partial order ranking encodes both quantitative and qualitative information of the trends analysed. As an illustration, the application of partial order ranking to the set of 323 phthalates identified nine levels of PBT hazard concern (Figures 8-9). In level 8, all 19 chemicals have moderate/high concern for one of the three properties and high concern for the other two. However, the level contains two clusters, distinguishing between 17 chemicals with moderate/high concern for P and high concern for B and T, and two chemicals with high concern for P and B, and moderate/high concern for T (Figure 8).

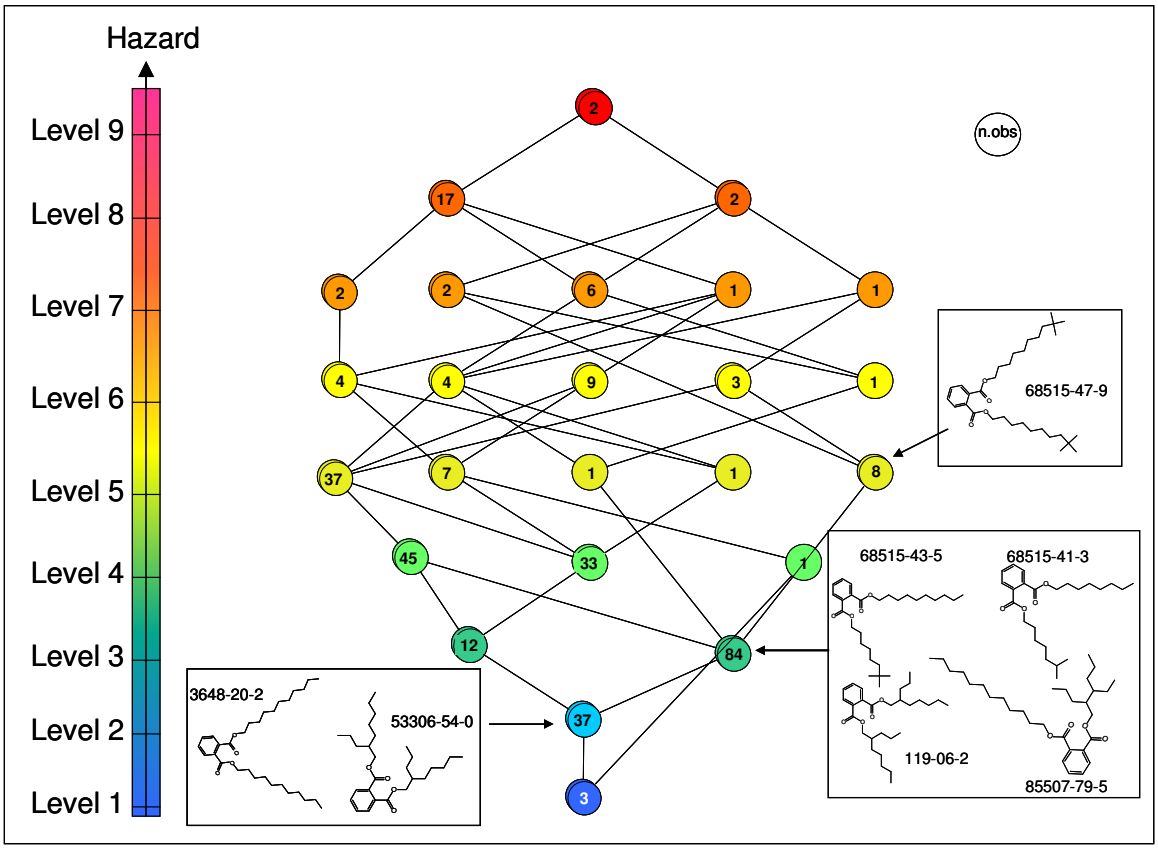

Figure 8. Partial order ranking of phthalates using the Hasse diagram

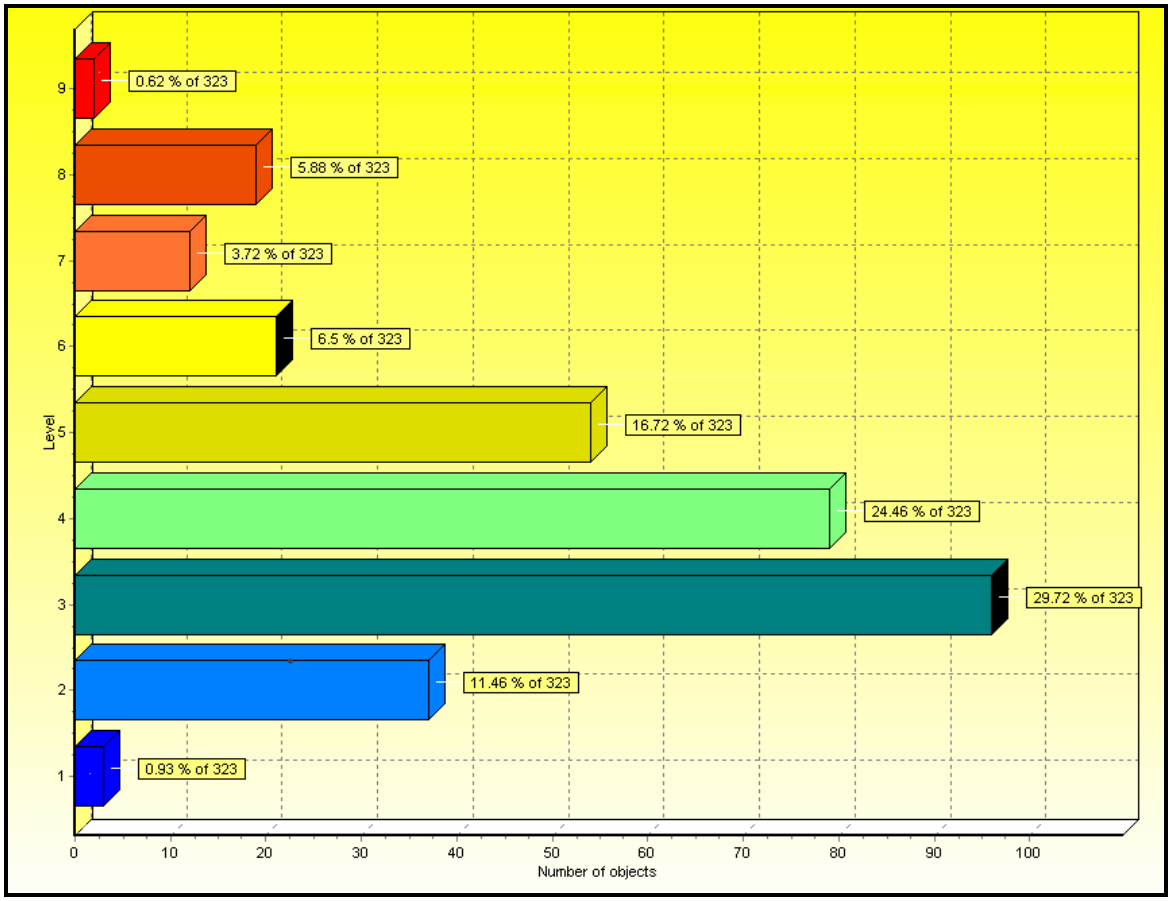

Figure 9. Distribution of phthalates across levels of concern defined by partial order ranking

4.5.3 Visualisation of toxicological profile by principal components analysis

Another way of visualising the toxicological profile of a set of chemicals (in this case the PBT profile of the phthalate analogues) is to apply principal component analysis (PCA) to the different levels of concern (Table 2). This method provides an additional means of visualising similarities and dissimilarities in PBT profiles.

PCA was applied to the predicted PBT data for the 323 phthalate analogues, to identify the orthogonal directions of maximum variance in the original data set and to project the data into a two-dimensional space formed by the two highest-variance components. Figure 10 shows the biplot of the first and second components. The cumulative explained variance of the first two principal components is 84.3%. The Hotelling T2 ellipse (in red) indicates the distance of each chemical from the model hyperplane. The ellipse was computed with a 95% confidence level.

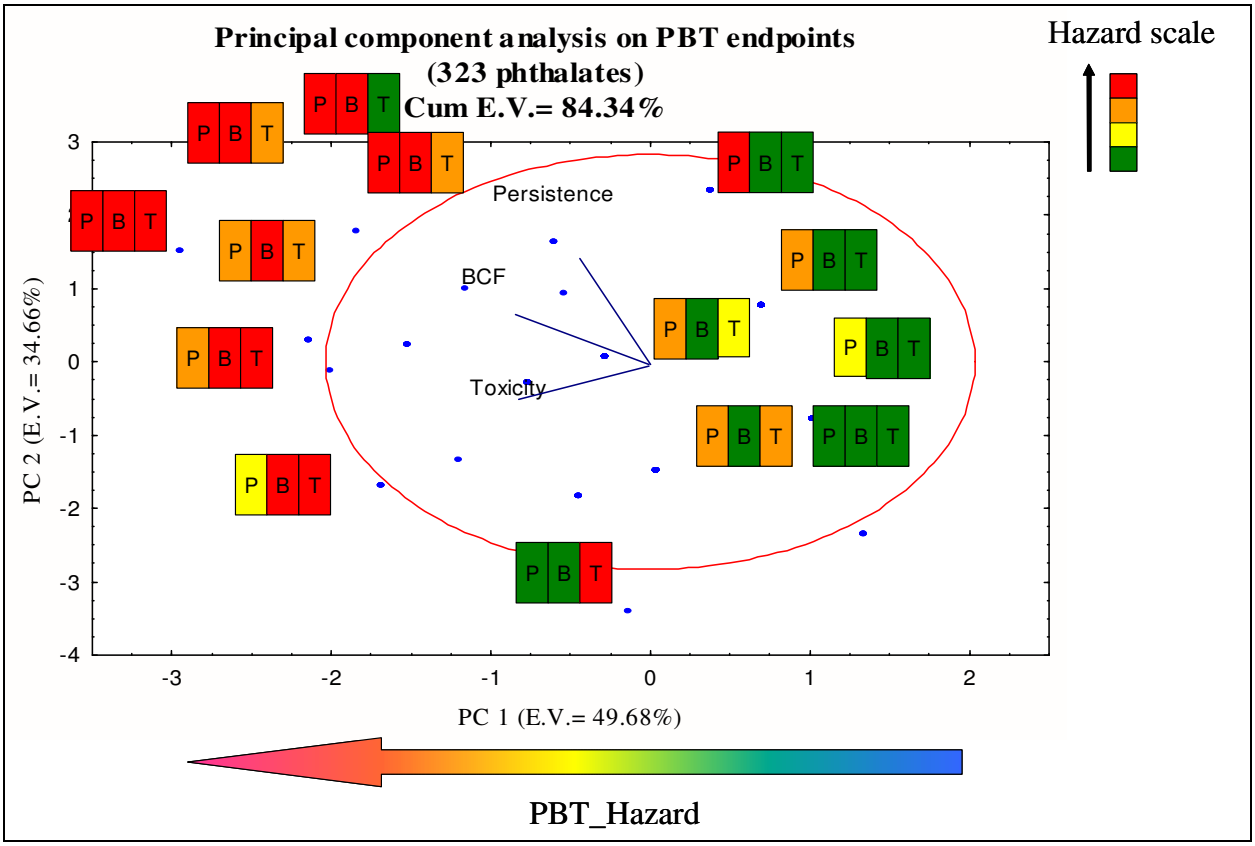

Figure 10. Visualisation of PBT profile by Principal Components Analysis.

It can be seen that the first principal component (PC1), explaining 49.7% of the total information, corresponds to a quantitative macrovariable, which can be interpreted as a PBT hazard score. High values of the first component are associated with compounds having a globally safe PBT profile, while low values of the first component are associated with compounds of high concern based on their PBT profile. Thus, PC1 separates the safest compounds ones (right hand side of the plot) from the more hazardous ones (left hand side of the plot).

The second principal component (PC2), explaining 34.7% of the total information, discriminates between different profiles of PBT behaviour. In particular, PC2 separates persistence and bioaccumulation from toxicity. High values of PC2 are associated with high persistence and bioconcentration but low toxicity, whereas low values correspond with high toxicity but low persistence and bioconcentration. Thus, the upper left part of the plot contains chemicals characterised by high persistence and bioconcentration, but relatively low or moderate toxicity, whereas the lower left part of the plot contains compounds with high toxicity, but relatively low or moderate persistence and bioconcentration.

4.6 Conclusions on the applicability of ranking methods to organic chemicals

Ranking methods allow chemicals to be sorted and sub-grouped according to their relative levels of concern. It should be noted that the numerical values of ranking scores have no absolute meaning, because if chemicals are added or deleted from the

dataset, and the ranking algorithm is performed again, the scores will change. However, the ranking scores are meaningful with respect to each other, and can be used to sort the chemicals (according to their numerical values) and to define sub-groups of chemicals (having the same scores).

Rankings based entirely on QSAR data can be used to predict chemicals with the highest level of concern as well as the lowest level of concern. Chemicals at the extremes of the predicted trend could be selected for strategic testing to confirm the boundaries of the trend. In addition, selected chemicals in the middle of the predicted trend could also be selected for testing, to check whether there are any deviations.

The different levels of concern identified by ranking methods for subgroups which could be used as the basis for identifying subcategories.[4] In particular, the ability of ranking methods to combine quantitative information from multiple properties could be exploited to define different subgroups based on multiple endpoints, e.g. different levels of the PBT hazard ranking could be regarded as different subcategories. TOR based on the *desirability function* provides a means of ranking and sub-grouping chemicals in a conservative manner, reflecting a high level of concern for any single endpoint. In contrast, TOR based on the *utility function* provides a useful means of ranking and sub-grouping chemicals based on their "average" behaviour across multiple toxicological endpoints.

Ranking methods can also be used to identify subgroups based on different toxicological profiles (e.g. high P & B & T at one extreme *vs* low P & B & T at the other extreme). TOR based on the *dominance function* was found to be useful in this respect.

If it is desirable to compare chemicals both in terms of the quantitative differences in their hazard rankings and the qualitative differences in their hazard profiles, the method of choice is *partial order ranking*. The qualitative and quantitative differences can be visualised by using the Hasse diagram.

In this investigation, only estimated properties were used as the input to the ranking algorithms. This demonstrates how ranking methods could be used in combination with QSAR methods in cases where there are insufficient experimental data to develop the initial category hypothesis (or proposal). It is proposed that the trends, boundaries, and subcategories predicted by using QSARs and ranking methods could be used to develop the initial category hypothesis, and to identify chemicals for strategic testing, in order to assess the robustness of the category.

Finally, while this investigation focussed on environmental properties, the same general approach could also be applied to combinations of human health endpoints (e.g. carcinogenicity, mutagenicity and reproductive toxicity).

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[4] This makes the assumption that subcategories can be defined directly on the basis of toxicological endpoints, rather than on underlying physicochemical or structural properties.

5. RANKING OF POTENTIAL PBT SUBSTANCES

5.1 Introduction

The general purpose of this investigation was to explore and illustrate how chemometric ranking methods could be used to supplement the use of QSAR methods in the context of toxicological assessments.

As basis for the investigation, a list of "existing" chemicals (put on the market before 1981), screened by a panel of EU scientists as potential persistent, bioaccumulative and toxic (PBT) substances, has been analysed for their potential PBT behaviour.
It was *not* the purpose to re-evaluate any substance-specific data or conclusions made in the regulatory assessments performed by the EU scientists, which may include additional considerations, such as expert judgement and concerns by regulatory authorities.

A total of 125 substances are currently identified in the list of potential PBT substances. From this list 38 substances could not be evaluated because mixture or polymer. A total of 87 substances, listed in Table 5, were analysed.

PBT list No.	CAS	Name	ECOSA class
1	001506-02-1	1-(5,6,7,8-tetrahydro-3,5,5,6,8,8-hexamethyl-2-naphthyl)ethan-1-one	Neutral Organics
2	001222-05-5	1,3,4,6,7,8-hexahydro-4,6,6,7,8,8-hexamethylindeno[5,6-c]pyran	Neutral Organics
3	000087-61-6	1,2,3-trichlorobenzene	Neutral Organics
4	000120-82-1	1,2,4-trichlorobenzene	Neutral Organics
5	000118-82-1	2,2',6,6'-tetra-tert-butyl-4,4'-methylenediphenol	Phenols
6	005102-83-0	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2,4-dimethylphenyl)-3-oxobutyramide]	Neutral Organics
7	005468-75-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(2-methylphenyl)-3-oxobutyramide]	Neutral Organics
8	005567-15-7	2,2'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[N-(4-chloro-2,5-dimethoxyphenyl)-3-oxobutyramide]	Neutral Organics
9	003520-72-7	4,4'-[(3,3'-dichloro[1,1'-biphenyl]-4,4'-diyl)bis(azo)]bis[2,4-dihydro-5-methyl-2-phenyl-3H-pyrazol-3-one]	Hydrazines
10	000088-06-2	2,4,6-trichlorophenol	Phenols
11	000121-14-2	2,4-dinitrotoluene	Dinitrobenzenes
12	000096-76-4	2,4-di-tert-butylphenol	Phenols
13	000128-39-2	2,6-di-tert-butylphenol	Phenols
14	000497-39-2	4,6-di-tert-butyl-m-cresol	Phenols
15	015571-58-1	2-ethylhexyl 10-ethyl-4,4-dioctyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate	Esters
16	003542-36-7	Dichlorodioctylstannane	Neutral Organics

PBT list No.	CAS	Name	ECOSA class
19	005208-93-5	3-methyl-1-(2,6,6-trimethylcyclohex-1-en-1-yl)penta-1,4-dien-3-ol	Vinyl/Allyl Alcohols
20	005124-30-1	4,4'-methylenedicyclohexyl diisocyanate	Isocyanates
21	002392-48-5	4-chloro-1-(2,4-dichlorophenoxy)-2-nitrobenzene	Neutral Organics
22	050849-47-3	5-nonylsalicylaldehyde oxime	Aliphatic Amines + Phenols
25	005216-25-1	alpha,alpha,alpha,4-tetrachlorotoluene	Benzyl Halides
32	000120-12-7	anthracene, pure	Neutral Organics
33	001103-38-4	barium bis[2-[(2-hydroxynaphthyl)azo]naphthalenesulphonate]	Phenols
37	039489-75-3	bis(2,4-dichloro-5-nitrophenyl) carbonate	Esters
38	000050-29-3	Clofenotane (= p,p-DDT)	Benzyl Halides
39	004904-61-4	Cyclododeca-1,5,9-triene	Neutral Organics
40	000294-62-2	Cyclododecane	Neutral Organics
41	011138-60-6	Decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate	Esters
42	031565-23-8	Di(tert-dodecyl) pentasulphide	Neutral Organics
43	026898-17-9	Dibenzyltoluene	Neutral Organics
44	000115-32-2	Dicofol	Benzyl Alcohols + Benzyl Halides
45	001762-27-2	diethyldimethylplumbane	Neutral Organics
46	025550-98-5	Diisodecyl phenyl phosphite	Esters + Esters (phosphate)
47	012578-12-0	Dioxobis(stearato)trilead	Neutral Organics
48	001163-19-5	bis(pentabromophenyl) ether	Neutral Organics
49	032536-52-0	Diphenyl ether, octabromo derivative	Neutral Organics
55	027193-86-8	Dodecylphenol	Phenols
56	000115-29-7	Endosulfan	Vinyl/Allyl Halides
58	025637-99-4	Hexabromocyclododecane	Neutral Organics
59	000118-74-1	Hexachlorobenzene	Neutral Organics
60	000087-68-3	hexachlorobuta-1,3-diene	Vinyl/Allyl Halides
64	051338-27-3	methyl 2-(4-(2,4-dichlorophenoxy)phenoxy)propionate	Esters
65	006386-38-5	methyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	Esters + Phenols
66	004979-32-2	N,N-dicyclohexylbenzothiazole-2-sulphenamide	Neutral Organics
67	014861-17-7	4-(2,4-dichlorophenoxy)aniline	Aromatic Amines
68	001836-75-5	Nitrofen	Neutral Organics
69	025154-52-3	Nonylphenol	Phenols
70	084852-15-3	Phenol, 4-nonyl-, branched	Phenols
72	000095-31-8	N-tert-butylbenzothiazole-2-sulphenamide	Neutral Organics
73	001843-05-6	octabenzone	Phenols
74	002082-79-3	octadecyl 3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate	Esters + Phenols
75	000556-67-2	octamethylcyclotetrasiloxane	Neutral Organics
76	000133-49-3	pentachlorobenzenethiol	Phenols
77	006683-19-8	pentaerythritol tetrakis(3-(3,5-di-tert-butyl-4-hydroxyphenyl)propionate)	Esters + Phenols
78	000128-69-8	perylene-3,4:9,10-tetracarboxylic dianhydride	Neutral Organics
79	061788-44-1	Phenol, styrenated	Phenols
86	026140-60-3	Terphenyl	Neutral Organics

PBT list No.	CAS	Name	ECOSA class
88	001461-25-2	Tetrabutyltin	Neutral Organics
89	003590-84-9	Tetraoctyltin	Neutral Organics
90	000117-08-8	Tetrachlorophthalic anhydride	Neutral Organics
91	000078-00-2	Tetraethyllead	Neutral Organics
92	000075-74-1	Tetramethyllead	Neutral Organics
94	000603-35-0	Triphenylphosphine	Neutral Organics
95	000056-35-9	Bis(tributyltin)oxide (TBTO)	Neutral Organics
96	000693-36-7	Dioctadecyl 3,3'-thiodipropionate	Esters
97	000793-24-8	N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD)	Neutral Organics
98	025103-58-6	tert.dodecanethiol	Thiols(mercaptans)
99	027107-89-7	2-Ethylhexyl 10-ethyl-4-[[2-[(2-ethylhexyl)oxy]-2-oxoethyl]-thio]-4-octyl-7-oxo-8-oxa-3,5-dithia-4-stannatetradecanoate	Esters
100	031570-04-4	Tris(2,4-di-tert-butylphenyl)phosphite	Neutral Organics
101	032588-76-4	Ethylene-bistetrabromophthalimide	Imides
104	000469-61-4	1H-3a,7-Methanoazulene, 2,3,4,7,8,8a-hexahydro-3,6,8,8-tetramethyl-, 3R-(3.alpha.,3a.beta.,7.beta.,8a.alpha.) -	Neutral Organics
105	000058-89-9	Lindane	Neutral Organics
106	000091-57-6	Methylnaphthalene	Neutral Organics
108	000077-47-4	Hexachlorocyclopentadiene	Vinyl/Allyl Halides
109	001217-08-9	1H-Indene-5-ethanol, 2,3-dihydro-beta.,1,1,2,3,3-hexamethyl-	Neutral Organics
113	000096-69-5	4,4'-Thio-bis(2-t-butyl-5-methylphenol)	Phenols
114	000608-71-9	Pentabromophenol	Phenols
115	013560-89-9	Dodecachlorodimethan-o-dibenzocyclooctane	Vinyl/Allyl Halides
116	026040-51-7	Phthalic acid, tetrabromo-, bis(2-ethylhexyl) ester	Esters
117	000119-47-1	6,6'-Di-tert-butyl-2,2'-methylenedi-p-cresol	Phenols
119	026272-76-4	N-[2-(2-Heptadecyl-4,5-dihydro-1H-imidazol-1-yl)ethyl] stearamide	Neutral Organics
120	051000-52-3	Vinyl neodecanoate	Esters
121	000128-37-0	2,6-di-tert-butyl-p-cresol (BHT)	Phenols
122	000330-54-1	Diuron	Neutral Organics + Ureas(substituted)
123	000095-76-1	3,4-dichloroaniline	Aromatic Amines
124	000541-02-6	Decamethylcyclopentasiloxan	Neutral Organics
125	038640-62-9	DIPN	Neutral Organics

Table 5 - List of potential PBT substances.

