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Evaluation of EU Risk Assessments Existing Chemicals (EC Regulation 793/93)

C.W.M. Bodar, F. Berthault[1], J.H.M. de Bruijn[1], C.J. van Leeuwen[2], M.E.J. Pronk and T.G. Vermeire

[1] European Chemicals Bureau JRC, Ispra, Italy
[2] Institute for Health and Consumer Protection, Ispra, Italy

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RIVM, P.O. Box 1, 3720 BA Bilthoven, telephone: 31 - 30 - 274 91 11; telefax: 31 - 30 - 274 29 71

Abstract

An evaluation was performed on the first group (41) of completed risk assessments for chemicals of the EU priority lists (Existing Chemicals; EC Regulation 793/93). The evaluation focussed on the conclusions of the risk assessments. The EU risk assessment process detected a high number of substances of concern. Furthermore priority chemicals may pose (potential) risks to the whole range of protection goals of the risk assessment. The predictability of the risk assessments for priority chemicals was investigated. Our *a priori* knowledge on possible risks of priority chemicals is found to be poor, especially for consumers. Both for environment and human health the (potential) risks were linked with a broad spectrum of use patterns. It is concluded that no industry category can in advance be excluded from performing risk assessments. For a great number of chemicals, additional testing was found to be needed to finalise the risk assessment. This evokes questions about the completeness of the current base-set, but also about the suitability of some of the submitted human health tests that should initially fulfil the base-set needs. The results of this evaluation are useful for future discussions on risk assessment processes for chemicals.

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Samenvatting

Vanaf 1993 is de EG-Verordening 793/93 van kracht die zich richt op de risico´s van 'bestaande stoffen'. Sindsdien worden er voor deze stoffen, de zogenaamde High Production Volume Chemicals in het bijzonder, EU-risicobeoordelingen gemaakt.
De inhaalslag om op EU-niveau de risico´s van bestaande stoffen te beoordelen blijkt een zeer intensief en tijdrovend proces te zijn. De vraag is echter wat levert het nu allemaal op? Het RIVM, in samenwerking met het Europees Chemicaliën Bureau te Ispra (It), heeft een evaluatie-onderzoek gedaan naar de 'overall' uitkomsten van het werk tot nu toe. Deze groep van afgeronde risicobeoordelingsrapporten (totaal 41 d.d. 1-1-2001) omvat diverse, economisch zeer belangrijke chemicaliën, zoals broombrandvertragers, ftalaten (weekmakers) en MTBE (antiklopmiddel in benzine).
Het EU risicobeoordelingsproces heeft een groot aantal stoffen naar voren gebracht die aanleiding geven tot zorg. Dit gold maar liefst voor 34 van de 41 beoordeelde chemicaliën. Bovendien beperkten de risico's zich niet tot één van de onderzochte beschermingsdoelen (milieu, consument, algemene volksgezondheid en werknemer). Op alle terreinen kwamen potentiële risico's aan het licht: het voordeel van een integrale beoordeling van mens en milieu.
Stoffen worden geselecteerd voor een EU risicobeoordeling (prioritering), omdat men op basis van o.a. nationale programma's verwacht dat de stof mogelijk risico's vormt voor milieu, consument, werknemer en/of algemene volksgezondheid. De vraag is nu of de uitkomst van de risicobeoordeling altijd strookt met de verwachte risico's van een stof. Een stof die bijvoorbeeld om milieu-redenen wordt beoordeeld, kan aan het eind van de risicoschatting ook tot zorg blijken te leiden voor consument of werknemer. Komen we nu veel van dit soort 'onverwachte' resultaten tegen? Dit blijkt inderdaad zo te zijn. Vooral bij de consument treden veel 'onderschattingen' op, d.w.z. dat we aanvankelijk geen enkel vermoeden hadden dat die stof wel eens een consumentenprobleem zou kunnen zijn. Stoffen komen blijkbaar in producten terecht waar ze totaal niet thuis horen. Onze kennis hierover is gering: een belangrijk signaal richting beleid.
Verder is gekeken of er een relatie bestaat tussen de potentiële risico´s van de stoffen en het type gebruik van de stof. Gaat het bijvoorbeeld vaak mis in de verf- of polymeerindustrie? Zo ja, dan zou je je daar in de toekomst speciaal op kunnen richten. Duidelijk werd echter dat de risico's gekoppeld zijn aan een zeer breed scala van gebruikscategorieën. Het lijkt erg moeilijk om op voorhand een gebruikscategorie uit te sluiten van het maken van een risicobeoordeling. Zelfs het gebruik van een stof als 'intermediair', een toepassing waarvan de risico´s minimaal worden geacht (gesloten systeem), geeft regelmatig reden tot zorg.
De industrie is wettelijk verplicht om een zogenaamde basis-set van gegevens aan te leveren voor een stof. Deze basis-set omvat een (minimale) hoeveelheid informatie over fysisch-chemische en (eco)toxicologische eigenschappen van die stof. Ondanks deze basis-set bleek dat voor veel stoffen aanvullende testen noodzakelijk waren om de risicoschatting goed te kunnen afronden. Bij milieu werden bijvoorbeeld vele aanvullende testen verricht met sediment- of bodemorganismen, omdat de basis-set alleen maar testen met waterorganismen omvat. Bij de risicoschatting voor de mens daarentegen bleken extra testen regelmatig noodzakelijk te zijn, omdat niet aan alle vereisten van basis-set werd voldaan (m.n. reproductie toxiciteit). Deze resultaten roepen vragen op over de juistheid en compleetheid van de huidige basis-set. Moet de basis-set voor bestaande stoffen niet worden uitgebreid?
Momenteel worden, zowel op nationaal als internationaal niveau, de lijnen uitgestippeld voor een nieuw stoffenbeleid (o.a. SOMS, White Paper). De resultaten van dit onderzoek blijken uiterst bruikbaar te zijn bij de voorbereidende discussies.

Summary

An evaluation was performed on the first group (41) of completed risk assessments for chemicals of the EU priority lists (Existing Chemicals; EC Regulation 793/93). The evaluation focussed on the conclusions of the risk assessments. Not so much on the results of each individual risk assessment, but particularly on the overall picture.
The EU risk assessment process detected a high number of substances of concern. For 34 out of 41 chemicals the risk assessment resulted in either a conclusion i) (more data needed) or iii) (risk reduction needed). These conclusions i) or iii) are not restricted to one particular endpoint (environment, man indirectly exposed via the environment, consumers or workers). Apparently, priority chemicals may pose (potential) risks to the whole range of protection goals of the risk assessment.
The predictability of the risk assessments for priority chemicals was investigated. If a chemical was selected for the priority list because of expected risks for a particular endpoint (e.g. environment), do we then always end up with the same endpoint being at risk? Or do we find a lot of unexpected results? A great number of 'underestimations' and 'overestimations' was found, particularly for consumers. This means that our *a priori* knowledge on possible risks of priority chemicals is poor. In this context the pros and cons of comprehensive versus targeted risk assessments were discussed.
It was further examined if the (potential) risks of the priority chemicals were associated with one or more use patterns of the chemicals. The outcome was that both for environment and human health the (potential) risks were linked with a broad spectrum of use patterns. One may conclude that no industry category can in advance be excluded from performing risk assessments. Even the use of chemicals as an intermediate, of which exposure is expected to be at a minimum (closed systems), frequently resulted in concern for priority chemicals.
The base-set (Annex VIIA), containing a number of physico-chemical and (eco)toxicological test results, is a minimum data requirement for HPVCs on the priority lists. Despite this base-set, for a great number of chemicals additional testing was found to be needed to finalise the risk assessment. For human health this mostly referred to additional testing in order to comply with one or more of the original base-set requirements, reproductive toxicity in particular. For environment the additional testing in most cases consisted of post base-set testing (sediment, soil or plant fumigation testing). These results evoke questions about the completeness of the current base-set, but also about the suitability of some of the submitted human health tests that should initially fulfil the base-set needs.
The results of this evaluation may be useful for future discussions on the risk assessment process for chemicals (e.g. the implementation of the EU White Paper).