5.2. Endpoint prediction : P – B – T

5.2.1 Persistence

Persistence of the potential PBT substances was evaluated by the Biodegradation Probability Program, BIOWIN software (Syracuse Research Corporation, Bioconcentration Factor Program BIOWIN) downloadable from the U.S. EPA website. BIOWIN estimates the probability for the rapid aerobic biodegradation of an organic chemical in the presence of mixed populations of environmental microorganisms. Estimates are based upon fragment constants that were developed using multiple linear and non-linear regression analyses. Experimental biodegradation data for the multiple linear and non-linear regressions were obtained from Syracuse Research Corporation's (SRC) data base of evaluated biodegradation data (Howard et. Al., 1987).

In BIOWIN version 4.02 comprises six models designated as follows (Boethling et al, 2003):

Biowin1 = linear probability model
Biowin2 = nonlinear probability model
Biowin3 = expert survey ultimate biodegradation model
Biowin4 = expert survey primary biodegradation model
Biowin5 = Japanese MITI linear model
Biowin6 = Japanese MITI nonlinear model

The results provided by the linear and nonlinear probability model, as well as the Japanese MITI linear and nonlinear models are in terms of biodegradation probability: a value greater than 0.5 is considered as "biodegrades fast", a biodegradation probability less than 0.5 is considered as " does not biodegrades fast".

Primary and ultimate biodegradation models are expert based models using structural fragments to provide information on the time required to achieve primary (transformation of a parent compound to an initial metabolite) and ultimate biodegradation (transformation of a parent compound to carbon dioxide and water), respectively. The ultimate and primary biodegradation of each chemical is rated on a scale of 1 to 5, corresponding to the following time units: 5 – hours; 4 – days; 3 – weeks; 2 – months; 1 – longer.

5.2.1.1 EU Persistence criteria.

According to the PBT criteria defined in Annex XII of REACH regulation a substance *fulfils* the persistence criterion (P-) when:

- the half-life in marine water is higher than 60 days, or
- the half-life in fresh- or estuarine water is higher than 40 days, or
- the half-life in marine sediment is higher than 180 days, or
- the half-life in fresh- or estuarine water sediment is higher than 120 days, or
- the half-life in soil is higher than 120 days.

According to the preliminary guidance document on preparing the Chemical Safety Assessment under REACH (Technical Guidance Document on Information Requirements and Chemical Safety Assessment, 2008.). the assessment of the potential for persistency in the marine environment should in principle be based on actual half-life data determined under marine environmental conditions. Depending on whether a substance has a half-life smaller or greater than the cut-off criterion it is decided if a substance fulfils the P criterion. When these key data are not available other types of available information on the degradability of a substance can be used to decide if further testing is needed to assess the potential persistence. In this approach three different levels of information are defined according to their perceived relevance to the criteria:

- experimental data on persistence in the marine environment;
- other experimental data;
- data from biodegradation estimation models.

For those substances with no available data or with information difficult to interpret, QSAR models can be applied to estimate the potential for biodegradation in the environment. In a preliminary assessment whether a substance has a potential for persistence in the marine environment and hence for asking for actual test data it is proposed to consider use of the BIOWIN program.

The use of the results of these programs in a conservative way may fulfil the needs for evaluating the potential for persistency. The use of three out of the six models is suggested as follows:

- non-linear model prediction: does not biodegrade fast (<0.5) **or**
- MITI non-linear model prediction: not readily degradable (<0.5) **and**
- ultimate biodegradation timeframe prediction: > months (<2.2)

When predictions of these three models are combined relatively few not readily biodegradable substances will not be identified, without in the same time causing a significant increase in the number of falsely included readily biodegradable substances.

The preliminary character of this method to identify potentially persistent substances in the marine environment is emphasised, and further possible development of a suitable methodology is recommended. The BIOWIN program is available from the US EPA's internet site (http://www.epa.gov/opptintr/exposure/pubs/episuite.htm).

5.2.1.2 P predictions conversion in levels of concern

The predictions generated by BIOWIN were coded into a scale of 1 to 4, corresponding to low (score=1), low/moderate (score=2), moderate/high (score=3) and high concern (score=4), as shown in Table 6. The coding was set in such a way that a high concern score equal to 4 was assigned to those substances that fulfil the P criterion as established by the REACH legislation.

Ultimate persistence prediction	Chemical evaluation	Concern score
non-linear model < 0.5 **or** MITI non-linear model < 0.5 **and** Ultimate biodegradation < 2.2	High persistent	4
2.2 ≤ Ultimate biodegradation < 3	High/ Moderate persistent	3
3 ≤ Ultimate biodegradation < 3.5	Moderate/Low persistent	2
Ultimate biodegradation ≥ 3.5	Not persistent	1

Table 6. Conversion of P predictions in different levels of concern.

The predicted persistence values were used for chemical classification in one of the four categories: high persistent, high/moderate persistent, moderate / low persistent, and low persistent. The result of the initial classification is shown in Figure 11. Table 7 gives the exact numbers of the chemicals in each persistence category, as well as the percentage of the total.

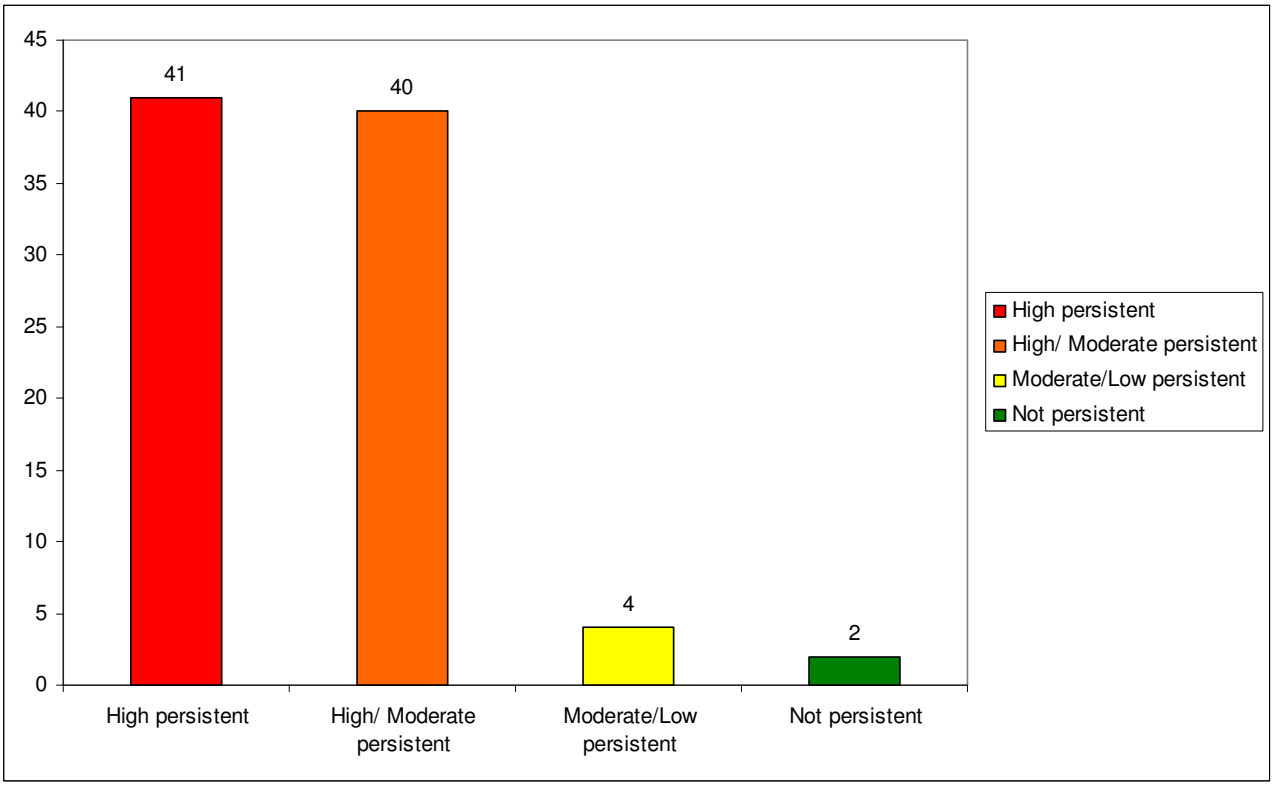

Figure 11. Initial classification of potential PBT substances in four persistence groups.

Category	**Number of Chemicals**	**Percentage of total**
High persistent	41	47.13
High/ moderate persistent	40	45.98
Moderate / low persistent	4	4.60

Low persistent	2	2.30
Total	**87**	**100**

Table 7. Number of chemicals classified into four persistence groups.

5.2.2 Bioconcentration factor

BCF values of the potential PBT substances were computed by BCFWIN software (Syracuse Research Corporation, Bioconcentration Factor Program BCFWIN) downloadable from the U.S. EPA website. BCFWIN estimates the bioconcentration factor (BCF) of an organic compound using the compound's log octanol-water partition coefficient (K_{ow}) (Meylan *et al*., 1999).

The estimation methodology used by BCFWIN consists in a suite of log BCF/logK_{ow} models based on a fragment approach and derived from a large data set of 694 training chemicals. Measured BCFs and other experimental details for 694 chemicals were collected in the Syracuse BCFWIN database and used to support BCFWIN software. Chemicals with significant deviations from the line of best fit were analyzed carefully dividing them into subset of data for non-ionic, ionic, aromatic and azo compounds, tin and mercury compounds. Because of the deviation from rectilinearity (linearity?), different models were developed for different logK_{ow} ranges, and a set of 12 correction factors and rules were introduced to improve the accuracy of BCF predictions. On average, the goodness of fit of the derived methodology by Meylan et al. is within one-half log unit for the compounds under study.

The BCFWIN method classifies a compound as either ionic or non-ionic. Ionic compounds include carboxylic acids, sulfonic acids and salts of sulfonic acids, and charged nitrogen compounds (nitrogen with a +5 valence such as quaternary ammonium compounds). All other compounds are classified as non-ionic.

Non-ionic compounds are predicted by the following relationships:

log BCF = 0.77 log Kow - 0.70 + Sum F(i) (log Kow 1.0 to 7.0)

log BCF = -1.37 log Kow + 14.4 + Sum F(i) (log Kow > 7.0)

log BCF = 0.50 (log Kow < 1.0)

where Sum F(i) is the summation of structural correction factors.

Ionic compounds are predicted as follows:

log BCF = 0.50 (log Kow < 5.0)

log BCF = 0.75 (log Kow 5.0 to 6.0)

log BCF = 1.75 (log Kow 6.0 to 7.0)

log BCF = 1.00 (log Kow 7.0 to 9.0)

log BCF = 0.50 (log Kow > 9.0)

Metals (tin and mercury), long chain alkyls and aromatic azo compounds require special treatment.

5.2.2.1 EU Bioconcentration criteria.

According to the PBT criteria defined in Annex XII of REACH regulation a substance *fulfils* the bioaccumulation (B-) criterion when:

- the bioconcentration factor (BCF) is higher than 2000.

According to the preliminary guidance document on preparing the Chemical Safety Assessment under REACH (Technical Guidance Document on preparing the Chemical Safety Report under REACH, 2005), the assessment of the potential for bioconcentration in the marine environment should in principle be based on measured data on bioconcentration in aquatic species. When measured BCF values are not available the K_{ow} or the BCF based on modelling can be used to indicate the liability to bioaccumulate from water. For substances with log K_{ow} < 6 assessment on the basis of Kow or estimated BCF does not make a real difference since all available BCF models are linear. The B criterion for log K_{ow} is therefore directly derived from this linear relationship. A substance is considered to potentially fulfil the B criterion when log K_{ow} exceeds a value of 4.5.

For highly hydrophobic substances, with log K_{ow} > 6, experimentally derived BCF values tend to decrease with increasing log K_{ow}. Several explanations can be given for this decline. For these substances the available BCF models can lead to very different results. As a consequence the potential for bioaccumulation is assessed by expert judgement on the basis of the log K_{ow} value and the estimated BCF using the available BCF models.

5.2.2.2 B predictions conversion in levels of concern

The predictions generated by BCFWIN were coded into a scale of 1 to 4, corresponding to low (score=1), low/moderate (score=2), moderate/high (score=3) and high concern (score=4), as shown in Table 8. The different levels of concern were set so that a high concern was assigned to those chemicals that fulfil the B criterion under REACH.

BCFWIN prediction	Chemical evaluation	Concern score
BCF > 2000	High bioconcentrative	4
1500 < BCF ≤ 2000	High/ Moderate bioconcentrative	3
1000< BCF ≤ 1500	Moderate/Low bioconcentrative	2
BCF ≤ 1000	Not bioconcentrative	1

Table 8. Conversion of B predictions in different levels of concern

The predicted bioconcentration values were used for chemical classification in one of the four categories: high bioconcentrative, high/ moderate bioconcentrative, moderate / low bioconcentrative, and low bioconcentrative. The result of the initial classification is shown in Figure 12. Table 9 gives the exact numbers of the chemicals in each bioconcentration category, as well as the percentage of the total.

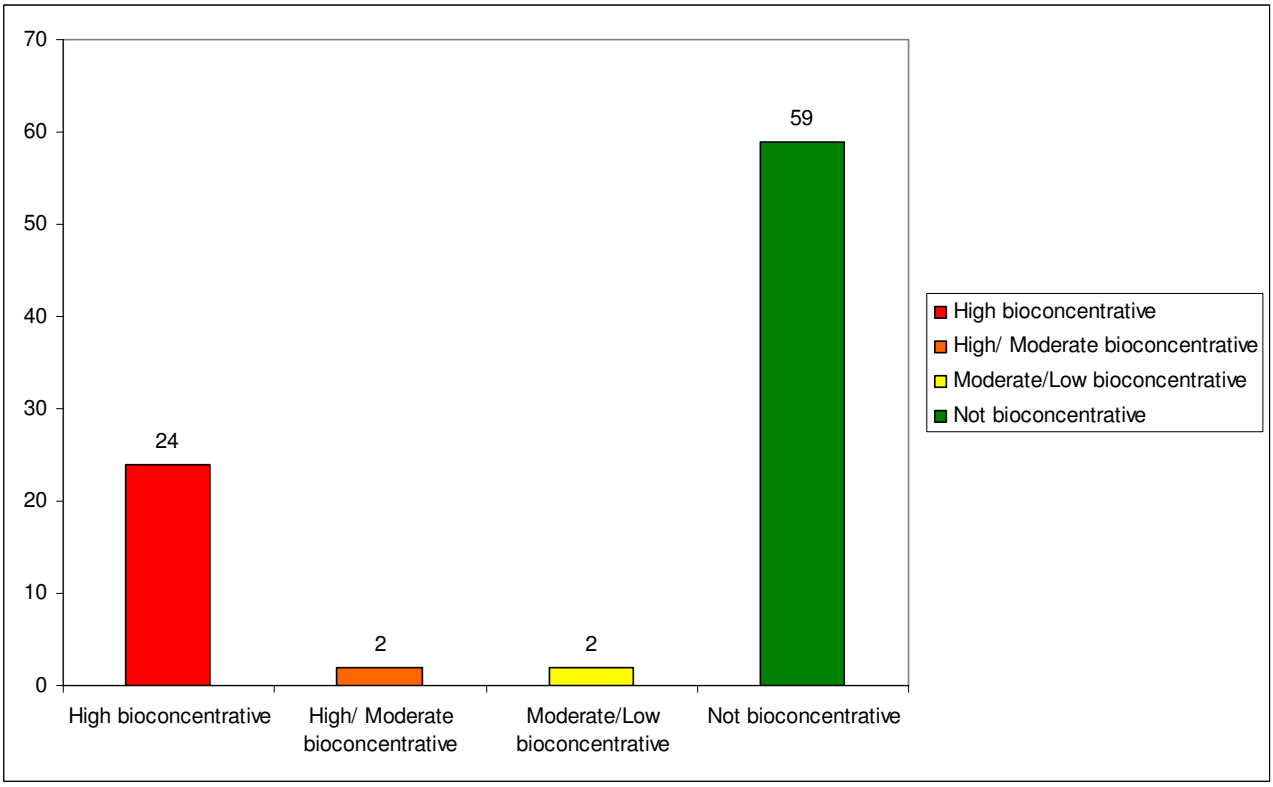

Figure 12. Initial classification of potential PBT substances in four bioconcentration groups.

Category	Number of Chemicals	Percentage of total
High bioconcentrative	24	27.59
High/ Moderate bioconcentrative	2	2.30
Moderate/Low bioconcentrative	2	2.30
Not bioconcentrative	59	67.82
Total	**87**	**100**

Table 9. Number of chemicals classified into four bioconcentration groups.

5.2.3 Toxicity

Toxicity values of the potential PBT substances were computed by ECOSAR software downloadable from the U.S. EPA website (ECOSAR). The standard ECOSAR aquatic toxicity profile consists of 3 acute values (fish LC_{50}, daphnid LC_{50}, and algae EC_{50}), 3 chronic values (fish ChV, daphnid ChV, and algae ChV), and determination of a chronic COC value.

Organism	Acute Toxicity Values	Chronic Toxicity Values
Fish	96-hour LC_{50}	30-day ChV
Daphnid (Aquatic Invertebrate)	48-hour LC_{50}	ChV or 16-day EC50
Algae	72- or 96-hour EC_{50}	ChV
Chronic Concentration of Concern (COC)	Lowest ChV* value/10	

Table 10. ECOSAR standard aquatic toxicity profile.

ECOSAR program uses QSAR models to predict the aquatic toxicity of chemicals based on their similarity of structure to chemicals for which the aquatic toxicity has been previously measured. Most QSAR calculations in the ECOSAR Class Program are based upon the octanol/water partition coefficient (K_{ow}).