1. Introduction

1.1 Background

Chemicals are integrated in all sections of our technical society. Opposed to the many (economical) benefits, there is the continuous awareness that chemicals may pose risks to environment and human health. Risk assessment and risk management are needed to control these potential risks of chemicals to man and environment. This holds especially for the so-called 'existing'[1] chemicals, i.e. those chemicals which were already on the market in the period before the legal submission of a basic profile on the potential hazards etc. of a chemical (notification system). In contrast to 'new' chemicals, 'existing' chemicals did not pass the sieve filtering out possibly dangerous substances as much as possible.
The concern regarding the potential risks of chemicals and in particular 'existing' chemicals, was already a policy priority in the late 1980's. The Council of the European Communities, in approving the Fourth Community Action Programme on the Environment (1987-1992), stated that one of the priority areas was the evaluation of the risks to the environment and human health posed by chemical substances. This Action Programme underlined the need for a legislative instrument, which would provide a comprehensive structure for the evaluation of the risks posed by existing chemicals. In particular, the Action Programme stated that such a legislative instrument "will establish a procedure for treating priority lists of chemicals for immediate attention, as well as setting out the means for gathering information, requiring testing and evaluating the risks to people and the environment". Consequently, the European Commission proposed a series of legal instruments, which were aimed at meeting the objectives outlined in the Action Programme. One of these instruments was the Existing Substances Regulation.
In 1993 the Council adopted Council Regulation (EEC) 793/93 or the Existing Substances Regulation (EEC, 1993), thereby introducing a comprehensive framework for the evaluation and control of 'existing' chemical substances. The Regulation was intended to complement the already existing rules governed by Council Directive 67/548/EEC for 'new' chemical substances. The Regulation 793/93 foresees that the evaluation and control of the risks posed by existing chemicals will be carried out in four steps: 1. Data collection; 2. Priority setting; 3. Risk assessment and 4. Risk reduction

The Regulation was initially concerned with the so-called High Production Volume Chemicals (HPVCs). HPVCs are those substances which have been imported or produced in quantities exceeding 1000 tonnes per year between March 23, 1990 and March 23, 1994.
Article 8 of the Regulation states that the Commission, in consultation with the Member States, will regularly draw up lists of priority substances which require immediate attention because of their potential effects to man or the environment. Since 1994, four such priority lists have been published.
Substances on priority lists must undergo an in-depth risk assessment covering the risks posed by the priority chemical to man (covering workers, consumers and man exposed via the environment) and the environment (covering the terrestrial, aquatic and atmospheric eco-systems and accumulation through the food chain). This risk assessment follows the framework set out in Commission Regulation (EC) 1488/94 and implemented in the detailed Technical Guidance Documents (TGD) on Risk Assessment for New and Existing

[1] In the EU an 'Existing' chemical substance is officially defined as any chemical substance listed in the European INventory of Existing Commercial Substances (EINECS), an inventory containing 100,195 substances.

Substances. The first draft of the risk assessment reports are written by the Member States which act as 'rapporteurs'.

The scope of the risk assessment covers emissions and consequent environmental impact and human exposures at each stage of the life-cycle of a chemical, from production, through processing, formulation and use, to recycling and disposal. Protection goals for the environment include the atmosphere, aquatic organisms, sediment dwelling organisms, soil-dwelling organisms, micro-organisms in waste water treatment plants, and mammals and birds exposed via accumulation up the food chain.

Exposure of humans from all relevant sources is considered, including exposures from consumer products, (e.g. solvents in paints during use, but also after use as volatiles leach into the air, migration from food contact materials, air freshener blocks slowly vaporizing in a house), through ambient air, food, and drinking water (man exposed via environment) and exposure at the workplace. Each exposure scenario is assessed individually, and where appropriate, an overall combined exposure is also estimated.

1.2 Evaluation

The work on risk assessments for HPVCs within the framework of EC Regulation 793/93 is running now for about six years. The progress of the program has been criticized heavily, especially by policymakers. This depends, however, on the way one looks at the process. If one is only interested in numbers of risk assessment reports (RARs) that are produced by the system this may be true to some extent. The UNCED Agenda 21 goal of hundreds of chemicals being addressed in a relatively short period of time is indeed still miles ahead (UN, 1992). But from another, more scientific angle, a lot has been achieved. Member States have been able to complete a considerable number of high quality RARs for a group of 'difficult' HPVCs. 'Difficult' as in many cases data rich chemicals were assessed with e.g. a wide dispersive use or initially controversial opinions about certain hazard characteristics (e.g. carcinogenicity). Furthermore the comprehensive and integrated risk assessments were carried out following transparent, harmonized guidelines (TGD) and all went through the same uniform reviewing process (EU Technical Meetings).

It is felt that the time is ripe now to use the batch of (nearly) finalized, uniform RARs for a general evaluation. Basic questions will be addressed like what the 'overall score' of the RARs is and to what extent additional testing was needed to complete the risk assessment. Important lessons, both for risk assessors and policy makers, may be learnt from this evaluation, especially with the view of the ongoing discussions on a new EU chemicals policy (White Paper, 2001) and the ICCA activities within the OECD. The evaluation will focus in essence on the conclusions of the risk assessments. It is felt that pure policy aspects of the EU-HPVC program are already being dealt with in other fora. The same is true for pure technical issues, namely in the TGD update working groups.

Each risk assessment ends up with one of the following conclusions for each of the various protection goals:

conclusion i: there is need for further information and/or testing

conclusion ii: there is at present no need for further information and/or testing or for risk reduction measures beyond those which are being applied

conclusion iii: there is a need for limiting the risks: risk reduction measures which are already being applied shall be taken into account

The conclusion iii) can be split up in a conclusion iiia) and iiib) in the human health part of the risk assessment. This is done for non-threshold carcinogens. Conclusion iiia) then indicates that for this type of chemicals risks are always expected because of intrinsic genotoxic properties, but that the exposure assessment (either for consumers, man indirectly exposed via the environment or workers) points to acceptable concentrations. Conclusion iiib) refers to the possibility that significant exposure to the compound may occur. In the underlying report only conclusions iiib) are reckoned among conclusions iii).
(It should be noted that the above-mentioned split up between conclusion iiia) and iiib) for non-threshold carcinogens is no longer practice in EU RARs).