ECOSAR has been used by the U.S. Environmental Protection Agency since 1981 to predict the aquatic toxicity of new industrial chemicals in the absence of test data. The acute toxicity of a chemical to fish (both fresh and saltwater), water fleas (daphnids), and green algae has been the focus of the development of SARs, although the program provides predictions also for chronic effects. ECOSAR is developed for more than 50 chemical classes. These chemical classes range from the very large, e.g., neutral organics, to the very small, e.g., aromatic diazoniums.

Details on the applicability and limitations of the suggested models are provided in ECOSAR output. A list of chemical classes identified by ECOSAR and used for the toxicity predictions of the potential PBT substances is provided in Table 11.

Model	N. Compounds
Aliphatic amines + Phenols	1
Aromatic Amines	2
Benzyl Alcohols + Benzyl Halides	1
Benzyl Halides	2
Dinitrobenzenes	1
Esters	8
Esters Phosphate	1
Esters + Phenols	3
Hydrazines	1
Imides	1
Isocyanates	1
Neutral organics	42
Neutral organics + ureas	1
Phenols	16

Thiols (mercaptans)	1
Vinyl/Allyl Alcohols	1
Vinyl/Allyl Halides	4

Table 11. A list of models used at least once for prediction of the fish toxicity.

5.2.3.1 EU toxicity criteria.

[1] A substance *fulfils* the toxicity (T-) criterion when:

- the long-term no-observed effect concentration (NOEC) for marine or freshwater organisms is less than 0.01 mg/l, or
- the substance is classified as carcinogenic (category 1 or 2), mutagenic (category 1 or 2), or toxic for reproduction (category 1, 2, or 3), or
- there is other evidence of chronic toxicity, as identified by the classifications: T, R48, or Xn, R48 according to Directive 67/548/EEC.

According to the preliminary guidance document on preparing the Chemical Safety Assessment under REACH (Technical Guidance Document on preparing the Chemical Safety Report under REACH, 2005), where data on chronic effects are not available short-term toxicity data for marine or freshwater organisms can be used to determine whether a substance is a potential PBT provided the screening criteria for P and B are fulfilled. In the context of the PBT assessment a substance is considered to be potentially toxic when the L(E)C50 to aquatic organisms is less than 0.1 mg/l. If a substance is confirmed to fulfil the ultimate P and B criteria chronic toxicity data are required to deselect this substance from being considered as a PBT. In principle chronic toxicity data, when obtained for the same species, should override the results from the acute tests.

In case where no acute or chronic toxicity data are available the assessment of the T criterion at a screening level can be performed using data obtained from quantitative structure activity relationships (QSARs).

5.2.3.2 T predictions conversion in levels of concern

The predictions generated by ECOSAR were coded into a scale of 1 to 4, corresponding to low (score=1), low/moderate (score=2), moderate/high (score=3) and high concern (score=4), as shown in Table 12.

ECOSAR ChV prediction (mg/L)	Chemical evaluation	Concern score
ChV < 0.1	High toxic	4
0.1 ≤ ChV < 1	High/ Moderate toxic	3
1 ≤ ChV < 10	Moderate/Low toxic	2
ChV > 10	Not toxic	1

Table 12. Conversion of T predictions in different levels of concern

The predicted toxicity values were used for chemical classification in one of the four categories: high toxic, high/ moderate toxic, moderate / low toxic, and low toxic. The result of the initial classification is shown in Figure 13. Table 13 gives the exact numbers of the chemicals in each toxicity category, as well as the percentage of the total.

It can be noticed that for a few compounds, toxicity could not be estimated because they are not soluble enough to measure the predicted effect. An artificial precautionary high level of concern equal to 3.5 was arbitrary assigned to these chemicals to highlight that there was no proof for a low concern but at the same time to discriminate them from those with a documented real high toxic concern (score equal to 4).

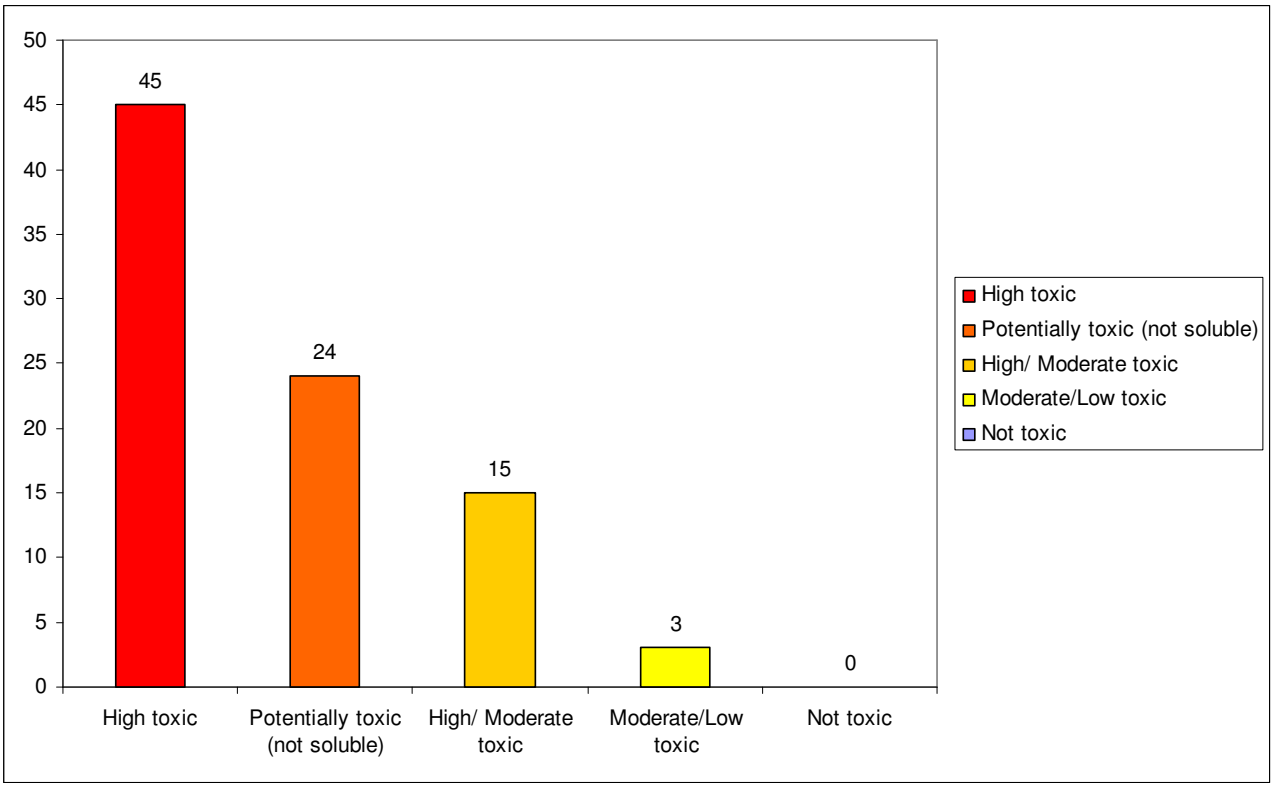

Figure 13. Initial classification of potential PBT substances in five toxicity groups.

Category	Number of Chemicals	Percentage of total
High toxic	45	51.72
Potentially toxic (not soluble)	24	27.59
High/ Moderate toxic	15	17.24
Moderate/Low toxic	3	3.45
Not toxic	-	0
Total	**87**	**100**

Table 13. Number of chemicals classified into toxicity groups.

5.3 Ranking of potential PBT substances according to their PBT properties

Total and partial ranking methods have been applied to order the potential PBT substances according to their environmental concern as PBT.

Total and partial ranking methods have been applied to the three relevant properties determining the PBT behaviour (persistence, BCF values and toxicity values) to screen the high number substance in the list of potential PBT and identify compounds that are, at the same time, highly persistent, bioaccumulative and toxic.

The persistence, bioconcentration factor and toxicity were estimated by BIOWIN, BCFWIN and ECOSAR, respectively. Persistence, BCF and toxicity predictions were coded into a scale of 1 to 4, corresponding to low, moderate/low, moderate /high and high concern score, by using respectively green, yellow, amber and red colours. (Table 14)

Persistence	BCF	Toxicity (ChV (mg/L)	Concern score
non-linear model < 0.5 **or** MITI non-linear model < 0.5 **and** Ultimate biodegradation < 2.2	BCF > 2000	ChV < 0.1	4
2.2 ≤ Ultimate biodegradation < 3	1500 < BCF ≤ 2000	0.1 ≤ ChV < 1	3
3≤ Ultimate biodegradation < 3.5	1000< BCF ≤ 1500	1 ≤ ChV < 10	2
Ultimate biodegradation ≥ 3.5	BCF ≤ 1000	ChV > 10	1

Table 14. Codification of P,B,T data into concern scores

Being, for each property, the "best" condition satisfied by a minimum value of the coded scale, each property was independently transformed into a desirability (and utility) by an inverse linear transformation which transforms the actual coded value of each chemical into a value between 0 and 1. Thus, the best condition, i.e. desirability equal to 1, corresponds to safe chemicals, i.e. code equal to 1; while the worst condition, i.e. desirability equal to 0, corresponds to code equal to 4.

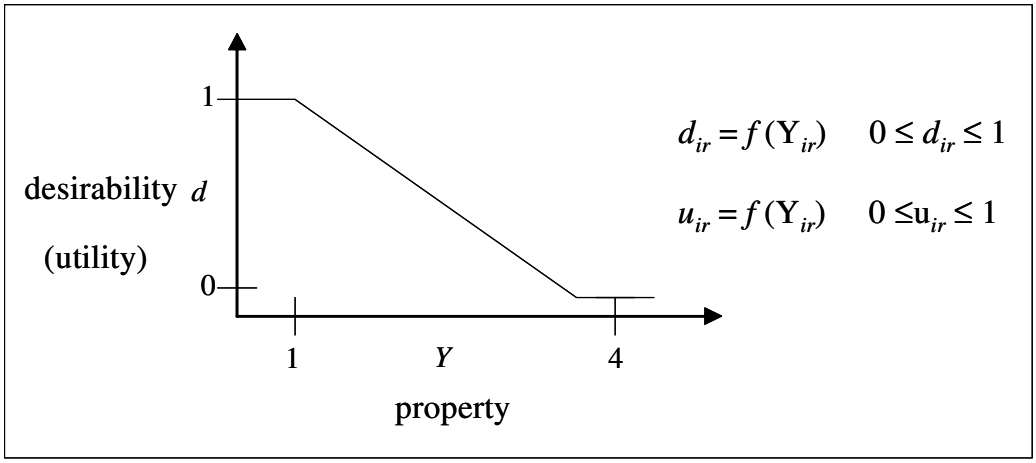

Figure 14 – Inverse transformation of desirability/utility values into hazard values

The three properties were equally weight in the ranking procedure and for each chemical the PBT hazard score was then calculated as $1 - D_i$ (U_i), being D_i (U_i) its overall desirability D_i (utility U_i).

Thus the defined PBT hazard score ranges from 0, for not PBT like chemicals, to a maximum of 1 for PBT like chemicals. The chemicals were ranked according to their decreasing PBT hazard score and a priority list of potential PBT chemicals was identified.

5.3.1 Ranking results based on "Desirability functions"

The results of the PBT hazard ranking evaluated by the "desirability functions" are illustrated in the Figure 15.

It has to be noted that this is the most severe ranking approach, where if a chemical has a high concern score for any P or B or T property, then its overall desirability D_i will be zero, resulting in the maximum PBT hazard score equal to 1. As an example, despite the 1,2,3-trichlorobenzene (87-61-6) low concern scores for BCF and toxicity, a high PBT hazard score is assigned to it being of high concern for persistence. On the contrary, the overall desirability D_i will be equal to one, and the PBT hazard score equal to 0, only if a chemical has a low concern score all the three considered properties.

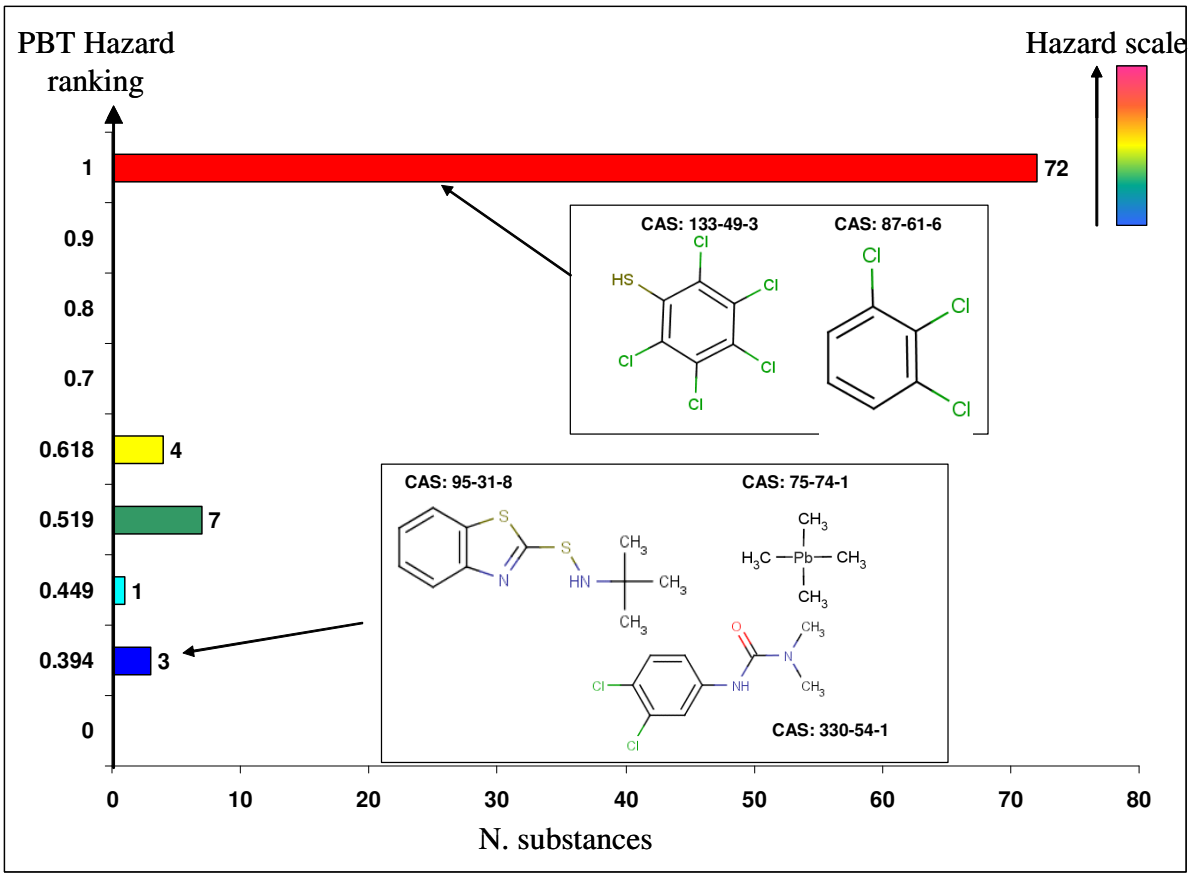

Figure 15 – Ranking results based on "Desirability functions"

The desirability functions ranking is generally used when a precautionary approach is demanded. However, the obtained ranking is poorly discriminating among the diverse PBT trends. Indeed, no distinction is accounted among chemicals that are of high concern for P and T but not for B and those of high concern for B and T, but not for P. For clarification, an example is illustrated in Table 15.

Persistence concern score	BCF concern score	Toxicity concern score	PBT Hazard score
4	1	3	1
1	4	3	1
4	4	4	1
4	1	4	1

Table 15 – Example of desirability calculation.

From the obtained results, it can be highlighted that a rather big number (72) of potential PBT were confirmed to be of high PBT concern. All the PBT hazard scores evaluated by desirability functions are provided in Appendix I.

5.3.2 Ranking results based on "Utility functions"

The application of the desirability function resulted in a large number of substances appearing to be of high concern, which was considered unrealistic in view of the known properties of some of these chemicals. Therefore, the utility function was applied to rank the chemicals in a less severe manner.

The ranking based on the utility function allows better discrimination between chemicals based on their overall PBT profile.

It can be noted that this ranking approach is calculated less severely: in fact, a PBT hazard score of 1 is assigned only to those chemicals which are of high concern for all three properties (P, B and T), thus if (and only if) *all three* properties (P, B and T) had a score of 4. This result was obtained for only nine chemicals of high concern for the P,B and T at the same time.

On the other hand utility a chemical can have assigned a low PBT hazard score even if it is of high concern for one out of three properties. As an example, despite the decanoic acid, ester with 2-ethyl-2-(hydroxymethyl)-1,3-propanediol octanoate (11138-60-6) high concern for toxicity, a relative low PBT hazard score (=0.445) is assigned to it being of low concern for BCF and persistence.

Because the utility function assigns the highest ranking only when all three hazard scores have maximal values, it could in principle be exploited in the identification of potential PBTs.

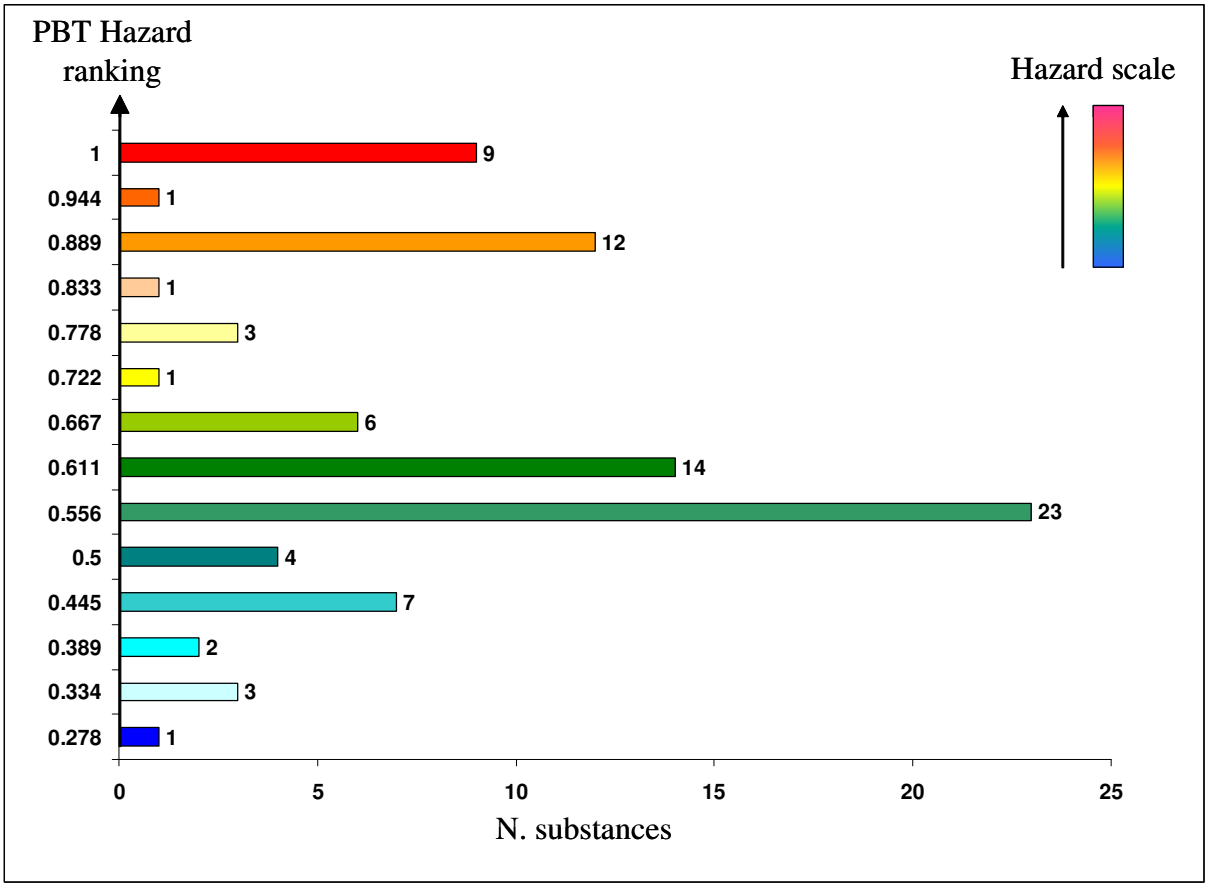

Figure 16 – Ranking results based on "Utility functions"

The utility functions approach provides a less severe ranking, but a better discrimination among the diverse PBT trends.

Persistence concern score	BCF concern score	Toxicity concern score	PBT Hazard score
4	4	4	1
3	4	4	0.889
3	3	4	0.778

Table 16 – Example of utility calculation.

The information encoded in the utility functions approach is quantitative: it does not resolve whether the concern results from P, B or T. For example, if one of the three properties has a score of 4 (high concern for a single property), and the other two properties have scores of 1 (low concern), the PBT hazard score is the same, irrespective of whether the high concern results from P, B or T.

An example is provided below: the same score is assigned to a chemical of high concern for P, low concern for B and medium/high concern for T, a chemical with high concern for T and low concern for B and medium/high concern for P and a chemical with high concern for B, low concern for P and medium/high concern for T being the three chemicals of high concern for one out of three properties.

Persistence concern score	BCF concern score	Toxicity concern score	PBT Hazard score
4	1	3	0.556
3	1	4	0.556
1	4	3	0.556

Table 17 – Example of utility calculation.

From the obtained results, it can be highlighted that only nine substances on the list are of high concern for all P, B and T at the same time; 13 chemicals are of high concern for two out of the three properties and moderate/high concern for the remaining.

All the PBT hazard scores evaluated by utility functions are provided in Appendix I.

5.3.3 Ranking results based on "Dominance functions"

To obtain a full discrimination between chemicals based on their individual P, B and T properties, i.e. to identify different profiles of PBT behaviour, total order ranking based on the dominance function can be used. Thus, the chemicals that have two properties with a score of 3, and one property with a score of 4, can be distinguished by a different PBT hazard score depending on their combinations of the scores.

An example is provided below.

Ultimate persistence concern score	BCF concern score	Toxicity concern score	PBT Hazard score
3	3	4	0.707
4	3	3	0.668

Table 18 – Example of dominance calculation.

All the PBT hazard scores evaluated by utility functions are provided in Appendix I.

As illustrated in Figure 17, the use of the dominance function enables qualitative differences between the phthalates to be detected, resulting in the identification of 19 different PBT profiles. This ranking approach accounts for qualitative information and allows the identification of different PBT trends.

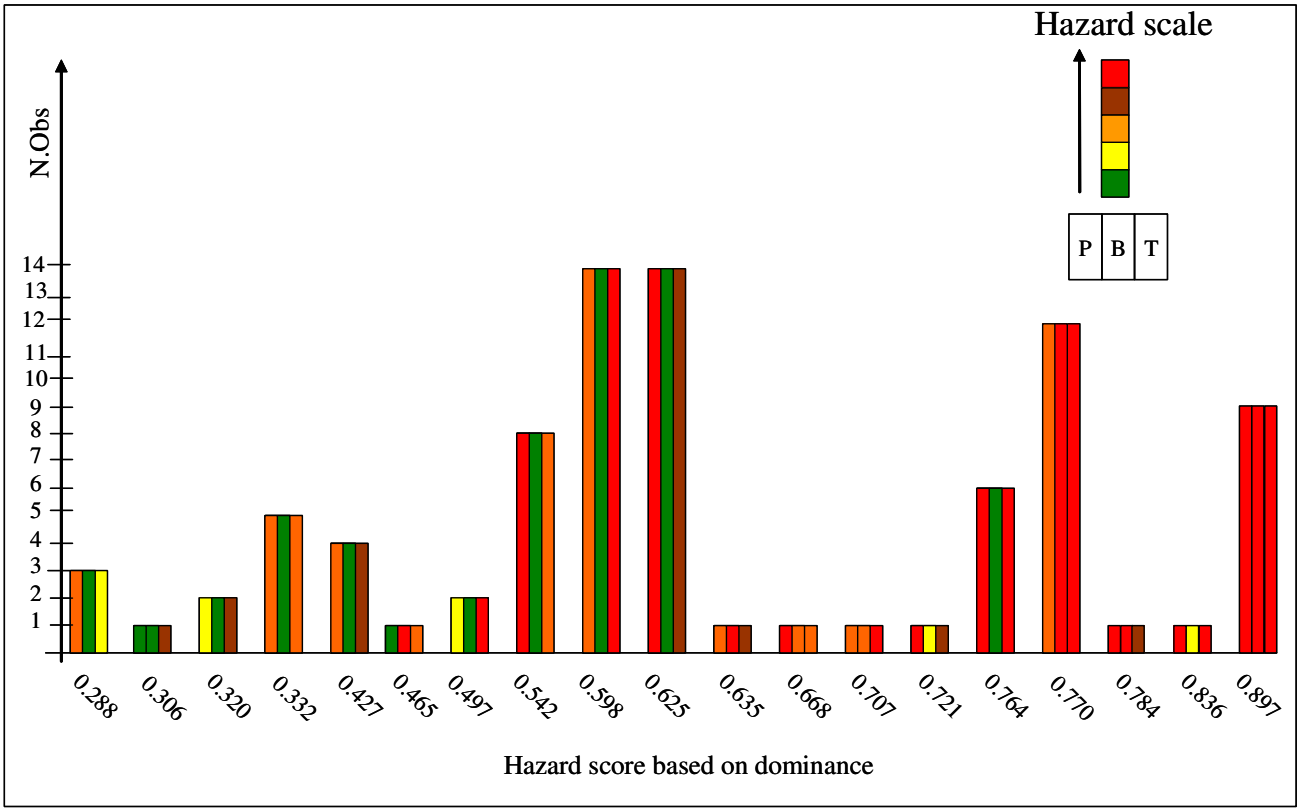

Figure 17 – Ranking results based on "Dominance functions"

5.3.4 Ranking results based on "Hasse diagram partial ranking"

The partial ranking provided by the Hasse diagram technique is illustrated in the Figure 18.

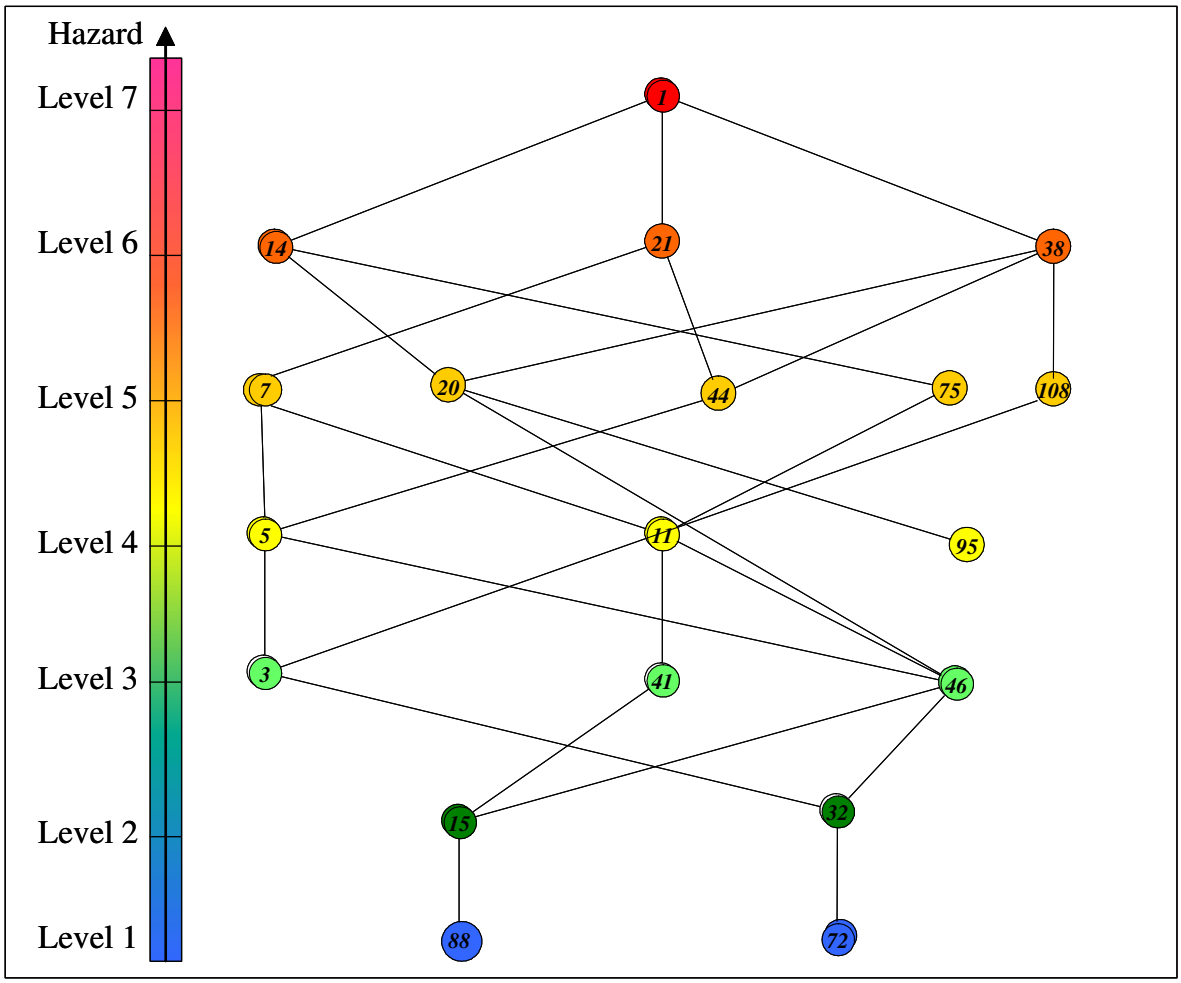

Figure 18 – Ranking results based on "Hasse diagram technique"

Each circle is designed by a double line in case that more than one chemicals fall in the same cluster.

As mentioned above, this technique overcomes the total order ranking methods limitation concerning the lost of information on conflicting properties. It encodes both quantitative and qualitative information of the PBT trends of the evaluated chemicals. The resulted diagram is structured on seven levels of PBT hazard concern.

As an example, it can be noted that the diagram is able to discriminate between the cluster of chemicals with high toxicity concern, moderate/high persistence and low concern for BCF and the chemical with high concern for BCF, moderate/high for toxicity and low concern for BCF. The two clusters are located at the same hazard level (level 4) being both of high concern for one out of the three analyzed properties, but at the same time the two clusters are distinguished.

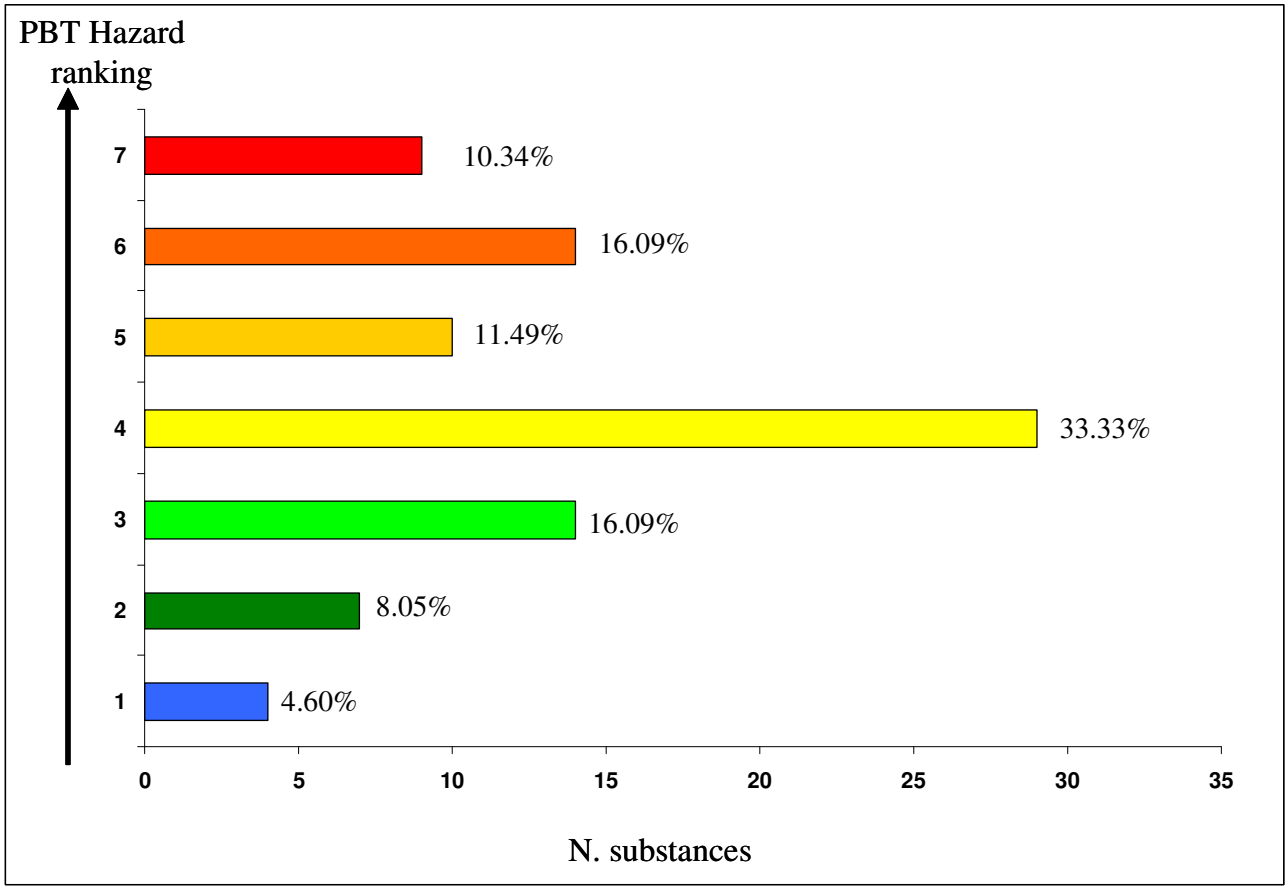

Figure 19 – PBT hazard levels identified by the "Hasse diagram technique"

The Hasse diagram ranking can be considered a more sophisticated ranking technique that recognizes the contradictions in the ranking, when many criteria are used.

It appears as a powerful tool to perform data analysis and multicriteria decision analysis. It has some relevant advantages: its evaluation can be represented as a graph; the mathematics is very simple; it can easily manage criteria of different scales (linguistic, ordinal and ratio-scaled criteria) since it does not perform any numerical aggregation of the criteria.

All the details of the chemicals assignments are illustrated in Appendix II.

5.4 Conclusions

1. Rankings based entirely on QSAR data can be used to predict chemicals with the highest level of concern as well as the lowest level of concern.
   Chemicals at the extremes of the predicted trend could be selected for strategic testing to confirm the boundaries of the trend. In addition, selected chemicals in the middle of the predicted trend could also be selected for testing, to check whether there are any deviations.
2. Ranking methods can also be used to identify different profiles of toxicological concern (e.g. high P & B & T at one extreme *vs* low P & B & T at the other extreme). TOR based on the *dominance function* was found to be useful in this respect.

3. If it is desirable to compare chemicals both in terms of the quantitative differences in their hazard rankings and the qualitative differences in their hazard profiles, the method of choice is *partial order ranking*. The qualitative and quantitative differences can be visualised by using the Hasse diagram.
4. In this investigation, only estimated properties were used as the input to the ranking algorithms. This demonstrates how ranking methods could be used in combination with QSAR methods in cases where there are insufficient experimental data to screen chemicals.
5. It is proposed that the ranking developed by using QSARs predictions could be used to develop a preliminary priority list, and to identify chemicals for strategic testing, in order to assess the robustness of the list.

6. COMPARISON OF COMMPS WITH TOTAL AND PARTIAL ALGORITHMS FOR RANKING OF CHEMICAL SUBSTANCES

6.1 Introduction

On July 18, 2000 the European Parliament and the Council adopted the EU Water Framework Directive, which establishes a framework for community action in the field of water policy. In addition to the directive, the European Commission and the German ‘‘Umweltbundesamt’’ (UBA) developed a proposal for a list of priority substances (European Commission, 1999). The methodology developed to generate the list of priority substances is the so-called Combined Monitoring-based and Modelling-based Priority Setting (COMMPS) scheme. This ranking method was used not only within the EU Water Framework Directive but also by the OSPAR Commission for the protection of the North Sea.

The COMMPS procedure for identifying priority substances was based on the identification of four sub-lists:

- a monitoring-based list for organic substances in the aquatic environment
- a modelling-based list for organic substances in the aquatic environment
- a monitoring-based list for organic substances in the sediment
- a monitoring-based list for metals.

Several substances appear on more than one list. From the four sub-lists the top substances (20 for the first list, 20 from the second one, 10 and 5 from the third and fourth ones, respectively) were selected as candidate for the final list of priority substances. All the 20 top substances examined on the monitoring-based list for organic substances in the aquatic environment were included in the final list of 32 substances (European Commission, 1999). Thus this sub-list is the one of major influence on the final list.

The COMMPS procedure belongs to the so-called scoring methods or index approaches, which are scalar techniques used to rank substances on the basis of more than one criterion. The different criteria values are combined into a single global ranking index, and substances are ordered sequentially according to the numerical value of the ranking index. Since criteria are not always in agreement, i.e. can be conflicting, there is a need to find an overall optimum that can deviate from the optima of one or more of the single criteria.

This study aims to compare the combined monitoring-based and modelling-based priority setting scheme (COMMPS) used to establish a first priority setting list within the EU Water Framework Directive with total and partial ranking methods for chemical substances. Thus the COMMPS procedure is compared with other types of scoring techniques, named total ranking techniques, as well as with a partial ranking method, named Hasse Diagram Technique (HDT). To better evaluate and interpret the reasons for the main differences among the applied techniques a short description of each ranking method is briefly presented. As a case study, this comparison analysis was performed on the 85 substances of the monitoring-based list for organic

substances in the aquatic environment (European Commission, 1999). This research is not the first attempt to compare the ranking using the partial order approach with the COMMPS index approach. A comparison of the COMMPS procedure with the Hasse diagram technique was previously published (Lerche, 2002).

In the present study a limited number of ranking methods were analyzed: the COMMPS priority scheme, three types of scoring methods and the partial ranking derived by Hasse diagram technique. Further a correlation analysis of the different rankings resulting from the different techniques was performed All the computations were performed by using the DART (Decision Analysis by Ranking Techniques) software (DART, 2008), developed by Talete srl and funded by ECB in the context of the 2006 IHCP exploratory research project on the investigation of computational approaches for the ranking of chemicals according to their environmental and toxicological concern.

6.2 Combined Monitoring-based and Modelling-based Priority Setting scheme

COMMPS was developed to prioritise substances on the basis of their risk to the aquatic environment and to human health via the aquatic environment as required by Article 21 of the Water Framework Directive (2000/60/EC).

The COMMPS procedure is based on an approach to combine an automated risk based ranking and a subsequent expert judgement, which can be considered as a simplified risk assessment. The COMMPS procedure can be classified as a so called scoring method or an index approach, where the various descriptors are aggregated into a single score for each substance. The applied functional relationship and weight factors are established based on judgements provided by experts from the EU Member States.

In the present case study the comparison among ranking techniques was performed by applying them to the candidate list of 85 substances that were previously examined on the monitoring-based list for organic substances in the aquatic environment. In the COMMPS procedure, the ranking of substances is based on priority indices (I_PRIO) obtained by multiplication of a substance's exposure index (I_EXP) with the corresponding effect index (I_EFF) as follows:

$$I\_PRIO = I\_EXP * I\_EFF$$

The higher the score the higher the associated risk.

The exposure scores of the organic substances in the aquatic phase are calculated on the basis of the arithmetic means obtained at each sampling station (i.e. on average 810 measurements were used with concentrations higher than the corresponding analytical determination limit). The 90^{th} percentile C_i of these sampling station values was used for the calculation of the exposure score at EU level. The aggregated levels were scored with a maximum score of 10. A logarithmically scaled exposure index was calculated for each substance as follows:

$$I\_EXP(\text{substance i}) = \frac{\log(C_i/(C_{min} * 10^{-1}))}{\log(C_{max}/(C_{min} * 10^{-1}))} * 10$$

The exposure index was scaled by defining an upper and a lower limit (minimum and maximum concentration). The multiplication of the lower limit (C_{min}) by a factor of 0.1 was introduced to avoid zero as a value of the exposure index for the substance with the highest concentration ($C_i = C_{max}$) because this would result in a priority index of zero (the priority index is obtained by multiplication of the exposure index with the effect index). The values of the exposure scores for the 85 substances were available (Table A14 European Commission, 1999).

The effects assessment in COMMPS essentially follows the EURAM method. It was modified insofar as the indirect effects to man via the aquatic environment were included in the effects scoring. The overall effect index for organic compounds is calculated as a combined score, sum of the scores of the three effect parameters, i.e. EFS_d (direct effects) indirect effects (EFS_i) and effects on humans (EFS_h).

$$I\_EFF = EFS_d + EFS_i + EFS_h$$

The direct effect score, EFS_d, is based on the PNEC and is scaled by a logarithmic function to be in a suitable range for multiplication. The indirect effect EFS_i is assumed to be correlated with the substance's ability to bioaccumulate and is derived from the bioconcentration factor (BCF) or alternatively from log Kow. The human effect score EFS_h is established using CMR properties (carcinogenicity, mutagenicity and effect on reproduction) and chronic effects (due to oral intake). The EFS_h score was established using official R-phrases for labelling of chemical substances.