Table 1. Finalized EU Risk assessment reports.

First Priority List (Published July, 1994)	Dimethyldioctadecylammonium chloride
Benzene, C10-13-alkyl derivs.	3,4-Dichloroaniline
2-(2-Methoxyethoxy)ethanol	Cyclohexane
2-(2-Butoxyethoxy)ethanol	Diphenyl ether, octabromo der.
Alkanes, C10-13 , Chloro-	Bis(pentabromophenyl)ether
Cumene	Methyl acetate
Acrylaldehyde	Aniline
Hydrogen fluoride	**Second Priority List** (Published September, 1995)
4,4'-Methylenedianiline	Diphenyl ether, pentabromo derivate
4-Chloro-2-Methyl Phenol	Dimethyl sulphate
1,4-Dichlorobenzene	1,4-Dioxane
Methacrylic acid	o-Anisidine
Acetonitrile	Nonylphenol (Phenol, 4-nonyl-, branched)
Acrylonitrile	1,2,4-Trichlorobenzene
Acrylamide	Hydrogen peroxide
Dibutyl phthalate	Methyloxirane
Methyl methacrylate	Toluene
Acrylic acid	Bis(2-ethylhexyl) phthalate
Naphthalene	Di-"isononyl" phthalate
Trichloroethylene	Di-"isodecyl" phthalate
But-2-yne-1,4-diol	**Third Priority List** (Published January, 1997)
Ethyl acetoacetate	Tert-butyl methyl ether

1.3 Research objectives

The evaluation will focus on the five main aspects listed below. The individual RARs (see Table 1) were checked on these points. The information was gathered by sending out a questionnaire to the rapporteurs. Although most information can be found in the RARs which are publicly available, certain aspects are not addressed in the reports (e.g. the reason why a chemical was originally put on the priority list). The questionnaire template is given in Appendix 1.

1. Endpoints at risk
(Questionnaire issue 5A)
An overall inventory will be made of the endpoints, i.e. environment, consumers, man indirectly exposed to environment or workplace, for which conclusion i), iii) or iiia/b) is

drawn. What is the 'overall score' of the group of finalized EU-RARs? Do we find a lot of conclusions i), iii) or iiia/b)? And, additionally, are e.g. consumers mostly at risk or is it the environment?

2. Difference between reason for P-list nomination and final results risk assessment
(Questionnaire issues 3 and 5A)
It will be investigated to what extent the reason(s) for putting a chemical on the P-list matches with the final outcomes of the risk assessment. Do we find a lot of 'unexpected' results? That is when at the end a chemical turns out to result in risks for (an)other endpoint(s) (environment, consumers or workers) than thought at the very beginning. If this happens to be true, we apparently have insufficient knowledge of potential risks of chemicals in our society.

3. Scope environmental risk (Industry and Use categories)
(Questionnaire issue 5B)
Several aspects will be analyzed to examine the scope of the RAR conclusions for environment (incl. man indirect). Which Industry Categories (IC) are mostly related to a final conclusion i) or iii) for environment. If particular IC's show to result in risks for various chemicals, extra attention should be paid to those in future.

4. Scope human health risk (Industry and Use categories)
(Questionnaire issues 5C and 5D)
Several aspects will be analyzed to examine the scope of the RAR conclusions for human health. Is the conclusion i) or iii(b)) for consumers related to specific consumer products? Is the conclusion i) or iii(b)) for workers related to specific Industry and Use Categories?

5. Additional testing
(Questionnaire issue 4)
For each HPV chemical on the P-list a base-set has to be submitted. This base-set contains information about a.o. important physicochemical, toxicological and ecotoxicological properties. Although this base-set literally forms the basis for the risk assessment, if needed, additional tests can be asked for during the process. It will be examined in how many cases the base-set turned out to be insufficient to complete the RAR. And what type of additional (eco)toxicity or fate tests have been carried out during the risk assessment process. Are for specific classes of chemicals additional tests (e.g. sediments) always asked for?
For the overview of additional testing both tests that were carried out during the RA process and tests that are required on the basis of a formal conclusion i) decision are taken into account. In a number of cases a base-set test has been repeated during the process due to e.g. technical shortcomings of the initial test. In our evaluation these tests are counted as 'additional'. The term 'additional' therefore refers to both base-set and post-base-set.

2. Results

2.1 General

All questionnaires that were sent out, were completed by the rapporteurs. The data were analyzed and the main results are presented in sections 2.2 to 2.6. All individual data can be found in Appendix 2. A number of issues in the questionnaires have not (yet) been elaborated in this evaluation.
It is emphasized that the analysis reflects the situation of spring 2001. Afterwards changes in the conclusions of the RARs may have occurred that have not been taken into account in this evaluation. Besides the outcomes of the questionnaires, also the then RARs were investigated (mainly for checking the types of additional testing in relation to a conclusion i).

2.2 Endpoints at risk

Figure 1 gives the overall conclusions of the finalized RARs. It shows that for seven EU-RARs a conclusion ii) for all endpoints was drawn. For the remaining 34 substances either a conclusion i) or iii) was drawn for one or more endpoints.

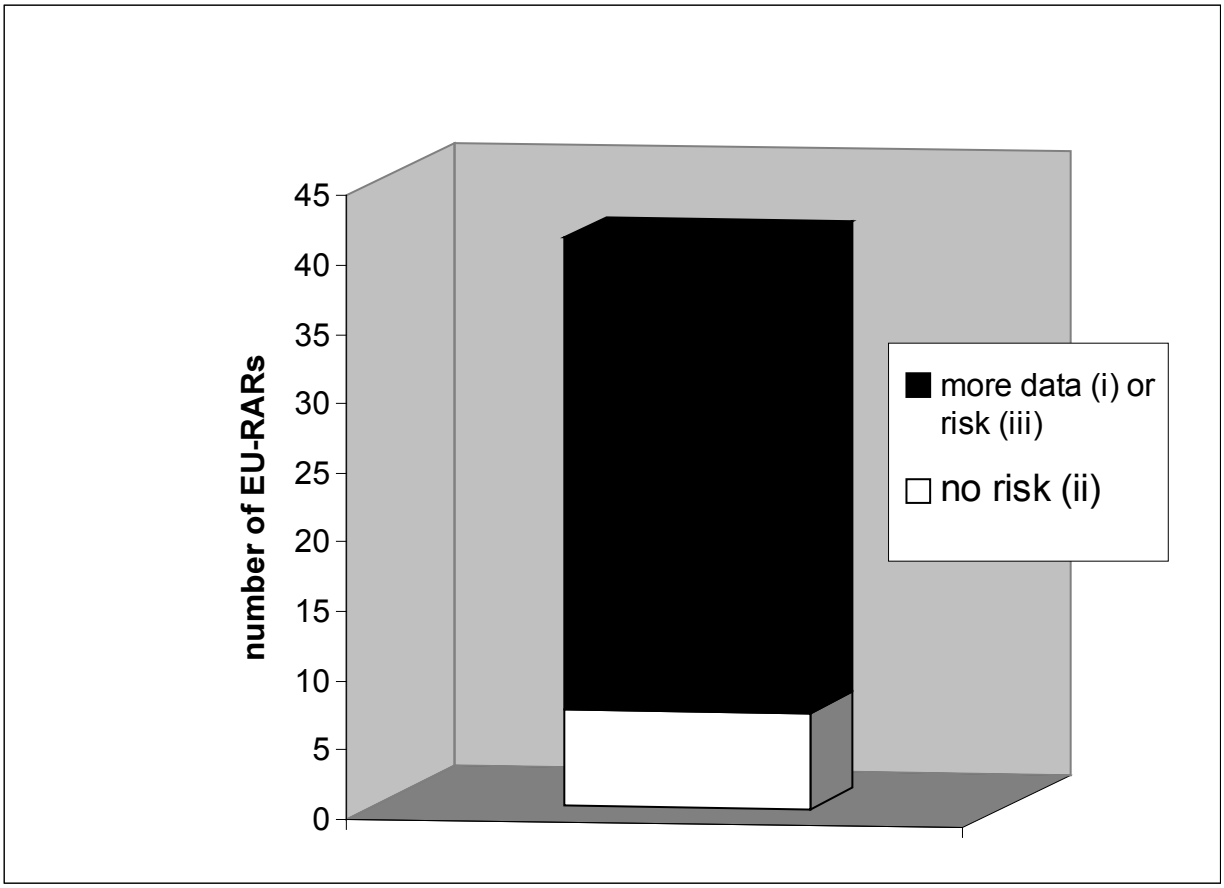

Figure 1. 'Overall score' of conclusions EU-RARs.

The next question is how the conclusions are distributed over the various endpoints (environment, consumers, man indirectly exposed via the environment and workers). This information is given in Figure 2. The figure clearly shows that the conclusions i) or iii) are not restricted to one particular endpoint: they are spread over all endpoints. For most priority

chemicals (80%!) it is workers for which a potential risk is indicated or at least more data are needed. This figure amounts to 65% for the environment and approximately 35% for both consumers and man indirectly exposed via the environment.

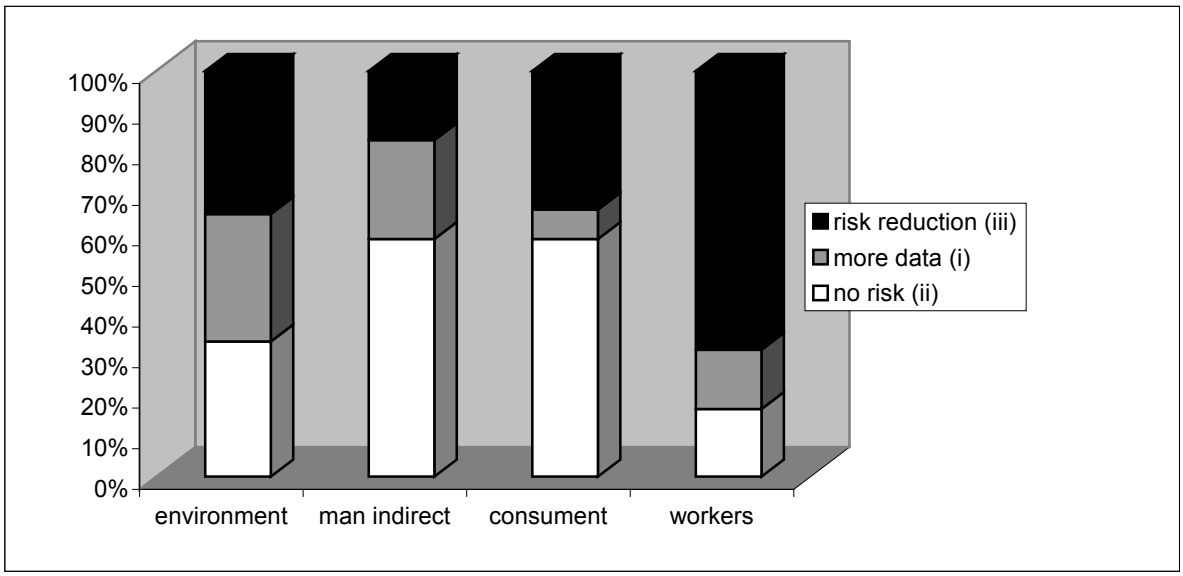

Figure 2. Distribution of the conclusions of the EU-RARs per endpoint.

2.3 Difference between reason for P-list nomination and conclusions risk assessment

Substances have been placed on one of the priority list because of expected potential risks or important data gaps. Member States were asked in the questionnaire to give the reason why 'their' substance was originally selected for one of the priority lists. This was done by selecting 'environment', 'consumers', 'man indirectly exposed via the environment' or 'workers' (or a combination). If for example a chemical was selected because of expected risks at the workplace due to reprotoxic characteristics of the chemical, the reason falls under 'workers'. Subsequently the reason for selection was compared with the final outcomes of the RAR: The results of this comparison are presented in TableTable 2. This table is split up in two parts, I. 'underestimations' and II. 'overestimations'. The 'underestimations' give the number of substances for which a particular endpoint was found to be at risk, but this endpoint appeared not to be the selection criterion (or one of the selection criteria) for that substance. For example: conclusion iii) is drawn for consumers, but it was because of environment that the substance was originally put on the P-list. Part II 'overestimations' presents the number of substances that ended up with a conclusion ii) (no risk) for a particular endpoint, but for which this particular endpoint was just the selection criterion.

From Table 2 part I. it can be concluded that for a relatively small number (n=3) of EU chemicals the outcome of the environmental risk assessment was a conclusion i) or iii), whereas environment was not a selection criterion. A relatively low number of 'underestimations' therefore occur for environment. A much higher incidence of 'underestimations' was found for the human health endpoints, with a maximum of 14 chemicals for workers.

The incidence of 'overestimations' for man indirectly exposed via the environment (n=3) and workers (n=3) was rather low as is illustrated in Part II of Table 2. The score is somewhat higher for environment (n=7). Consumers having the highest score (n=11) in the overestimations. Consumers appeared to have relatively 'high scores' in both the

underestimations and the overestimations. The difference of the sum of underestimations and overestimations in Table 2 with the total number of chemicals gives the number of 'good' predictions. The term 'good' refers in this context to the number of cases where the selection criterion matched with the conclusions of the RAR. This number of 'good' predicted chemicals is thus low for consumers (41-21=20 (50%)) in comparison with e.g. environment (41-10=31 (75%)).
A nuance should be made with respect to the 'overestimations' in Table 2. For a number of chemicals the conclusion ii) was only reached after additional testing was carried out (see also Figure 6), which makes the term 'overestimation' somewhat arguable. The figures between brackets in Table 2 refer to the number of such cases. For environment, man indirectly exposed via the environment and workers the number of 'soft' overestimations is relatively high. For consumers the number of 'real' overstimations exceeds the 'soft' ones.

Table 2. Reason for selecting chemical on P-list versus final conclusions of EU-RARs Figures refer to number of chemicals (see text for further explanation).