6.3 Dataset

In this study, the comparative analysis of the COMMPS procedure with the other ranking methods was performed on the 85 substances of the monitoring-based list for organic substances in the aquatic environment (European Commission, 1999).

Exposure data expressed in terms of the 90 percentile of the observed concentration in the waters of the EU Members States, interpreted as a ''realistic worst case'' in the technical guidance document on risk assessment for existing substances ((European Commission, 1996), together with the EU-level median and the EU-level arithmetic mean are provided in Table 18. These values were taken from Table A9 of the European Commission document (European Commission, 1999). Effect data expressed in terms of direct effect (EFS_d), indirect effect (EFS_i) and human effect (EFS_h) are also provided in Table 18. These values were taken from Table A22 of the European Commission document (European Commission, 1999).

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
1	71-55-6	1,1,1-trichloroethane	0.141	0.049	0.052	1.35	0	1.8
2	87-61-6	1,2,3-trichlorobenzene	0.031	0.008	0.014	1.98	1	0
3	120-82-1	1,2,4-trichlorobenzene	0.157	0.012	0.053	2.43	2	1.8
4	95-50-1	1,2-dichlorobenzene	0.544	0.026	0.260	1.74	1	0
5	107-06-2	1,2-dichloroethane	8.243	0.847	3.021	1.93	0	2
6	108-70-3	1,3,5-trichlorobenzene	0.034	0.008	0.025	1.93	2	0
7	541-73-1	1,3-dichlorobenzene	7.100	0.012	1.194	1.8	1	0
8	106-46-7	1,4-dichlorobenzene	0.422	0.098	0.139	1.93	1	0
9	93-76-5	2,4,5-	0.323	0.145	0.175	2.14	0	0

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
		trichlorophenoxyacetic ac.						
10	94-75-7	2,4-dichlorophenoxyacetic ac.	0.370	0.049	0.312	1.83	0	0
11	121-73-3	3-chloronitrobenzene	37.500	18.760	18.760	2.78	0	1.4
12	83-32-9	acenaphthene	0.417	0.010	0.062	2.63	1	0
13	15972-60-8	alachlor	0.150	0.053	0.079	3.57	0	1.8
14	309-00-2	aldrin	0.022	0.005	0.009	4.7	3	1.8
15	120-12-7	anthracene	0.083	0.004	0.014	4.09	2	0
16	1912-24-9	atrazine	0.334	0.052	0.330	2.94	0	1.8
17	6190-65-4	atrazine desethyl	0.078	0.039	0.043	3.07	0	0
18	2642-71-9	azinphos-ethyl	0.013	0.010	0.011	4.97	0	0
19	86-50-0	azinphos-methyl	0.013	0.011	0.011	4.03	0	0
20	25057-89-0	bentazon	0.086	0.018	0.034	1.5	0	0
21	56-55-3	benzo-a-anthracene	0.083	0.021	0.028	4.29	3	2
22	50-32-8	benzo-a-pyrene	0.027	0.007	0.012	4.5	3	2
23	205-99-2	benzo-b-fluoroanthene	0.048	0.009	0.018	4.29	3	2
24	191-24-2	benzo-g,h,i-perylene	0.047	0.008	0.017	5	3	1.8
25	207-08-9	benzo-k-fluoroanthene	0.025	0.004	0.009	4.9	3	2
26	470-90-6	chlorfenvinphos	0.103	0.003	0.020	4.29	2	0
27	2921-88-2	chlorpyrifos	0.128	0.020	0.035	5	2	0
28	15545-48-9	chlortoluron	0.117	0.061	0.070	3.14	0	0
29	21725-46-2	cyanazine	0.125	0.049	0.053	3.36	0	0
30	53-19-0	DDD, 2,4'- isomer	0.022	0.001	0.006	5	3	0
31	72-54-8	DDD, 4,4'- isomer	0.048	0.002	0.009	5	3	0
32	72-55-9	DDE, 4,4'- isomer	0.044	0.003	0.013	5	3	1.8
33	789-02-6	DDT, 2,4'- isomer	0.004	0.001	0.001	3.94	3	1.8
34	50-29-3	DDT, 4,4'- isomer	0.007	0.005	0.006	5	2	1.8
35	1007-28-9	desisopropylatrazine	0.145	0.047	0.068	2.45	0	0
36	333-41-5	diazinon	0.032	0.008	0.040	4.62	1	0
37	75-09-2	dichloromethane	10.250	0.933	2.133	2.11	0	1.8
38	62-73-7	dichlorvos	0.048	0.012	0.021	5	0	0
39	60-57-1	dieldrin	0.006	0.003	0.004	4.94	3	1.8
40	60-51-5	dimethoate	0.154	0.014	0.055	3.36	0	0
41	330-54-1	diuron	1.076	0.235	0.561	3.79	0	1.2
42	959-98-8	endosulfan, alpha-isomer	0.058	0.007	0.017	5	1	0
43	33213-65-9	endosulfan, beta isomer	0.019	0.005	0.009	4.39	1	0
44	1031-07-8	endosulfan-sulfate	0.019	0.007	0.009	4.1	1	0
45	72-20-8	endrin	0.007	0.005	0.005	5	3	0
46	100-41-4	ethylbenzene	0.332	0.115	0.147	0.7	0	0
47	60-00-4	ethylenediamine-tetraacetic acid	45.590	9.822	17.630	1.71	0	0
48	122-14-5	fenitrothion	0.030	0.010	0.017	4.32	1	0
49	55-38-9	fenthion	0.015	0.010	0.039	4.46	1	0
50	206-44-0	fluoroanthene	0.082	0.016	0.065	2.43	3	0
51	319-84-6	HCH, alpha- isomer	0.025	0.004	0.009	3.57	1	1.8
52	319-85-7	HCH, beta- isomer	0.038	0.006	0.013	3.04	1	1.8
53	319-86-8	HCH, delta- isomer	0.022	0.003	0.009	2.64	2	1.8
54	58-89-9	HCH, gamma- isomer	0.037	0.008	0.017	3.24	2	0

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
		(lindane)						
55	76-44-8	heptachlor	0.013	0.005	0.006	5	3	1.8
56	118-74-1	hexachlorobenzene	0.010	0.005	0.010	4.29	3	2
57	87-68-3	hexachlorobutadiene	0.007	0.005	0.009	3.07	3	1.8
58	67-72-1	hexachloroethane	0.002	0.000	0.001	2.87	2	1.2
59	193-39-5	indeno(1,2,3-cd)pyrene	0.094	0.034	0.036	4.29	3	2
60	465-73-6	isodrin	0.012	0.005	0.006	4.44	3	0
61	34123-59-6	isoproturon	0.370	0.115	0.162	3.23	0	1.8
62	121-75-5	malathion	0.040	0.010	0.041	4.07	1	0
63	94-74-6	MCPA	0.156	0.040	0.051	1.21	0	0
64	93-65-2	mecoprop	0.811	0.070	0.582	2.36	0	0
65	67129-08-2	metazachlor	0.080	0.007	0.031	3.14	0	0
66	72-43-5	methoxychlor	0.001	0.001	0.001	5	3	1.8
67	51218-45-2	metolachlor	0.313	0.065	0.123	3.36	1	0
68	91-20-3	naphthalene	1.683	0.065	0.267	2.59	2	0
69	56-38-2	parathion-ethyl	0.020	0.012	0.013	4.5	1	0
70	298-00-0	parathion-methyl	0.013	0.010	0.013	4.07	0	0
71	608-93-5	pentachlorobenzene	0.001	0.001	0.001	3.36	3	0
72	87-86-5	pentachlorophenol	0.135	0.071	0.451	3.34	3	1.8
73	7287-19-6	prometryn	0.033	0.014	0.021	3.07	0	2
74	139-40-2	propazine	0.052	0.021	0.030	1.97	0	1.8
75	7286-69-3	sebuthylazine	0.055	0.009	0.021	4.29	1	0
76	122-34-9	simazine	0.218	0.047	0.113	2.96	0	1.8
77	5915-41-3	terbuthylazine	0.170	0.036	0.191	3.07	0	0
78	886-50-0	terbutryne	0.279	0.037	0.070	2.14	1	0
79	127-18-4	tetrachloroethene	1.092	0.164	0.836	1.64	0	0
80	56-23-5	tetrachloromethane	1.049	0.116	0.685	2.25	0	1.8
81	108-88-3	toluene	10.796	0.418	2.549	1.5	0	1.8
82	79-01-6	trichloroethene	2.500	0.238	1.548	1.39	0	1.8
83	67-66-3	trichloromethane	1.173	0.281	0.793	2.93	0	1.8
84	1582-09-8	trifluralin	0.031	0.006	0.027	3.94	3	0
85	95-47-6	xylene, o- isomer	0.146	0.127	0.112	2.5	1	0

Table 18 – Substances of the monitoring-based list for organic substances in the aquatic environment (European Commission, 1999).

6.4 Ranking results

6.4.1 COMMPS results

COMMPS results are illustrated in Figure 20. To simplify the comparison with the other priority techniques a rank equal to 1 correspond to the most desirable compound, and thus with the least concern, while a rank of 85 correspond to the least desirable compound, with the highest concern. In this graph, also called a Pareto plot, substances are plotted on the *x* axis versus their COMMPS rank and on the *y* axis according to descending value of their COMMPS rank. Thus the first 20 substances on the *x* axis are the 20 top substances examined on the monitoring-based list for

organic substances in the aquatic environment and included in the final list of 32 substances.

The list of these substances ranked according to their descending value of COMMPS ranks are shown in Table 19 together with their exposure and effect scores.

ID	CAS	Compound	I_EXP	I_EFF	COMMPS Rank
59	193-39-5	indeno(1,2,3-cd)pyrene	5.67	9.29	85
21	56-55-3	benzo-a-anthracene	5.6	9.29	84
24	191-24-2	benzo-g,h,i-perylene	5.25	9.8	83
32	72-55-9	DDE, 4,4'- isomer	5.21	9.8	82
23	205-99-2	benzo-b-fluoroanthene	5.26	9.29	81
72	87-86-5	pentachlorophenol	5.9	8.14	80
25	207-08-9	benzo-k-fluoroanthene	4.85	9.9	79
22	50-32-8	benzo-a-pyrene	4.91	9.5	78
14	309-00-2	aldrin	4.78	9.5	77
55	76-44-8	heptachlor	4.42	9.8	76
31	72-54-8	DDD, 4,4'- isomer	5.26	8	75
27	2921-88-2	chlorpyrifos	5.87	7	74
56	118-74-1	hexachlorobenzene	4.29	9.29	73
11	121-73-3	3-chloronitrobenzene	9.39	4.18	72
39	60-57-1	dieldrin	3.92	9.74	71
30	53-19-0	DDD, 2,4'- isomer	4.77	8	70
3	120-82-1	1,2,4-trichlorobenzene	6	6.23	69
26	470-90-6	chlorfenvinphos	5.74	6.29	68
41	330-54-1	diuron	7.19	4.99	67
34	50-29-3	DDT, 4,4'- isomer	4.03	8.8	66

Table 19 – Top 20 substances selected by COMMPS procedure.

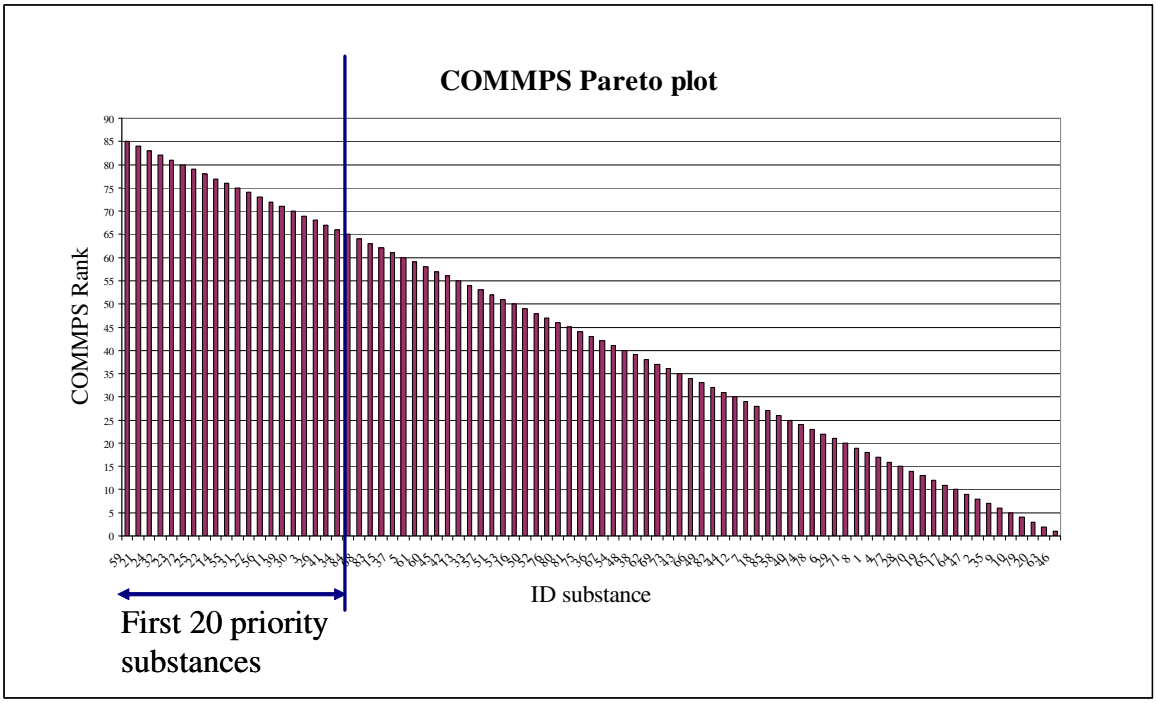

Figure 20 – COMMPS Pareto plot.

In the same way Figure 21 illustrates COMMPS results with respect to its priority index instead with the rank, providing additional information about the distribution of the chemicals in the entire hazard range.

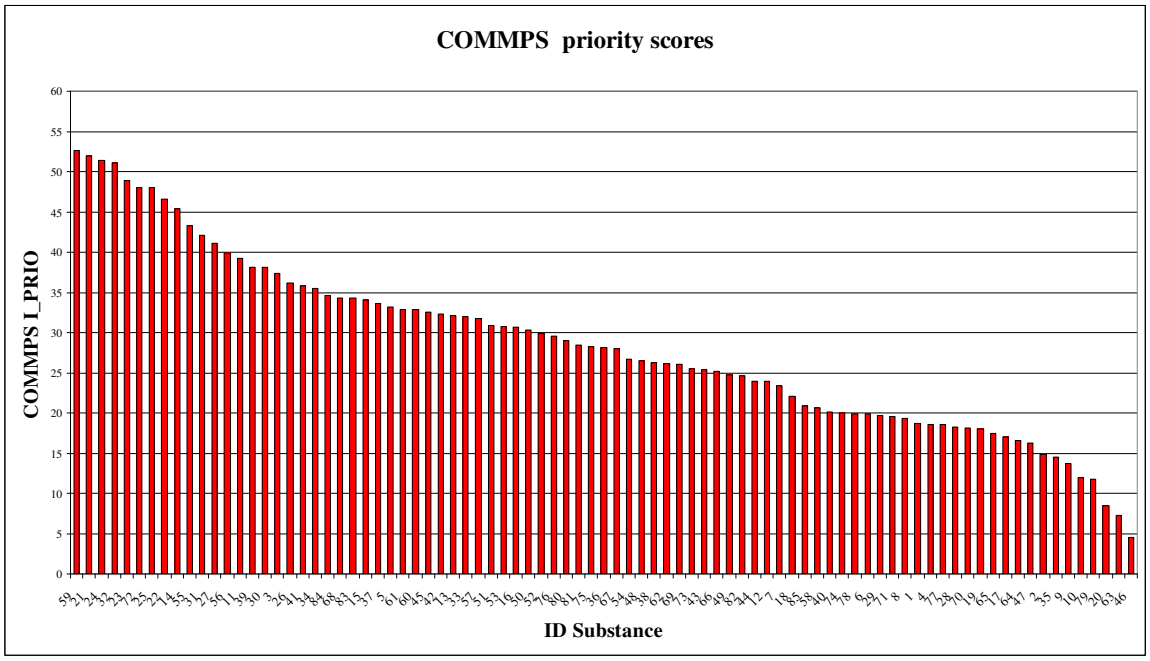

Figure 21 – COMMPS results.

6.4.2 Desirability and Utility function results

The desirability and utility function approaches were applied on the same dataset of 85 substances described by three exposure criteria, i.e. the 90 percentile of the observed concentration in the waters of the members states of the EU, the EU-level median and the EU-level arithmetic mean and by three effect criteria, i.e. the direct effect (EFS_d), indirect effect (EFS_i) and human effect (EFS_h). To transform the values of the six criteria to the same scale and to make the criteria unidirectional and oriented so that optimal values are assumed as the highest ones, the six criteria were transformed by an inverse linear transformation. These transformations are needed because the optimal values, the most desirable values, correspond to low values of the considered criteria. An illustrative picture of the inverse linear transformation of EFS_d is illustrated in Figure 22. By this transformation high desirabilities/utilities were assigned to those substances characterised by low direct effect score. The same transformation was applied to the other criteria. The six criteria, equally weighted, were then merged according to desirability and utility methods to provide the overall desirability/utility scores of each substance.

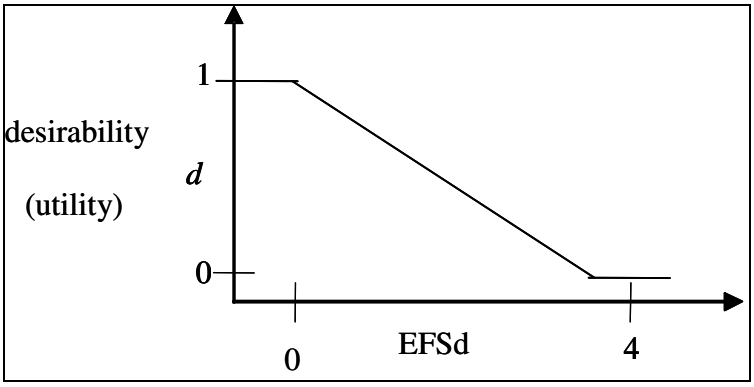

Figure 22 – Inverse linear transformation of EFS_d.

It has to be noted that Desirability ranking approach is the most severe ranking approach, which identifies 30 substances as priority substance, characterised by the lowest value of Desirability equal to 0, due to the fact that they are of high concern score for any exposure or effect criteria. On the contrary, the overall desirability Di is equal to the maximum value of 1, and the substance is considered of no concern, only if it has a low concern score for all the six considered criteria.

This approach, being based on a highly conservative assumption, is probably not the best one to be adopted in the context of a risk assessment evaluation, which is based on the assumption that a high risk is provided only by substances which have at the same time high exposure and high effect.

Thus, as an example, benzo-g,h,i-perylene (CAS 191-24-2; Substance ID = 24) is ranked in the list of the highest 30 priority substances because it is of high concern for the effects (EFS_d = 5 (maximum value); EFS_i = 3 (maximum value); EFS_h = 1.8 (maximum value = 2) despite its low concern for the exposure (90 percentile of the observed concentration in the waters = 0.047 µg/l; EU-level median = 0.008 µg/l; EU-level arithmetic mean = 0.017 µg/l).

The Desirability Pareto plot is illustrated in Figure 23. A rank equal to 1 correspond to the most desirable compound, i.e. with the least concern, while a rank of 85 correspond to the least desirable compound, i.e. the highest concern.

The 30 substances of high priority are highlighted in the left part of the plot, before the vertical line.