I. Underestimations			
Environment	Man indirectly exposed via environment	Consumers	Workers
3	12	10	14
II. Overestimations			
Environment	Man indirectly exposed via environment	Consumers	Workers
7 (5)	3 (2)	11 (5)	3 (3)

2.4 Scope environmental risks

The EU-RARs were examined on the relation between conclusions i) or iii) and the industry categories (IC). The EU distinguishes 16 IC's, covering all areas of society where chemicals are used (as such or applied in products). Figure 3 shows the IC's and the number of cases that a conclusion i) or iii) is drawn within the group of finalized EU-RARs. IC's with no conclusions i) or iii) are not shown in this figure. It should be noted that the number of cases does not necessarily correspond with the number of substances. This because per compound more than one IC can be covered.
It is clear from Figure 3 that a broad spectrum of IC's is associated with potential risks. For 15 out of the total number of 16 defined IC's either a conclusion i) or iii) is drawn. The IC's 'Polymers', 'Basic chemicals' and 'Chemical synthesis' show the highest number of conclusions i) or iii). The IC 'personal/domestic' is the only IC that lacks an environmental conclusion i) or iii).
Within each IC, several Use Categories (UC) can be distinguished giving a further specification of a particular process (e.g. chemical is used a solvent (UC48) in the 'Paints, lacquers and varnishes industry' (IC14). In this report no further subdivision is made between the various UC's, but it is known that the conclusions i) or iii) in a particular IC are indeed linked with several UC's (e.g. IC13 'Textile processing industry' in combination with UC22 flame retardant, UC48 solvent or UC43 process regulator).

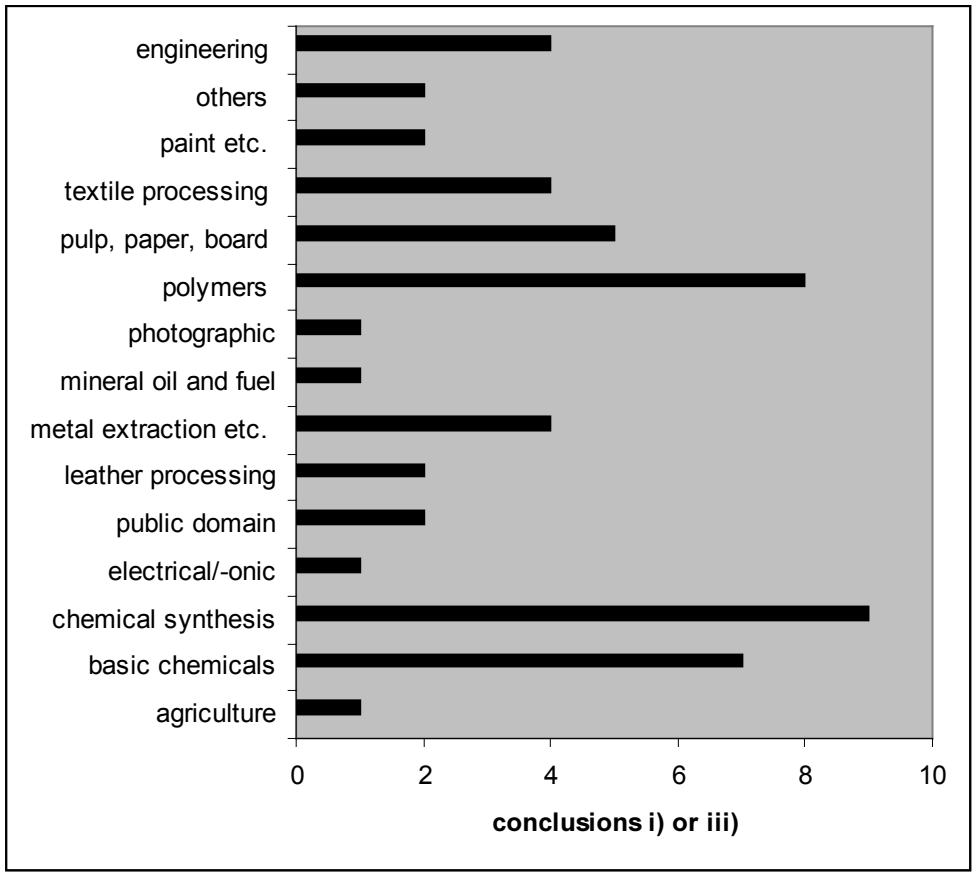

Figure 3. Industry categories associated with conclusion i) or iii) (environment).

It should be noted that unintentional sources are not taken into account in the overview of the IC/UC's. The same holds for human health (below).

2.5 Scope human health risks

Figure 4 shows the Industry Categories (IC) and the number of cases that a conclusion (i) or (iii) is drawn in the finalized EU-RARs for human health. IC's with a conclusion ii) have also been shown in this figure. This is different from the IC overview for environment (Figure 3). An IC is scored as a conclusion (ii) if for all three endpoints a conclusion (ii) was reached for a particular chemical, and considered as a conclusion (iii) or (i) if one of the endpoints had reached a conclusion (i) or (iii).

The same remark can be made as in the environment part, i.e. that the number of cases may exceed the number of substances since one substance can of course cover more than one IC.

Figure 4 indicates that all the 16 IC's defined in the TGD are associated with a potential risk for human health. The IC 'Chemical synthesis' shows the highest number of conclusion (i) or (iii), followed by 'Basic Chemicals', 'Polymers' and 'Others'. The figure also shows that the IC 'Personal/domestic' is the most common IC for human health, but the number of conclusions i) or iii) is relatively low for this IC. The ratio between the number of conclusions i or iii) and the number of conclusions ii) is different, however, for most other IC's: the number of conclusions i) or iii) being relatively high.

It is remarkable that the most common IC for human health, 'Personal/domestic', was the only IC for environment without any conclusion i) or iii) (see section 2.4).

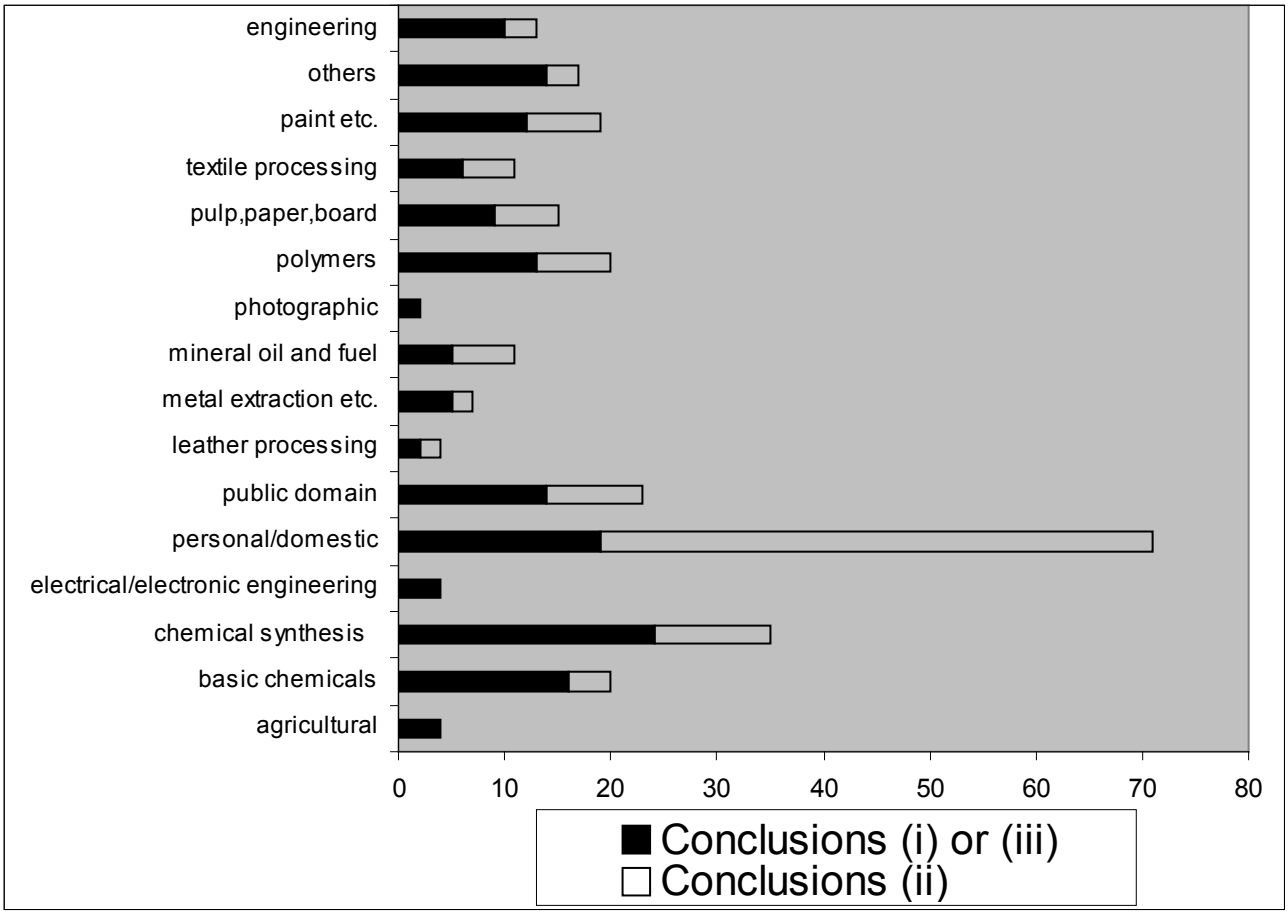

Figure 4. Industry categories associated with final conclusions of RAR) (human health).

Within each IC, several Use Categories (UC) can be distinguished. No further subdivision has been made between the various UC's. The potential risks related to the 'Chemicals synthesis' are, however, mostly associated with chemicals used as intermediate (IC3/UC33). Also for the 'Polymers' the majority is represented by the combination IC11/UC33.

Some further distinction has been made between the different endpoints for human health, in particular workers and man exposed via environment (data not shown). On average the ratio between conclusions i) or iii) and conclusions ii) is found to be higher for workers than for man indirectly exposed via the environment. On the other hand, no risks occurred for workers in three IC's, 'Agriculture', 'Leather processing' and 'Photographic industry', whereas for man indirect all IC's were, more or less, associated with potential concern. Interestingly, the IC 'Chemical synthesis' is linked with the highest number of conclusions i) or iii) for workers, but for man indirect this number is one of the lowest observed.

2.6 Additional testing

It was investigated to what extent additional testing was (or is) needed in order to draw up the final conclusions for the EU chemicals. In the overview, tests that were actually carried out during the RA process are put together with those required in the conclusion i). Figure 5 indicates that for about 50% of the EU-chemicals the base-set turned out to be not sufficient for completing the RAR. In about 20% of the cases, additional testing was related to either

environment or human health. For 12% of the chemicals both environmental and human health tests were needed before completion of the risk assessments.

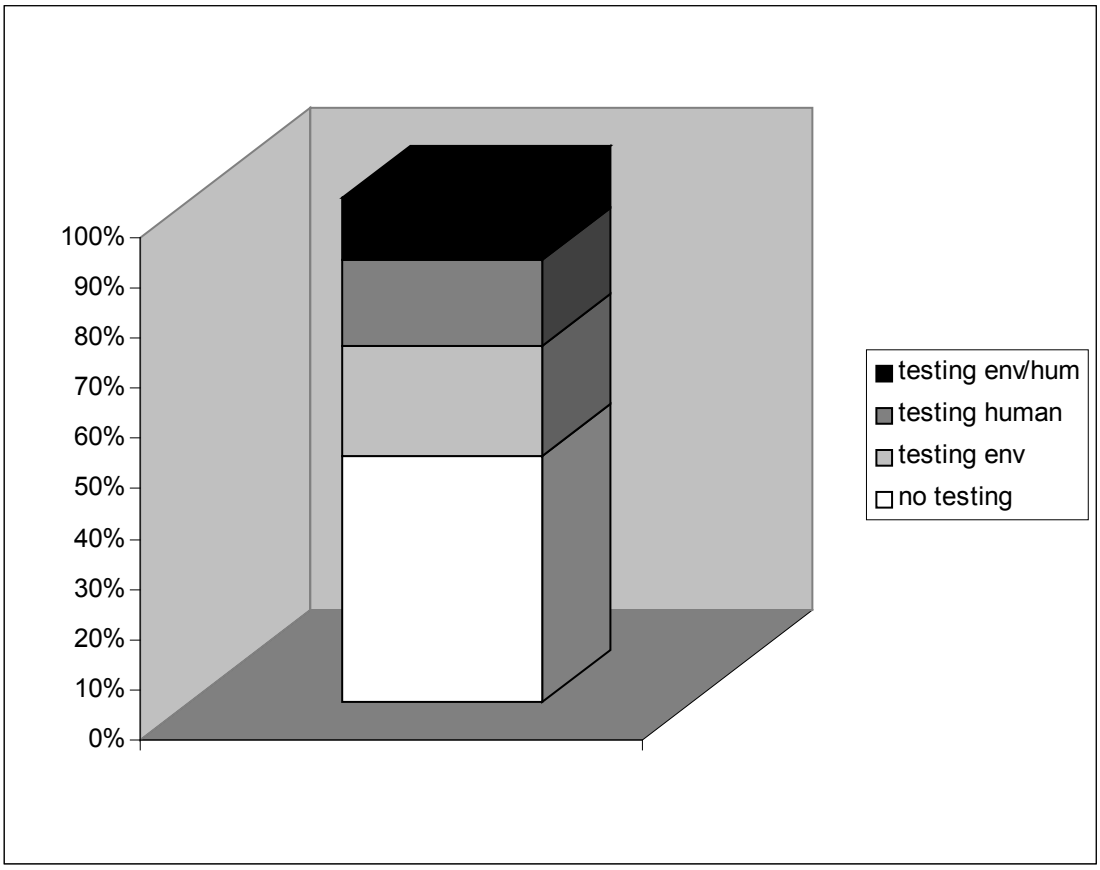

Figure 5. Additional testing for EU chemicals.