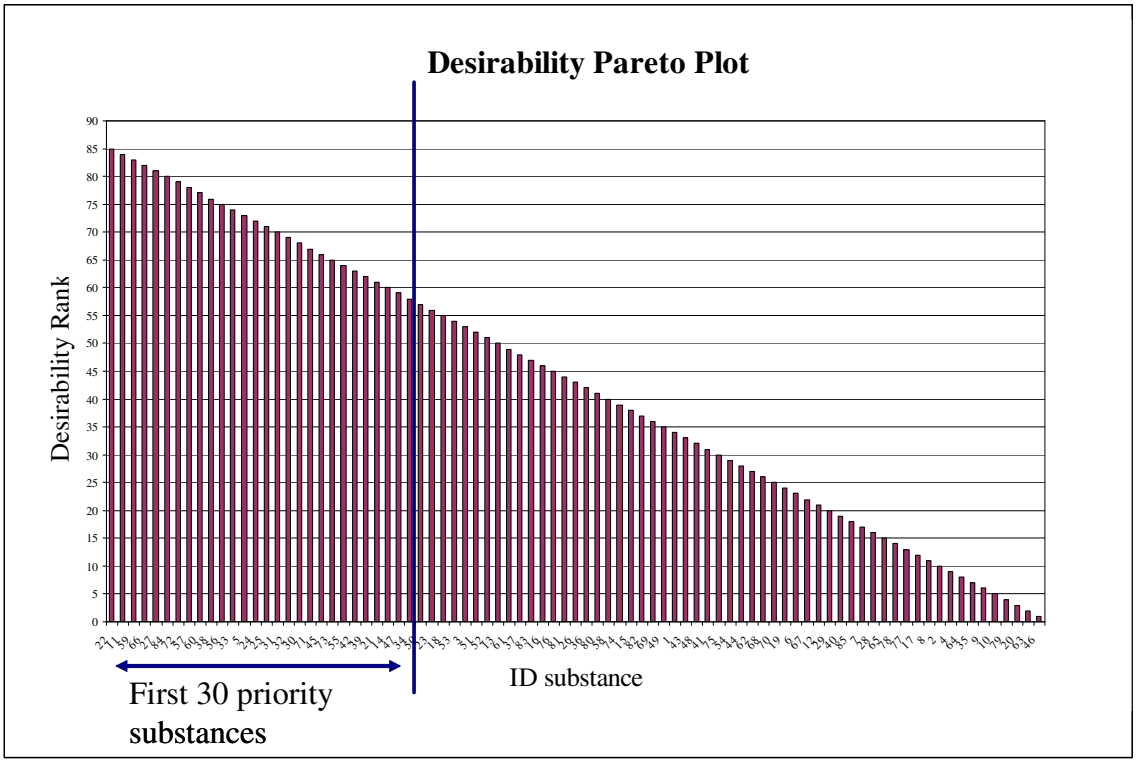

Figure 23 – Desirability Pareto plot.

The list of these 30 substances of Desirability values of 0 are shown in Table 20 together with their exposure and effect criteria. For each criterion the maximum value, i.e. highest value of exposure and effect, discovered in the COMMPS dataset is also reported. The criterion or criteria responsible for their high global level of concern are highlighted in bold.

ID	CAS	Compound	90-perc. Conc. [µg/l] max : 45.590	Median [µg/l] max: 18.760	Arit. Mean [µg/l] max: 18.760	EFS_d max: 5	EFS_i max:3	EFS_h max:2
5	107-06-2	1,2-dichloroethane	8.243	0.847	3.021	1.93	0	**2**
11	121-73-3	3-chloronitrobenzene	37.500	**18.760**	**18.760**	2.78	0	1.4
14	309-00-2	aldrin	0.022	0.005	0.009	4.7	**3**	1.8
21	56-55-3	benzo-a-anthracene	0.083	0.021	0.028	4.29	**3**	**2**
22	50-32-8	benzo-a-pyrene	0.027	0.007	0.012	4.5	**3**	**2**
23	205-99-2	benzo-b-fluoroanthene	0.048	0.009	0.018	4.29	**3**	**2**
24	191-24-2	benzo-g,h,i-perylene	0.047	0.008	0.017	**5**	**3**	1.8
25	207-08-9	benzo-k-fluoroanthene	0.025	0.004	0.009	4.9	**3**	**2**
27	2921-88-2	chlorpyrifos	0.128	0.020	0.035	**5**	2	0
30	53-19-0	DDD, 2,4'- isomer	0.022	0.001	0.006	**5**	**3**	0
31	72-54-8	DDD, 4,4'- isomer	0.048	0.002	0.009	**5**	**3**	0
32	72-55-9	DDE, 4,4'- isomer	0.044	0.003	0.013	**5**	**3**	1.8
33	789-02-6	DDT, 2,4'- isomer	0.004	0.001	0.001	3.94	**3**	1.8
34	50-29-3	DDT, 4,4'- isomer	0.007	0.005	0.006	**5**	2	1.8

ID	CAS	Compound	90-perc. Conc. [µg/l] max : 45.590	Median [µg/l] max: 18.760	Arit. Mean [µg/l] max: 18.760	EFS_d max: 5	EFS_i max:3	EFS_h max:2
38	62-73-7	dichlorvos	0.048	0.012	0.021	**5**	0	0
39	60-57-1	dieldrin	0.006	0.003	0.004	4.94	**3**	1.8
42	959-98-8	endosulfan, alpha-isomer	0.058	0.007	0.017	**5**	1	0
45	72-20-8	endrin	0.007	0.005	0.005	**5**	**3**	0
47	60-00-4	ethylenediamine-tetraacetic acid	**45.590**	9.822	17.630	1.71	0	0
50	206-44-0	fluoroanthene	0.082	0.016	0.065	2.43	**3**	0
55	76-44-8	heptachlor	0.013	0.005	0.006	**5**	**3**	1.8
56	118-74-1	hexachlorobenzene	0.010	0.005	0.010	4.29	**3**	2
57	87-68-3	hexachlorobutadiene	0.007	0.005	0.009	3.07	**3**	1.8
59	193-39-5	indeno(1,2,3-cd)pyrene	0.094	0.034	0.036	4.29	**3**	**2**
60	465-73-6	isodrin	0.012	0.005	0.006	4.44	**3**	0
66	72-43-5	methoxychlor	0.001	0.001	0.001	5	**3**	1.8
71	608-93-5	pentachlorobenzene	0.001	0.001	0.001	3.36	**3**	0
72	87-86-5	pentachlorophenol	0.135	0.071	0.451	3.34	**3**	1.8
73	7287-19-6	prometryn	0.034	0.014	0.021	3.07	0	**2**
84	1582-09-8	trifluralin	0.031	0.006	0.027	3.94	**3**	0

Table 20 – Top 30 substances selected by Desirability approach.

The application of the desirability function approach resulted in a large number of substances appearing to be of high concern, which is considered too conservative in view of the risk assessment assumption.

The ranking based on the utility function, on the contrary, allows better discrimination among the substances based on the risk they cause. This approach in fact is calculated less severely: a high level of concern, i.e. low utility value, is assigned only to those substances which are of high concern for all six criteria.

On the other hand a substance can have assigned a low concern score even if it is of high concern for one out of six criteria. As an example, despite the fact that dichlorvos (CAS 62-73-7; Substance ID = 38) is of high concern based on the human effect (EFS_h = 5), a relative low global score is assigned to it being of low concern for the other criteria.

Because the utility function assigns the highest ranking only when all six criteria have maximal values, it could in principle be exploited in the identification of highly risky substances.

The Utility Pareto plot is illustrated in Figure 24. As for the Desirability function, a rank equal to 1 correspond to the compound with the least concern, while a rank of 85 correspond to a compound with the highest concern.

The 20 substances of high priority are highlighted in the left part of the plot, before the vertical line.

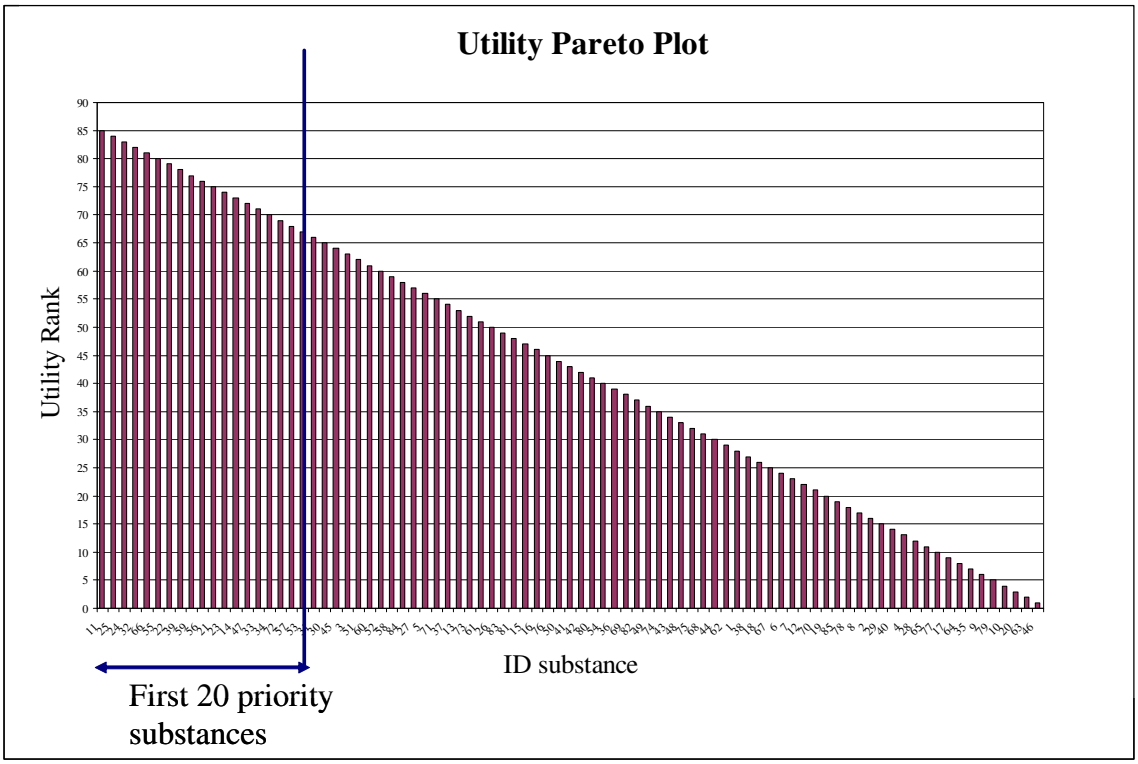

Figure 24 – Utility Pareto plot.

The list of the top priority 20 substances ranked according to their descending value of Utility score is shown in Table 21 together with their exposure and effect criteria.

ID	CAS	Compound	90-perc. Conc. [µg/l] max : 45.590	Median [µg/l] max: 18.760	Arit. Mean [µg/l] max: 18.760	EFS_d max: 5	EFS_i max:3	EFS_h max:2
11	121-73-3	3-chloronitrobenzene	37.500	18.760	18.760	2.78	0	1.4
25	207-08-9	benzo-k-fluoroanthene	0.025	0.004	0.009	4.9	3	2
32	72-55-9	DDE, 4,4'- isomer	0.047	0.008	0.017	5	3	1.8
24	191-24-2	benzo-g,h,i-perylene	0.044	0.003	0.013	5	3	1.8
55	76-44-8	heptachlor	0.013	0.005	0.006	5	3	1.8
66	72-43-5	methoxychlor	0.001	0.001	0.001	5	3	1.8
39	60-57-1	dieldrin	0.027	0.007	0.012	4.5	3	2
22	50-32-8	benzo-a-pyrene	0.006	0.003	0.004	4.94	3	1.8
23	205-99-2	benzo-b-fluoroanthene	0.083	0.021	0.028	4.29	3	2
21	56-55-3	benzo-a-anthracene	0.048	0.009	0.018	4.29	3	2
56	118-74-1	hexachlorobenzene	0.010	0.005	0.010	4.29	3	2

ID	CAS	Compound	90-perc. Conc. [µg/l] max : 45.590	Median [µg/l] max: 18.760	Arit. Mean [µg/l] max: 18.760	EFS_d max: 5	EFS_i max:3	EFS_h max:2
59	193-39-5	indeno(1,2,3-cd)pyrene	0.094	0.034	0.036	4.29	3	2
14	309-00-2	aldrin	0.022	0.005	0.009	4.7	3	1.8
47	60-00-4	ethylenediamine-tetraacetic acid	45.590	9.822	17.630	1.71	0	0
33	789-02-6	DDT, 2,4'- isomer	0.004	0.001	0.001	3.94	3	1.8
34	50-29-3	DDT, 4,4'- isomer	0.007	0.005	0.006	5	2	1.8
72	87-86-5	pentachlorophenol	0.135	0.071	0.451	3.34	3	1.8
57	87-68-3	hexachlorobutadiene	0.007	0.005	0.009	3.07	3	1.8
53	319-86-8	HCH, delta- isomer	0.022	0.003	0.009	2.64	2	1.8
31	72-54-8	DDD, 4,4'- isomer	0.048	0.002	0.009	5	3	0

Table 21 – Top 20 substances selected by Utility approach.

6.4.3 Dominance function results

The dominance function approach was also applied on the same dataset of 85 substances described by three exposure criteria and by three effect criteria.

As mentioned above, this approach is based on the comparison of the state of the different criteria for each pair of substances; it does not require the transformation of each criterion into a quantitative function and its computation is based on the comparison of the sets of criteria where a substance dominates the other, i.e. where a substance is better than the other, with the set of criteria where the substance is dominated by the other.

The dominance function approach is often used to obtain a full discrimination between substances based on their individual criteria selected for the analysis, i.e. to identify different profiles of behaviour of the substances with respect to the different criteria.

The Dominance Pareto plot is illustrated in Figure 25. The 20 substances of high priority are highlighted in the left part of the plot, before the vertical line.

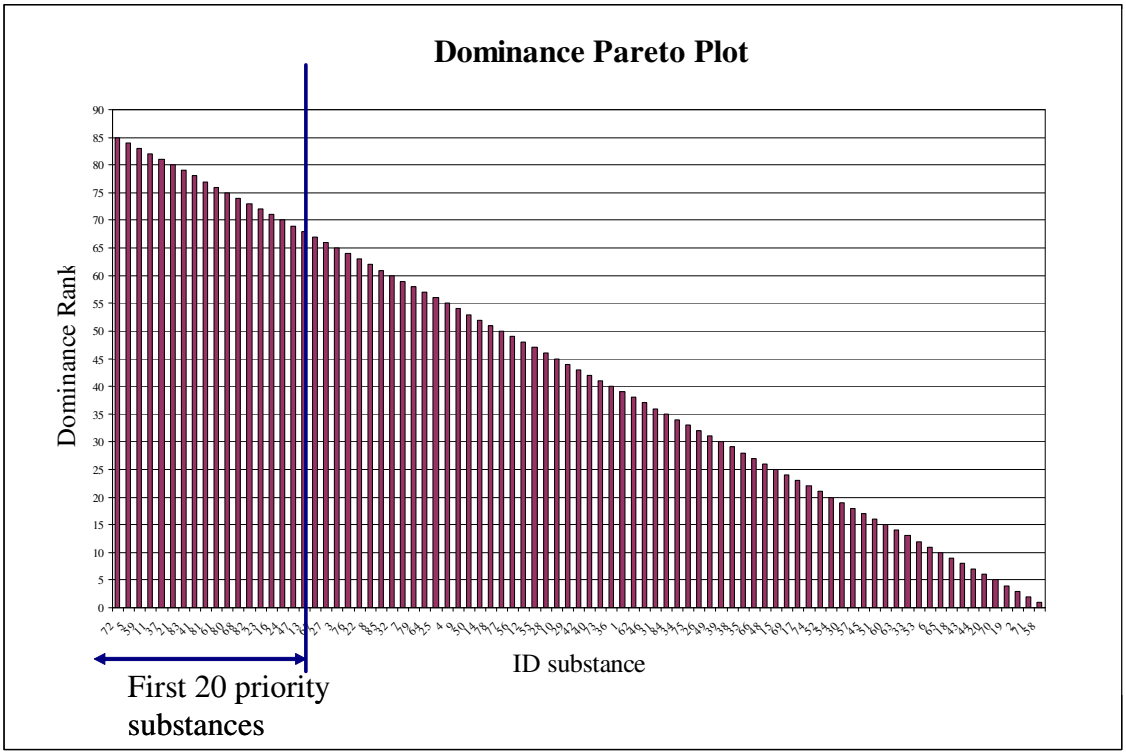

Figure 25 – Dominance Pareto plot.

The list of the top priority 20 substances ranked according to their descending value of Dominance score is shown in Table 22 together with their exposure and effect criteria.

ID	CAS	Compound	90-perc. Conc. [µg/l] max : 45.590	Median [µg/l] max: 18.760	Arit. Mean [µg/l] max: 18.760	EFS_d max: 5	EFS_i max:3	EFS_h max:2
72	87-86-5	pentachlorophenol	0.135	0.071	0.451	3.34	3	1.8
5	107-06-2	1,2-dichloroethane	8.243	0.847	3.021	1.93	0	2
59	193-39-5	indeno(1,2,3-cd)pyrene	0.094	0.034	0.036	4.29	3	2
11	121-73-3	3-chloronitrobenzene	37.500	18.760	18.760	2.78	0	1.4
21	56-55-3	benzo-a-anthracene	0.083	0.021	0.028	4.29	3	2
37	75-09-2	dichloromethane	10.250	0.933	2.133	2.11	0	1.8
83	67-66-3	trichloromethane	1.173	0.281	0.793	2.93	0	1.8
41	330-54-1	diuron	1.076	0.235	0.561	3.79	0	1.2
81	108-88-3	toluene	10.796	0.418	2.549	1.5	0	1.8
61	34123-59-6	isoproturon	0.370	0.115	0.162	3.23	0	1.8
80	56-23-5	tetrachloromethane	1.049	0.116	0.685	2.25	0	1.8
68	91-20-3	naphthalene	1.683	0.065	0.267	2.59	2	0
82	79-01-6	trichloroethene	2.500	0.238	1.548	1.39	0	1.8
23	205-99-2	benzo-b-fluoroanthene	0.048	0.009	0.018	4.29	3	2
16	1912-24-9	atrazine	0.334	0.052	0.330	2.94	0	1.8
24	191-24-2	benzo-g,h,i-	0.047	0.008	0.017	5	3	1.8

ID	CAS	Compound	90-perc. Conc. [µg/l] max : 45.590	Median [µg/l] max: 18.760	Arit. Mean [µg/l] max: 18.760	EFS_d max: 5	EFS_i max:3	EFS_h max:2
47	60-00-4	perylene ethylenediamine-tetraacetic acid	45.590	9.822	17.630	1.71	0	0
13	15972-60-8	alachlor	0.150	0.053	0.079	3.57	0	1.8
67	51218-45-2	metolachlor	0.313	0.065	0.123	3.36	1	0
27	2921-88-2	chlorpyrifos	0.128	0.020	0.035	5	2	0

Table 22 – Top 20 substances selected by Dominance approach.

6.4.4 Comparison COMMPS, Desirability, Utility and Dominance functions

A comparison of the different results provided by the applied techniques was performed by the correlation analysis of the ranks derived by COMMPS, Desirability, Utility and Dominance approaches, which provides information on the degree of agreement among the rankings. Two rank correlation coefficients, named the Spearman r and the Kendall τ (Kendall, 1948) were computed to quantify the correlation relationship among the ranking results. According to the Spearman coefficient *r*, two rankings are perfectly correlated if they provide the same ranks for all the elements, and the difference between two ranks (d_i) is taken as a measure of the ranking difference for the substance considered. For the whole set of substances, the rank differences are squared before summing them, in order to prevent differences with opposite signs from cancelling each other out. The general formula of the Spearman r coefficient is:

$$r_{rk} = 1 - \frac{6 \cdot \sum_{i=1}^{N} d_i^2}{N^3 - N} \qquad -1 \le r_{rk} \le +1$$

where d_i is the rank difference for the substance *i* in the two rank results *r* and *k* and *N* is the total number of substances. This coefficient ranges between +1 and –1. Rankings perfectly directly correlated, in terms of rank, assume values r = +1; inversely correlated values r = -1 and results not correlated values r = 0.

The Kendall coefficient τ is based on the sums of scores for pairs of substances in increasing and decreasing order. In rank correlation analysis Kendall defined a score for a pair of rankings of *N* items as +1 if any two are ranked in the same order by the two rankings, as -1 if in opposite order, and zero if tied to either or both rankings. The total score S is the algebraic sum of the ½ $N(N\text{-}1)$ contributions from pairs of items. Kendall's rank coefficient is the sum of scores for pairs in increasing and decreasing order, divided by the total number of pairs ($N(N\text{-}1)$) defined as:

$$\tau_{rk} = \frac{2S}{N(N-1)} \qquad -1 \le \tau_{rk} \le +1$$

Kendall's rank coefficient ranges from +1 in the case of complete agreement to –1 in the case of complete disagreement. If the two rankings are uncorrelated, it takes a value of 0.

Both the Spearman and Kendall rank correlation coefficients measure the correlation between two rankings, based on N elements.

The results of the correlation analysis by Spearman and Kendall coefficients are illustrated in the correlation matrices of Table 23 and 24, respectively.

	COMMPS	**Desirability**	**Utility**	**Dominance**
COMMPS	1	0.87	0.85	0.42
Desirability	0.87	1	0.94	0.25
Utility	0.85	0.94	1	0.24
Dominance	0.42	0.25	0.24	1

Table 23 – Spearman correlation matrix.

	COMMPS	**Desirability**	**Utility**	**Dominance**
COMMPS	1	0.74	0.71	0.29
Desirability	0.74	1	0.81	0.17
Utility	0.71	0.81	1	0.16
Dominance	0.29	0.17	0.16	1

Table 24 – Kendall correlation matrix.

Both Spearman and Kendall correlation analysis highlight a rather strong agreement between the rankings provided by the COMMPS procedure and the one provided by the Desirability approach and a slightly lower degree of agreement with the Utility ranking. These three prioritisation methods are based on a relatively similar aggregation scheme of the criteria: the COMMPS procedure provide a preliminary aggregation of the exposure and effect criteria, followed by a further aggregation of the two derived super-criteria (I_EXP and I_EFF); the Desirability technique aggregates all the criteria in the same step by a geometric mean, while the Utility technique provides an arithmetic mean aggregation.

Differently, the Dominance technique is based on a pair wise comparison of the behaviour of the substances and it clearly results in a rather different final ranking.

To explore further the degree of agreement among the prioritisation methods applied, the "consensus" among them was analysed. Table 25 provides the list of all the substances identified as priority substances by at least one of the method applied and sorted according to the overlap degree among the methods. The ranks (from 66 to 85) of the substances belonging to the COMMPS, Desirability, Utility and Dominance lists are highlighted in bold.

It can be noticed that a total consensus among the four prioritisation methods is achieved for six substances which are selected as priority substances: 3-chloronitrobenzene, benzo-a-anthracene, benzo-b-fluoroanthene, benzo-g,h,i-perylene, indeno(1,2,3-cd)pyrene and pentachlorophenol .In addition to these six substances, a consensus of the COMMPS, Desirability and Utility prioritisation methods is also achieved for aldrin, benzo-a-pyrene, benzo-k-fluoroanthene, DDD, 4,4'- isomer, DDE, 4,4'- isomer, DDT, 4,4'- isomer, dieldrin, heptachlor, hexachlorobenzene.

As a general comment it can be concluded that for those substances that are of high and evident risk, caused by their high exposure and high effect, a consensus among different aggregation methods can be achieved. However, if there is less evidence of the risk then depending on the method applied different results are derived. As a consequence of that, the selection of the aggregation method is a key point and strongly influences the ranking results.

ID	CAS	Compound	COMMPS Rank	Desirability Rank	Utility Rank	Dominance Rank
11	121-73-3	3-chloronitrobenzene	**72**	**72**	**85**	**82**
21	56-55-3	benzo-a-anthracene	**84**	**84**	**76**	**81**
23	205-99-2	benzo-b-fluoroanthene	**81**	**81**	**75**	**72**
24	191-24-2	benzo-g,h,i-perylene	**83**	**83**	**83**	**70**
59	193-39-5	indeno(1,2,3-cd)pyrene	**85**	**85**	**77**	**83**
72	87-86-5	pentachlorophenol	**80**	**80**	**69**	**85**
14	309-00-2	aldrin	**77**	**77**	**73**	52
22	50-32-8	benzo-a-pyrene	**78**	**78**	**79**	63
25	207-08-9	benzo-k-fluoroanthene	**79**	**79**	**84**	56
27	2921-88-2	chlorpyrifos	**74**	**74**	57	**66**
31	72-54-8	DDD, 4,4'- isomer	**75**	**75**	**66**	36
32	72-55-9	DDE, 4,4'- isomer	**82**	**82**	**82**	61
34	50-29-3	DDT, 4,4'- isomer	**66**	**69**	**70**	34
39	60-57-1	dieldrin	**71**	**71**	**78**	30
55	76-44-8	heptachlor	**76**	**76**	**81**	48
56	118-74-1	hexachlorobenzene	**73**	**73**	**74**	50
30	53-19-0	DDD, 2,4'- isomer	**70**	**70**	65	19
47	60-00-4	ethylenediamine-tetraacetic acid	9	56	**72**	**69**
3	120-82-1	1,2,4-trichlorobenzene	**69**	53	63	65
5	107-06-2	1,2-dichloroethane	60	**67**	56	84
13	15972-60-8	alachlor	55	50	53	**68**
16	1912-24-9	atrazine	50	46	46	**71**
26	470-90-6	chlorfenvinphos	**68**	43	50	33
33	789-02-6	DDT, 2,4'- isomer	54	63	**71**	13
37	75-09-2	dichloromethane	61	48	54	**80**
41	330-54-1	diuron	**67**	32	43	**78**
53	319-86-8	HCH, delta- isomer	51	54	**67**	12
57	87-68-3	hexachlorobutadiene	53	62	**68**	20
60	465-73-6	isodrin	58	**66**	61	15
61	34123-59-6	isoproturon	59	49	51	**76**
66	72-43-5	methoxychlor	34	58	**80**	27
67	51218-45-2	metolachlor	42	22	25	**67**
68	91-20-3	naphthalene	64	26	31	**74**
80	56-23-5	tetrachloromethane	46	41	41	**75**

81	108-88-3	toluene	45	44	48	**77**
82	79-01-6	trichloroethene	32	37	37	**73**
83	67-66-3	trichloromethane	63	47	49	**79**
84	1582-09-8	trifluralin	65	**68**	58	35

Table 25 – Priority substances identified by COMMPS, Desirability, Utility and Dominance methods. Highlighted in bold are the ranks from 66 to 85 of the substances belonging to the COMMPS, Desirability, Utility and Dominance lists.

The ranking overlap of the different methods over the substances listed in Table 25 is also showed in Figure 26.

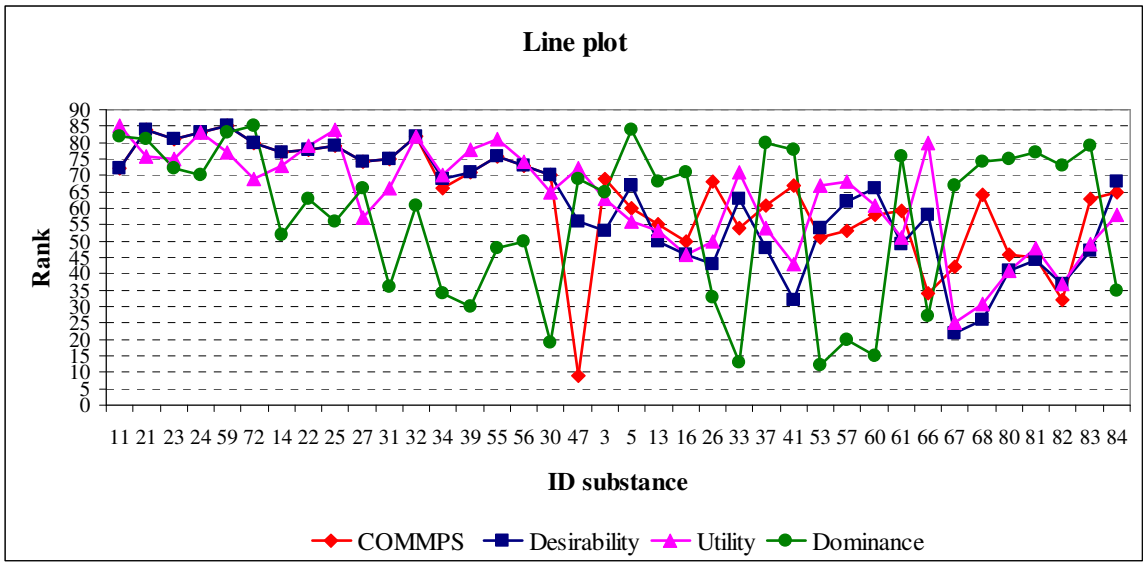

Figure 26 – Line plot of the substances identified as priority substances by at least one of the method applied and sorted according to the overlap degree among the methods.

6.4.5 Hasse diagram results

The Hasse diagram based on the six criteria, the 90 percentile of the observed concentration in the waters of the members states of the EU, the EU-level median, the EU-level arithmetic mean, EFS_d, EFS_i and EFS_h is shown in Figure 27.

The numbers correspond to the substances as listed in Table 18. The diagram might look complicated, but valuable information on the data set can easily be extracted. It is arranged in such a way that it has 6 levels of priority and there are 27 substances in the top level and 2 substances in the lowest level.

The substances located in the highest level (level 6) are the substances of highest risk. The full list of these 27 priority substances is provided in Table 26.

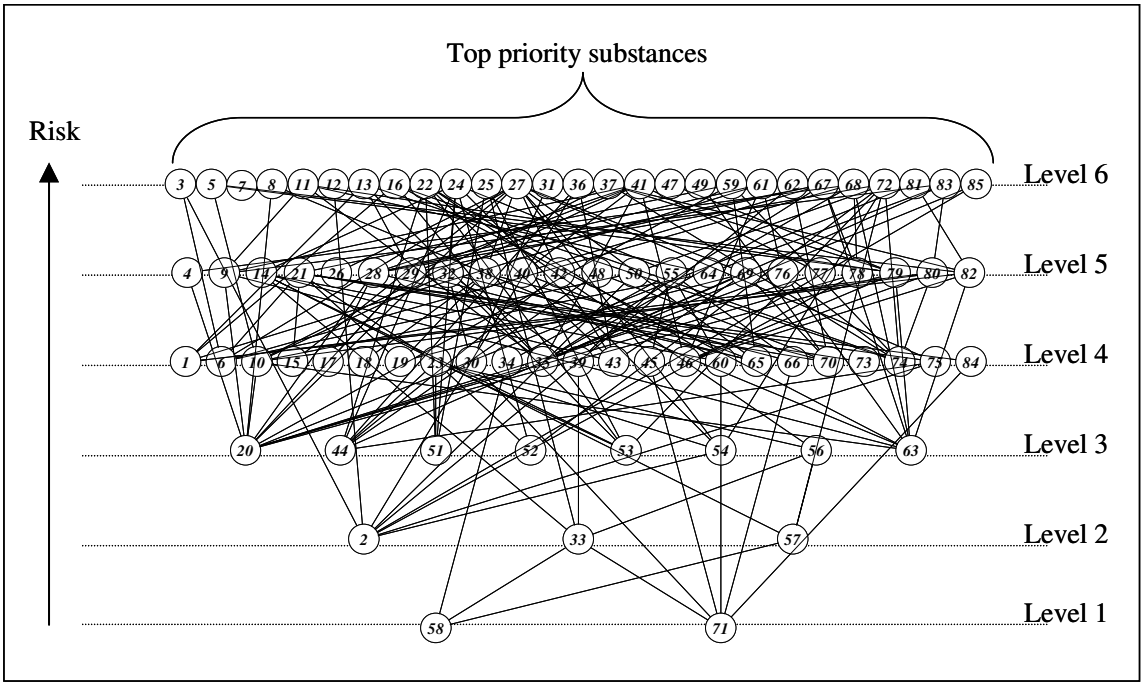

Figure 27 – Hasse diagram for the 85 substances from the COMMPS procedure. The criteria used are the 90 percentile of the observed concentration in the waters, the EU-level median, the EU-level arithmetic mean, EFS_d, EFS_i and EFS_h.

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
3	120-82-1	1,2,4-trichlorobenzene	0.157	0.012	0.053	2.43	2	1.8
5	107-06-2	1,2-dichloroethane	8.243	0.847	3.021	1.93	0	2
7	541-73-1	1,3-dichlorobenzene	7.100	0.012	1.194	1.8	1	0
8	106-46-7	1,4-dichlorobenzene	0.422	0.098	0.139	1.93	1	0
11	121-73-3	3-chloronitrobenzene	37.500	18.760	18.760	2.78	0	1.4
12	83-32-9	acenaphthene	0.418	0.010	0.062	2.63	1	0
13	15972-60-8	alachlor	0.150	0.053	0.079	3.57	0	1.8
16	1912-24-9	atrazine	0.334	0.052	0.330	2.94	0	1.8
22	50-32-8	benzo-a-pyrene	0.027	0.007	0.012	4.5	3	2
24	191-24-2	benzo-g,h,i-perylene	0.047	0.008	0.017	5	3	1.8
25	207-08-9	benzo-k-fluoroanthene	0.025	0.004	0.009	4.9	3	2
27	2921-88-2	chlorpyrifos	0.128	0.020	0.035	5	2	0
31	72-54-8	DDD, 4,4'- isomer	0.048	0.002	0.009	5	3	0
36	333-41-5	diazinon	0.032	0.008	0.040	4.62	1	0
37	75-09-2	dichloromethane	10.250	0.933	2.133	2.11	0	1.8
41	330-54-1	diuron	1.076	0.235	0.561	3.79	0	1.2
47	60-00-4	ethylenediamine-tetraacetic acid	45.590	9.822	17.630	1.71	0	0
49	55-38-9	fenthion	0.015	0.010	0.039	4.46	1	0
59	193-39-5	indeno(1,2,3-cd)pyrene	0.094	0.034	0.036	4.29	3	2
61	34123-59-6	isoproturon	0.370	0.115	0.162	3.23	0	1.8
62	121-75-5	malathion	0.040	0.010	0.041	4.07	1	0
67	51218-45-2	metolachlor	0.313	0.065	0.123	3.36	1	0
68	91-20-3	naphthalene	1.683	0.065	0.267	2.59	2	0

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
72	87-86-5	pentachlorophenol	0.135	0.071	0.451	3.34	3	1.8
81	108-88-3	toluene	10.796	0.418	2.549	1.5	0	1.8
83	67-66-3	trichloromethane	1.173	0.281	0.793	2.93	0	1.8
85	95-47-6	xylene, o- isomer	0.146	0.127	0.112	2.5	1	0

Table 26 – Top priority substances.

To have a clear understanding of how to interpret the diagram a few cases are explained. As mentioned above the diagram is a kind of dominance diagram, where if an order or cover relation exists then a line between the corresponding pairs of substances is drawn, the substances belonging to an order relation are "comparable". A set of comparable elements is called a chain. In the Hasse diagram of Figure 27 one of the chains is the one of indeno(1,2,3-cd)pyrene (ID: 59; Level 6), benzo-a-anthracene (ID: 21; Level 5), benzo-b-fluoroanthene (ID: 23; Level 4), hexachlorobenzene (ID: 56; Level 3), hexachlorobutadiene (ID: 57; Level 2), hexachloroethane (ID: 58; Level 1). Accordingly, indeno(1,2,3-cd)pyrene is associated with a higher risk than benzo-a-anthracene, which has a higher risk than benzo-b-fluoroanthene and so on up to hexachloroethane. The increasing risk caused by these substances can be easily identified from the data of Table 27. In this case a total or full order is identified: no conflict among the criteria is identified for these 6 substances.

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
59	193-39-5	indeno(1,2,3-cd)pyrene	0.094	0.034	0.036	4.29	3	2
21	56-55-3	benzo-a-anthracene	0.083	0.021	0.028	4.29	3	2
23	205-99-2	benzo-b-fluoroanthene	0.048	0.009	0.018	4.29	3	2
56	118-74-1	hexachlorobenzene	0.010	0.005	0.010	4.29	3	2
57	87-68-3	hexachlorobutadiene	0.007	0.005	0.009	3.07	3	1.8
58	67-72-1	hexachloroethane	0.002	0.000	0.001	2.87	2	1.2

Table 27 – Data of the chain example.

As mentioned above, the Hasse diagram is a partial ranking method which also detects incomparabilities, i.e. contradictions or conflicts among the criteria.

Incomparable substances are substances that cannot be directly ranked one above the other because of contradictions among the criteria used for the analysis, which means that they exhibit different patterns of risk. These incomparable substances are not connected by a line and are located at the same geometrical height and as high as possible in the diagram. Therefore all the top priority substances are incomparable. As an example, it can be noticed from Table 26 that 1,2,4-trichlorobenzene (ID: 3) is incomparable with 1,2-dichloroethane (ID: 5), since the former causes a higher direct and indirect effects than the latter but is characterised by a lower exposure than the latter. Thus, in this case a contradiction among the criteria exists and therefore the two substances are considered and ranked at the same level of priority but for different reasons. Another simple example is the one provided by 3-chloronitrobenzene (ID: 11) and fluoroanthene (ID: 25): the former is characterized by a very high exposure

but causes relatively low effects, while the latter is risky for the effects caused rather then for the exposure.

In the case of a rather complex diagram, such as Figure 27, a useful graph to analyse the results of the partial ranking is the one of Figure 28 describing the level structure. This is a bar chart graph representing the number of substances in the different levels of risk identified.

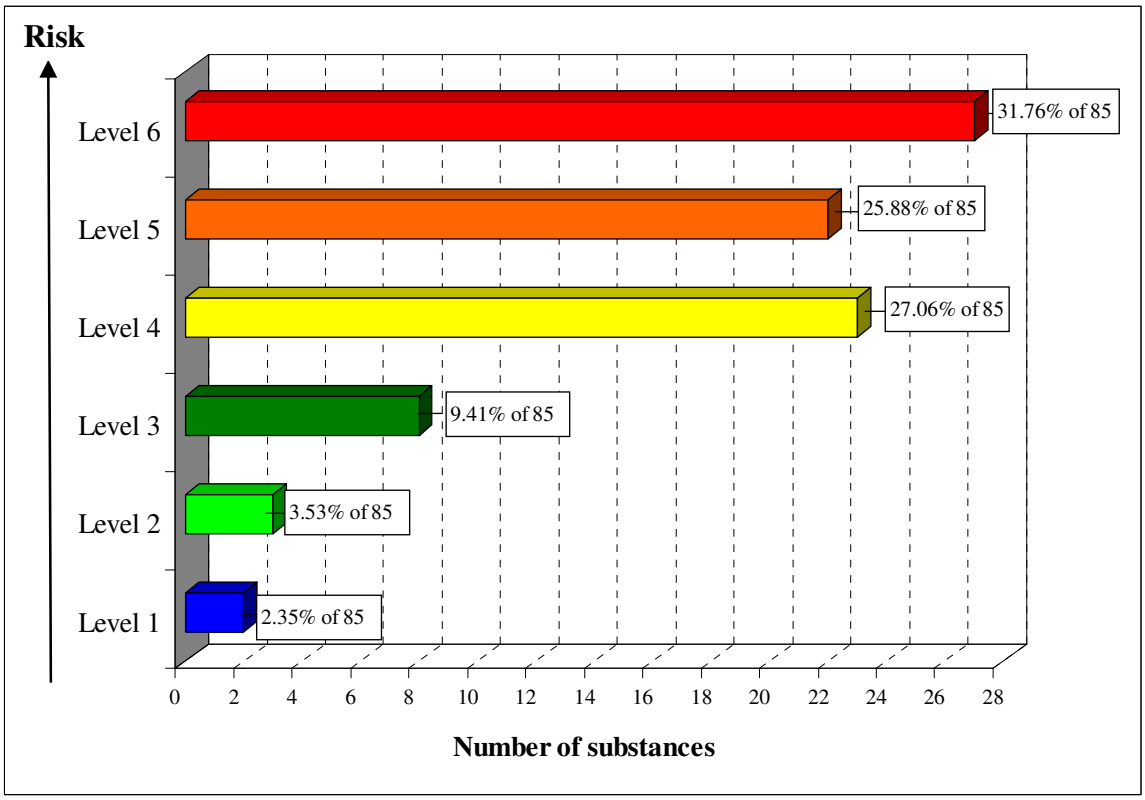

Figure 28 – Level structure graph of the Hasse diagram.

6.4.6 Comparison COMMPS scheme with Hasse diagram results

To compare the results provided by the Hasse diagram ranking with the ones derived by COMMPS procedure the attention should focus on the top 20 substances selected by the COMMPS ranking scheme. In Figure 29 the 20 substances selected by COMMPS are highlighted in orange in the Hasse diagram.

It can be noticed that 10 of the top 20 substances from the COMMPS scheme are also ranked within the top priority substances of the Hasse diagram. Thus, the choice of these substances is very consistent. The critical issue might be the other substances selected by the Hasse diagram technique but not by COMMPS scheme. These substances are listed in Table 28.

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
5	107-06-2	1,2-dichloroethane	8.243	0.847	3.021	1.93	0	2

ID	CAS	Compound	90-perc. Conc. [µg/l]	Median [µg/l]	Arit. Mean [µg/l]	EFS_d	EFS_i	EFS_h
7	541-73-1	1,3-dichlorobenzene	7.100	0.012	1.194	1.8	1	0
8	106-46-7	1,4-dichlorobenzene	0.422	0.098	0.139	1.93	1	0
12	83-32-9	acenaphthene	0.418	0.010	0.062	2.63	1	0
13	15972-60-8	alachlor	0.150	0.053	0.079	3.57	0	1.8
16	1912-24-9	atrazine	0.334	0.052	0.330	2.94	0	1.8
36	333-41-5	diazinon	0.032	0.008	0.040	4.62	1	0
37	75-09-2	dichloromethane	10.250	0.933	2.133	2.11	0	1.8
47	60-00-4	ethylenediamine-tetraacetic acid	45.590	9.822	17.630	1.71	0	0
49	55-38-9	fenthion	0.015	0.010	0.039	4.46	1	0
61	34123-59-6	isoproturon	0.370	0.115	0.162	3.23	0	1.8
62	121-75-5	malathion	0.040	0.010	0.041	4.07	1	0
67	51218-45-2	metolachlor	0.313	0.065	0.123	3.36	1	0
68	91-20-3	naphthalene	1.683	0.065	0.267	2.59	2	0
81	108-88-3	toluene	10.796	0.418	2.549	1.5	0	1.8
83	67-66-3	trichloromethane	1.173	0.281	0.793	2.93	0	1.8
85	95-47-6	xylene, o- isomer	0.146	0.127	0.112	2.5	1	0

Table 28 – Substances selected by the Hasse Diagram but not by COMMPS.