In Figure 1 it was shown that 7 out of 41 chemicals ended up with conclusions ii) for all endpoints. Figure 6 interestingly shows that in almost all cases (6 out of 7) this no risk conclusion was only reached after additional testing was carried out. So only one substance of the entire set, i.e. linear alkyl benzene LAB, went directly through the RA-process with all conclusions ii) without any additional testing!

Table 3. Types of additional tests for human health.

Additional test	**Number of test**
sensitization	3
irritation (eyes/skin)	2
90 d inhalation toxicity	2
reproductive toxicity (various types)	7
(sub)acute toxicity	5
mutagenicity	2
others	4
Total	*25*

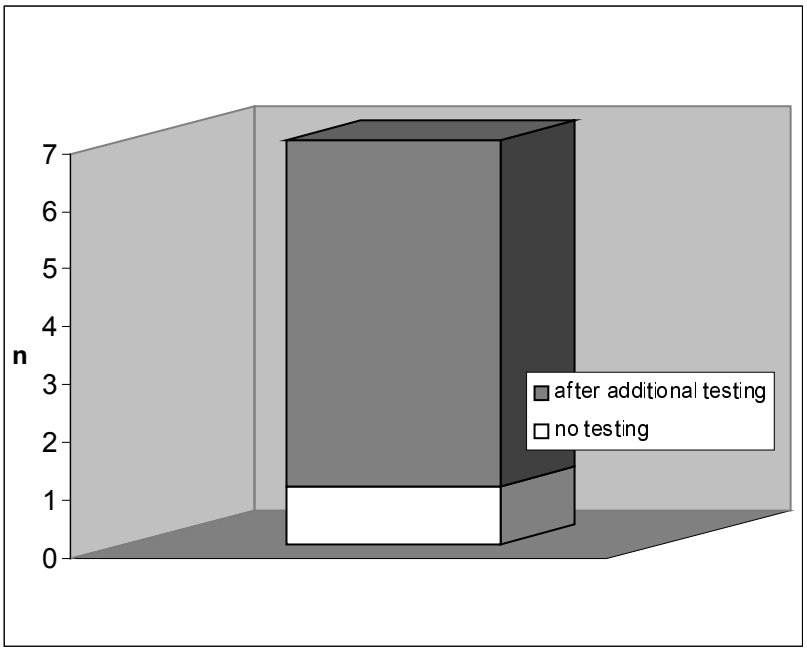

Figure 6. Number of chemicals (=n) with a conclusion ii) reached with or without additional testing.

The next issue is what type of additional testing was asked for in the RA process? A split up is made between human health and environment testing.
Table 3 gives the various types of additional tests that were carried out for human health during the RA process. In total 25 human health tests were performed. For some chemicals more than one test was performed. Most tests are linked with reproductive toxicity. It refers among others to the OECD 421 test.

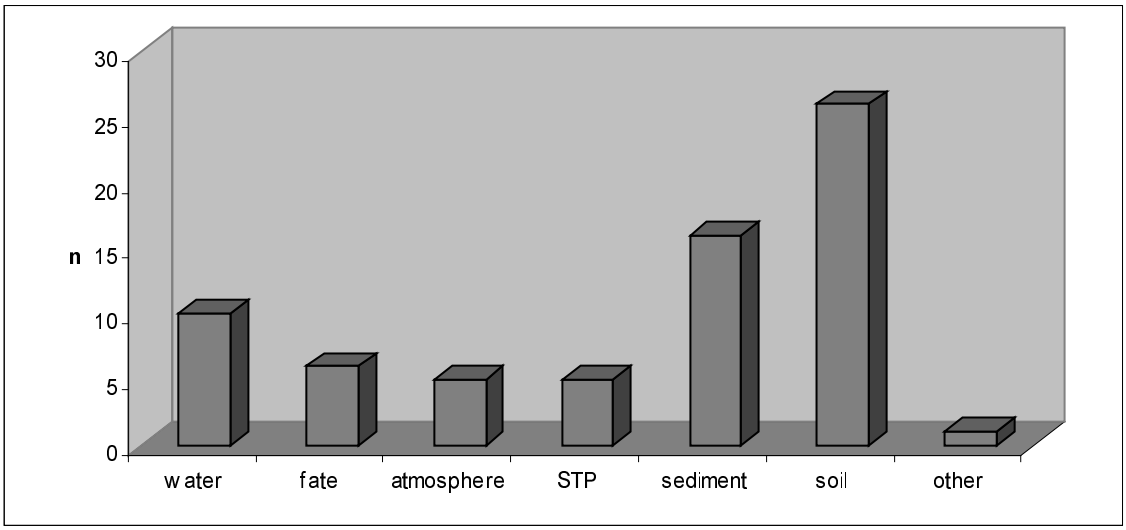

Figure 7. Types of additional testing for environment (n= number of tests).

The additional tests for environment are presented in Figure 7. A total number of 69 tests were carried out. Similar to human health more than one test per compound is possible.

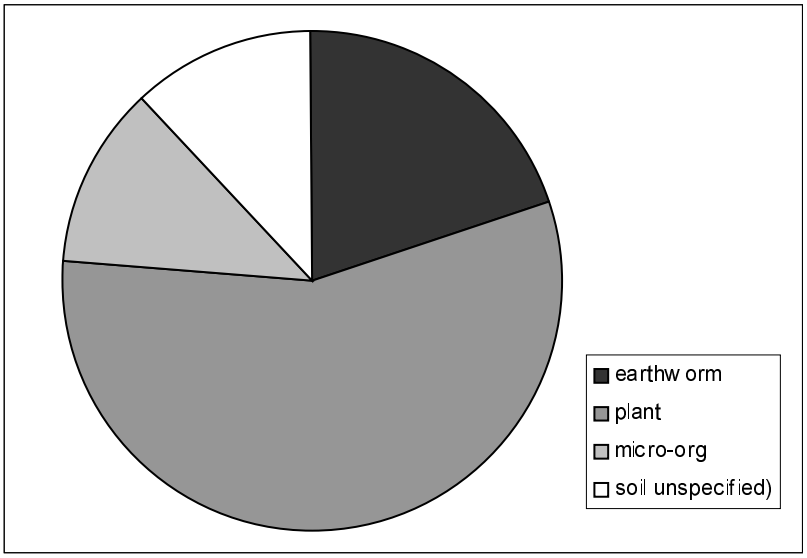

Figure 8. Types of additional testing for the terrestrial compartment.

For water, the additional tests were mostly chronic daphnid or fish studies. These test were performed in order to refine the PNEC for surface water. For atmosphere, plant fumigation tests (n=5) were carried out. In this type of tests plants are being exposed to the chemical via the airborne route. It refers to non-standardized tests under both laboratory and semi-outdoor conditions (i.c. the Open Top Chamber experiment for tetrachloroethylene). The base-set does not comprise any test for the atmospheric compartment. The additional tests for the risk assessment of Sewage Treatment Plant (STP) mostly refer to an activated sludge respiration inhibition or nitrification test conducted with adapted sludge from specific industrial sites. They were needed for refining the local risk characterization for these production or processing sites. Additional fate tests comprise a.o. an experimental K_{oc} determination or photodegradation or anaerobic degradation tests.