As an example a comment can be made on isoproturon (ID: 61) selected by HD technique and not by COMMPS, and on hexachlorobenzene (ID: 56) selected by COMMPS but not by HD technique.

For hexachlorobenzene the input from the functional relationship appears to be significant. From the data of Table 1, it can be noticed that the concentration found in the environment (90 percentile, median and arithmetic mean) are more critical for isoproturon and less for hexachlorobenzene, which has more critical direct, indirect and human effects. Because of this different behaviour, i.e. the contradiction among the criteria, the two substances are considered incomparable in the Hasse diagram.

It can also be noticed that, despite that, hexachlorobenzene is ranked by COMMPS on position 75, while isoproturon on position 59. In addition, from the Hasse diagram it can be noticed that hexachlorobenzene (ID: 56) is located on Level 3 and it belongs to the chain: indeno(1,2,3-cd)pyrene (ID: 59) – benzo-a-anthracene (ID: 21) – benzo-b-fluoroanthene (ID: 23) – hexachlorobenzene (ID: 56) – DDT, 2,4'- isomer (ID: 33) – hexachloroethane (ID: 58). Thus, a consensus among the criteria is identified in evaluating indeno(1,2,3-cd)pyrene (ID: 59) more risky than benzo-a-anthracene (ID: 21), which is more risky than benzo-b-fluoroanthene (ID: 23), the latter being more risky than hexachlorobenzene (ID: 56) and so on up to the less risky hexachloroethane (ID: 58).

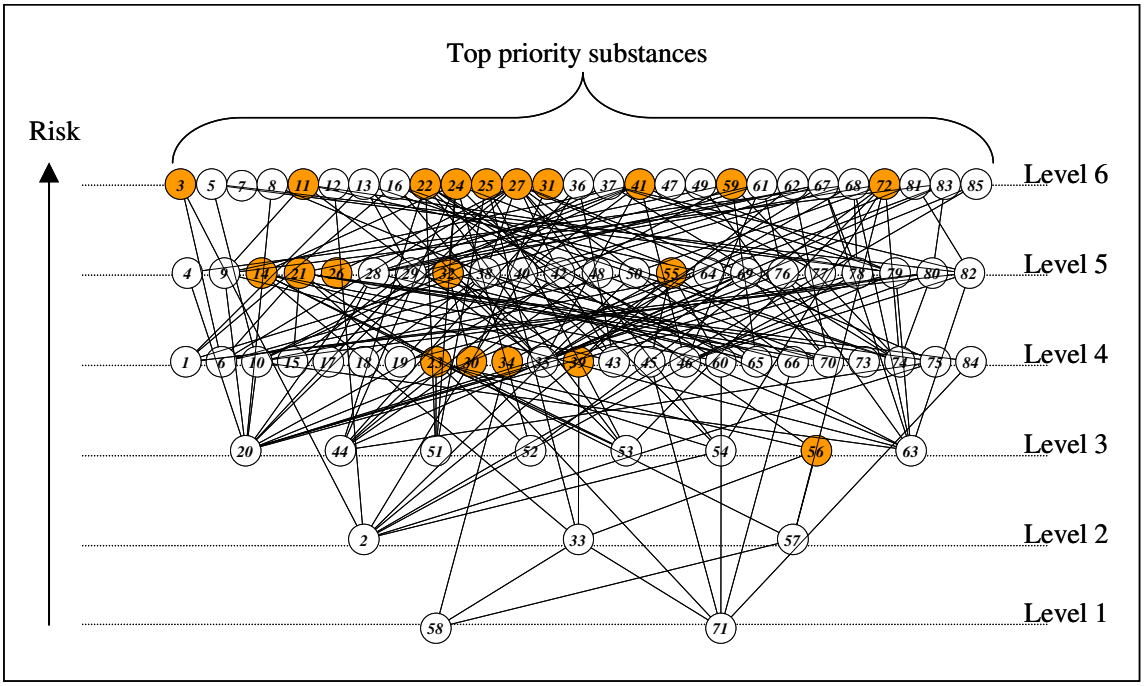

Figure 29 – Hasse diagram for the 85 substances from the COMMPS procedure. The criteria used are the 90 percentile of the observed concentration in the waters, the EU-level median, the EU-level arithmetic mean, EFS_d, EFS_i and EFS_h. The 20 substances selected by COMMPS are highlighted in orange.

Another comment can be related to naphthalene (ID: 68) selected by the HD technique and not by COMMPS, and to DDT, 4,4'- isomer (ID: 34) selected by COMMPS but not by HD technique. Again, for DDT, 4,4'- isomer the input from the functional relationship appears to play a significant role. From the data of Table 18, it can be noticed that the concentration found in the environment (90 percentile, median and arithmetic mean) are more critical for naphthalene and less for DDT, 4,4'- isomer, which has more critical direct and human effects (the indirect effect is the same). Because of this the contradiction among the criteria, the two substances are considered incomparable in the Hasse diagram.

It can also be noticed that, despite this incomparability, DDT, 4,4'- isomer is ranked by COMMPS on a higher position than naphthalene. In addition, from the Hasse diagram it can be noticed that DDT, 4,4'- isomer (ID: 34) is located on Level 4 and it belongs to the chain: benzo-g,h,i-perylene (ID: 24) – heptachlor (ID: 55) – DDT, 4,4'- isomer (ID: 34) – hexachloroethane (ID: 58). Thus, benzo-g,h,i-perylene (ID: 24) is consensually evaluated more risky than heptachlor (ID: 55), which is consensually more risky than DDT, 4,4'- isomer (ID: 34), the latter being consensually more risky than hexachloroethane (ID: 58).

6.4.7 Comparison among the different ranking methods

The comparison of the Hasse diagram results with all the other scoring methods is provided in Table 29, where the substances selected by each method are listed and sorted according to the degree of overlap among the methods.

ID	CAS	Compound	COMMPS Rank	Desirability Rank	Utility Rank	Dominance Rank	HDT Rank
11	121-73-3	3-chloronitrobenzene	x	x	x	x	x
24	191-24-2	benzo-g,h,i-perylene	x	x	x	x	x
72	87-86-5	pentachlorophenol	x	x	x	x	x
21	56-55-3	benzo-a-anthracene	x	x	x	x	
22	50-32-8	benzo-a-pyrene	x	x	x		x
23	205-99-2	benzo-b-fluoroanthene	x	x	x	x	
25	207-08-9	benzo-k-fluoroanthene	x	x	x		x
27	2921-88-2	chlorpyrifos	x	x		x	x
31	72-54-8	DDD, 4,4'- isomer	x	x	x		x
59	193-39-5	indeno(1,2,3-cd)pyrene	x	x	x	x	
5	107-06-2	1,2-dichloroethane		x		x	x
14	309-00-2	aldrin	x	x	x		
32	72-55-9	DDE, 4,4'- isomer	x	x	x		
34	50-29-3	DDT, 4,4'- isomer	x	x	x		
39	60-57-1	dieldrin	x	x	x		
41	330-54-1	diuron	x			x	x
47	60-00-4	ethylenediamine-tetraacetic acid			x	x	x
55	76-44-8	heptachlor	x	x	x		
56	118-74-1	hexachlorobenzene	x	x	x		
3	120-82-1	1,2,4-trichlorobenzene	x				x
13	15972-60-8	alachlor				x	x
16	1912-24-9	atrazine				x	x
30	53-19-0	DDD, 2,4'- isomer	x	x			
37	75-09-2	dichloromethane				x	x
61	34123-59-6	isoproturon				x	x
67	51218-45-2	metolachlor				x	x
68	91-20-3	naphthalene				x	x
81	108-88-3	toluene				x	x
83	67-66-3	trichloromethane				x	x
7	541-73-1	1,3-dichlorobenzene					x
8	106-46-7	1,4-dichlorobenzene					x
12	83-32-9	acenaphthene					x
26	470-90-6	chlorfenvinphos	x				
33	789-02-6	DDT, 2,4'- isomer			x		
36	333-41-5	diazinon					x
49	55-38-9	fenthion					x
53	319-86-8	HCH, delta- isomer			x		
57	87-68-3	hexachlorobutadiene			x		
59	193-39-5	indeno(1,2,3-cd)pyrene					x
60	465-73-6	isodrin		x			
62	121-75-5	malathion					x
66	72-43-5	methoxychlor			x		
80	56-23-5	tetrachloromethane				x	
82	79-01-6	trichloroethene				x	

ID	CAS	Compound	COMMPS Rank	Desirability Rank	Utility Rank	Dominance Rank	HDT Rank
84	1582-09-8	trifluralin		**x**			
85	95-47-6	xylene, o- isomer					**x**

Table 29 – Priority substances identified by COMMPS, Desirability, Utility, Dominance and Hasse diagram methods.

It can be highlighted that the Hasse diagram technique identified a higher number of priority substances than the COMMPS procedure (27 substances in the top priority level). In addition the results derived by the scoring methods and in particular by COMMPS, Desirability and Utility methods are much more similar than those derived by the Dominance and partial ranking method, being these latter based on a pair wise comparison of the behaviour of the substances against the considered criteria.

6.5 Conclusions

In the present study different ranking methods have been applied to the same data, the aim being to compare the results provided by different priority setting methodologies and to highlight how the results might be different depending on the algorithm used for the ranking.

To correctly apply ranking methods it is important to identify all additional and useful external information. Some arbitrariness related to the choice of the criteria is foreseen for all the methods. The choice of criteria is generally based on key parameters from risk assessment schemes, environmental fate and effect models, which have to be agreed by the decision makers involved in the priority setting procedure.

In the case of the Hasse diagram technique, the selection of the criteria is the main and only contribution of subjectivity. For the other scoring methods another level of subjectivity is added related to the choice of the transformation functions selected to transform values of the criteria to the same scale. Sometimes another level of arbitrariness is then added, by applying a weighting scheme to make some criteria play a more important role in the ranking than others. The choice of the weighting scheme is generally considered more subjective than the choice of criteria.

The Hasse diagram technique does not require any transformation function and the criteria are not weighted. In the above study, no weighting scheme was adopted for the scoring methods, i.e. the criteria were equally weighted, to allow a more precise and direct comparison with the Hasse diagram technique.

The analyzed ranking methods provided different ranking results. An agreement was achieved for the most risky substances, while several disagreements were identified for substances with a more controversial behaviour. These results highlight the importance to select the most appropriate method for prioritization and the convenience to apply sophisticated techniques, like the Hasse Diagram technique, to identify conflicting criteria, which are commonly encountered, incomparable substances as well as sequences of comparable substances. Also a good strategy is to apply several ranking methods to increase the confidence on the obtained results.

In those cases characterised by a huge number of substances to be prioritised a tiered approach could also be used, by applying in the first phase a scoring method to derive a preliminary rough ranking of the substances and in a second phase a partial ranking method to derive a more precise and detailed ranking which preserves useful information that would otherwise be lost.

Disclaimer

Any views and conclusions expressed in this report are those of the authors alone and do not represent an official position of the European Commission.

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APPENDICES

APPENDIX I: PRIORITY RANKING LIST

P: Ultimate persistence; B: BCF; T: ChV (mg/L);H_UTI: PBT hazard score defined by utility function; H_DOM: PBT hazard score defined by dominance function; H_DES: PBT hazard score defined by desirability function. The chemicals are ranked according to their decreasing PBT hazard score defined by utility function (H_UTI).

ID	CAS	P	B	T	H_UTI	H_DOM	H_DES
1	001506-02-1	4	4	4	1.000	1	0.897
2	001222-05-5	4	4	4	1.000	1	0.897
37	039489-75-3	4	4	4	1.000	1	0.897
58	025637-99-4	4	4	4	1.000	1	0.897
59	000118-74-1	4	4	4	1.000	1	0.897
76	000133-49-3	4	4	4	1.000	1	0.897
78	000128-69-8	4	4	4	1.000	1	0.897
114	000608-71-9	4	4	4	1.000	1	0.897
117	000119-47-1	4	4	4	1.000	1	0.897
38	000050-29-3	4	4	3.5	1.000	0.944	0.784
14	000497-39-2	3	4	4	1.000	0.889	0.770
19	005208-93-5	3	4	4	1.000	0.889	0.770
39	004904-61-4	3	4	4	1.000	0.889	0.770
40	000294-62-2	3	4	4	1.000	0.889	0.770
43	026898-17-9	3	4	4	1.000	0.889	0.770
66	004979-32-2	3	4	4	1.000	0.889	0.770
70	084852-15-3	3	4	4	1.000	0.889	0.770
86	026140-60-3	3	4	4	1.000	0.889	0.770
94	000603-35-0	3	4	4	1.000	0.889	0.770
104	000469-61-4	3	4	4	1.000	0.889	0.770
124	000541-02-6	3	4	4	1.000	0.889	0.770
125	038640-62-9	3	4	4	1.000	0.889	0.770
20	005124-30-1	3	4	3.5	1.000	0.833	0.635
21	002392-48-5	4	2	4	1.000	0.778	0.836
75	000556-67-2	3	3	4	1.000	0.778	0.707
108	000077-47-4	4	3	3	1.000	0.778	0.668
44	000115-32-2	4	2	3.5	1.000	0.722	0.721
7	005468-75-7	4	1	4	1.000	0.667	0.764
8	005567-15-7	4	1	4	1.000	0.667	0.764
10	000088-06-2	4	1	4	1.000	0.667	0.764
33	001103-38-4	4	1	4	1.000	0.667	0.764
60	000087-68-3	4	1	4	1.000	0.667	0.764
67	014861-17-7	4	1	4	1.000	0.667	0.764
5	000118-82-1	4	1	3.5	1.000	0.611	0.625
6	005102-83-0	4	1	3.5	1.000	0.611	0.625
9	003520-72-7	4	1	3.5	1.000	0.611	0.625
42	031565-23-8	4	1	3.5	1.000	0.611	0.625
47	012578-12-0	4	1	3.5	1.000	0.611	0.625
48	001163-19-5	4	1	3.5	1.000	0.611	0.625
49	032536-52-0	4	1	3.5	1.000	0.611	0.625

ID	CAS	P	B	T	H_UTI	H_DOM	H_DES
74	002082-79-3	4	1	3.5	1.000	0.611	0.625
77	006683-19-8	4	1	3.5	1.000	0.611	0.625
100	031570-04-4	4	1	3.5	1.000	0.611	0.625
101	032588-76-4	4	1	3.5	1.000	0.611	0.625
113	000096-69-5	4	1	3.5	1.000	0.611	0.625
115	013560-89-9	4	1	3.5	1.000	0.611	0.625
116	026040-51-7	4	1	3.5	1.000	0.611	0.625
3	000087-61-6	4	1	3	1.000	0.556	0.542
4	000120-82-1	4	1	3	1.000	0.556	0.542
11	000121-14-2	3	1	4	1.000	0.556	0.598
12	000096-76-4	3	1	4	1.000	0.556	0.598
13	000128-39-2	3	1	4	1.000	0.556	0.598
16	003542-36-7	3	1	4	1.000	0.556	0.598
22	050849-47-3	3	1	4	1.000	0.556	0.598
25	005216-25-1	4	1	3	1.000	0.556	0.542
55	027193-86-8	3	1	4	1.000	0.556	0.598
56	000115-29-7	4	1	3	1.000	0.556	0.542
64	051338-27-3	4	1	3	1.000	0.556	0.542
65	006386-38-5	3	1	4	1.000	0.556	0.598
68	001836-75-5	4	1	3	1.000	0.556	0.542
69	025154-52-3	3	1	4	1.000	0.556	0.598
73	001843-05-6	3	1	4	1.000	0.556	0.598
79	061788-44-1	3	1	4	1.000	0.556	0.598
90	000117-08-8	4	1	3	1.000	0.556	0.542
91	000078-00-2	3	1	4	1.000	0.556	0.598
95	000056-35-9	1	4	3	1.000	0.556	0.465
105	000058-89-9	4	1	3	1.000	0.556	0.542
109	001217-08-9	3	1	4	1.000	0.556	0.598
120	051000-52-3	3	1	4	1.000	0.556	0.598
121	000128-37-0	3	1	4	1.000	0.556	0.598
46	025550-98-5	3	1	3.5	0.618	0.5	0.427
96	000693-36-7	3	1	3.5	0.618	0.5	0.427
99	027107-89-7	3	1	3.5	0.618	0.5	0.427
119	026272-76-4	3	1	3.5	0.618	0.5	0.427
32	000120-12-7	3	1	3	0.519	0.445	0.332
41	011138-60-6	2	1	4	1.000	0.445	0.497
45	001762-27-2	3	1	3	0.519	0.445	0.332
97	000793-24-8	3	1	3	0.519	0.445	0.332
98	025103-58-6	2	1	4	1.000	0.445	0.497
106	000091-57-6	3	1	3	0.519	0.445	0.332
123	000095-76-1	3	1	3	0.519	0.445	0.332
15	015571-58-1	2	1	3.5	0.519	0.389	0.320
89	003590-84-9	2	1	3.5	0.519	0.389	0.320
72	000095-31-8	3	1	2	0.394	0.334	0.288
92	000075-74-1	3	1	2	0.394	0.334	0.288
122	000330-54-1	3	1	2	0.394	0.334	0.288
88	001461-25-2	1	1	3.5	0.449	0.278	0.306

APPENDIX II: PARTIAL RANKING ASSIGNEMENTS

Potential PBT substances	PBT hazard level	PBT trend
{1;2;37;58;59;76;78;114;117}	7	P B T
{14;19;39;40;43;66;70;86;94;104;124;125}	6	P B T
{21}	6	P B T
{38}	6	P B T
{7;8;10;33;60;67}	5	P B T
{20}	5	P B T
{44}	5	P B T
{75}	5	P B T
{108}	5	P B T
{5;6;9;42;47;48;49;74;77;100;101;113;115;116}	4	P B T
{11;12;13;16;22;55;65;69;73;79;91;109;120;121}	4	P B T
{95}	4	P B T
{3;4;25;56;64;68;90;105}	3	P B T
{41;98}	3	P B T
{46;96;99;119}	3	P B T
{15;89}	2	P B T
{32;45;97;106;123}	2	P B T
{72;92;122}	1	P B T
{88}	1	P B T

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Title: A Set of Case Studies to Illustrate the Applicability of DART (Decision Analysis by Ranking Techniques) in the Ranking of Chemicals

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Abstract

This report is based on exploratory research carried out during 2007 and 2008 within the JRC's Institute for Health & Consumer Protection. The research focused on the problem of ranking chemicals according to their environmental and toxicological concern, and aimed to develop a better understanding of how to apply such approaches in the implementation of chemicals legislation, such as REACH and the Water Framework Directive.

A number of limitations were identified in existing approaches for the prioritisation of chemicals. For example, the traditional EU tool, EURAM, was difficult to apply in a consistent way due to the fact that many of the data inputs needed were often missing, which meant that high priority was often given to data-poor chemicals, rather than chemicals that were inherently hazardous or likely to cause a significant risk. This project aimed to address limitations such as this by encoding novel ranking methods into a new user-friendly software tool, and by investigating the applicability of the tool in a number of case studies. The tool developed in this project, called DART (Decision Analysis by Ranking Techniques), is made freely downloadable from the JRC website.

The applicability of DART tool is illustrated through a set of case studies. The first case study aims to summarise and illustrate different ways in which chemometric ranking methods could be used to supplement the use of QSAR methods in the development of chemical categories. The second case study illustrates how ranking methods could be used to supplement the use of QSAR methods in the context of toxicological assessments of potential persistent, bioaccumulative and toxic (PBT) substances. Finally, the third case study, aims to investigate the compatibility of established and novel ranking approaches with the risk assessment paradigm, in which hazard and exposure assessments are integrated into a characterisation of risk. These case studies illustrate some potential applications of ranking techniques in the regulatory assessment of chemicals.

The mission of the JRC is to provide customer-driven scientific and technical support for the conception, development, implementation and monitoring of EU policies. As a service of the European Commission, the JRC functions as a reference centre of science and technology for the Union. Close to the policy-making process, it serves the common interest of the Member States, while being independent of special interests, whether private or national.