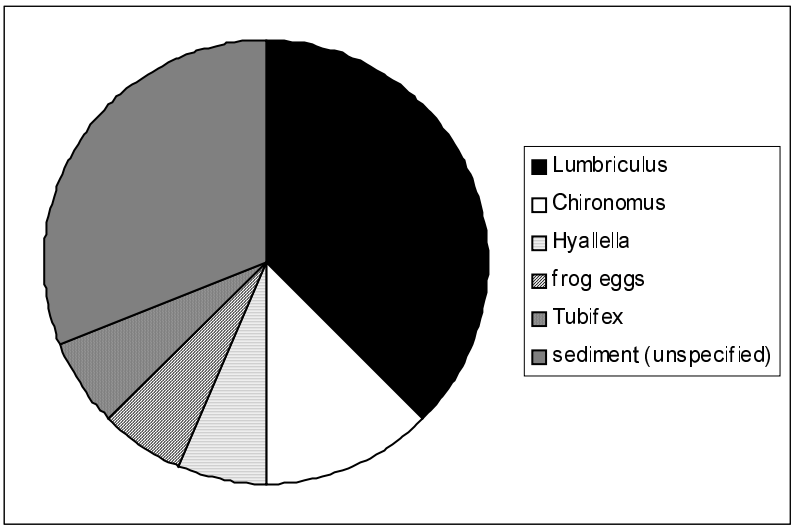

Figure 9. Types of additional testing for the sediment compartment.

Most additional testing for environments deals with the soil and sediment compartment. A more detailed insight in the types of tests that were performed for the soil and sediment is given in Figure 8 and Figure 9, respectively. For soil in most cases a plant test (OECD 208)

was performed, followed by earthworm tests or microbial tests. For a number of chemicals more than one (additional) soil tests was performed.
For the sediment compartment the midge larvae *Chironomus* or the oligochaete worm *Lumbriculus* are shown to be the most tested species. Frog egg studies were only performed occasionally for one chemical (the phthalate ester DEHP).

3. Discussion and conclusions

3.1 General

After the adoption of the EC-Regulation 793/93 a structure had to be built in order to facilitate the risk assessment process of the selected EU priority chemicals. Transparency, consistency and high quality standards were essential preconditions for a successful realization of the EC-Regulation. A clear technical framework was laid down in the Technical Guidance Documents, reflecting the current state-of-the-art on performing risk assessments within the EU. Further an open, (semi-)scientific communication structure was crystallized in the form of so-called Technical Meetings with all parties involved, i.e. Member States, industry, the Commission and NGO's, with industry and NGO's in the role as observers. Since then all contributors have spent large amounts of money and time on the actual work within the Regulation by making risk assessments. At a certain moment the almost obliged question should then be asked if the built RA structure really meets its goal. What is the output of the process? And are we on the right track? Which elements of the 793/93 RA process could be used in the design of a new chemicals policy? To answer these questions the current evaluation study was initiated. The emphasis falls on the final conclusions of the risk assessments. Not so much on the results of each individual RAR, but particularly on the overall picture.

3.2 Overall score: endpoints at risk?

The above-described EU RA-process detected a high number of substances of concern during the last six years. Figure 1 shows that for 34 out of 41 chemicals the risk assessment resulted in either a conclusion i) (= more data needed) or iii) (= risk reduction needed). On the one hand one could say that this result could be expected. This because the chemicals were selected beforehand as being compounds with a potential risk to man or environment. On the other hand new insights were brought forward during the process, additional testing was carried out in many cases (see below) and, importantly, the chemicals went through a (rather) new approach of performing risk assessments. The fact is that the EU follows a (semi-)quantitative approach with relatively much attention to the exposure assessment, especially in comparison with the more traditional, principally hazard-based risk assessments. Apparently, applying this advanced method to the priority chemicals resulted in a high number of compounds that needs either further information or direct risk reduction measures. Figure 2 showed that the conclusions i) or iii) are not restricted to one particular endpoint (environment, man indirectly exposed via the environment, consumers or workers). Evidently, priority chemicals may pose risks to the whole range of the protection goals of the risk assessment. Workers having the highest number (80%) of conclusions i) or iii) followed by environment (65%). These high scores might be related to the fact that both workers and environment were the endpoints most frequently mentioned as selection criteria for the P-lists. For 50% and 65% of the chemicals, respectively, workers and environment happened to be the selection criteria. For man indirectly exposed via the environment and consumers these figures amount to 12 and 35%, respectively. On the other hand this study also shows that the match between selection criterion and final results of the RAR can be poor (see below).

3.3 Priority setting and the outcome of the risk assessments

We investigated the predictability of the risk assessments for P-list chemicals. If a chemical is selected because of potential risks for a particular endpoint, by applying the current, rather arbitrary selection mechanism, do we then always end up with the same endpoint being at risk? Or do we find a lot of unexpected results? And, if yes, why, and what are the consequences? Table 2 presents the number of 'underestimations' and 'overestimations'. Regarding the number of 'underestimations' there is a clear difference between environment and human health. This number is low for environment, meaning that our insight in possible environmental risks is quite well reflected in the outcomes of the risk assessments. We don't stake too conservatively in priority setting, as the number of 'overestimations' is also relatively low (7) for environment. Especially when it is taken into account that for five out these seven cases, conclusion ii) could only be drawn after additional testing.
The great number of underestimations for consumers may be due to several reasons. One is that during the process unforeseen consumer applications showed up. Another reason may be that quantitative exposure assessments for consumers were carried out in a standard way for all chemicals with potential consumer exposure (a.o. by applying CONSEXPO). A more accurate exposure assessment, as prescribed in the TGD, may also be responsible for the great number of underestimations for man indirectly exposed via the environment and workers. The high number of 'underestimations' for human health in general is accompanied by a high number of 'overestimations' in case of consumers (overestimations are low for man indirectly exposed via the environment and workers). In simple terms one could therefore say that for chemicals for which we presume there is a risk for consumers there often appears to be no risk, whereas for chemicals we think there is no risk for consumers there appears to be a risk!
This all means that our *a priori* knowledge on possible risks of HPVCs is poor (especially for consumers) which is a very important signal to policy makers. The results further emphasize the need for a more objective, science-based priority setting system (e.g. EURAM). It should be stated of course that the success of every (priority) system is to a large extent determined by the quality of input data. If you don't know that a chemical is used in consumer products, the outcome of any priority setting system will be limited.

This brings us to an important question: what is the advantage of performing integrated risk assessments for a chemical? The term 'integrated' refers in this context to covering both environment and human health in one risk assessment. This holistic approach definitely has great advantages. First of all one gets a full picture of the potential risks of a chemical. Additionally, the exchange of information between human health and environment on e.g. the mode of action of a chemical improves the overall quality of the risk assessment. Furthermore, secondary poisoning and man indirectly exposed via the environment, being important issues on the interface between environment and human health, are properly dealt with via an integrated approach. The other side of the picture is of course that the preparation of the risk assessment demands much more time. In the EU a discussion is going on about the usefulness of so-called 'targeted' risk assessments (NL, 2001). This refers to risk assessments focusing on only one particular endpoint rather than evaluating the whole life cycle of a chemical for both man and environment. A targeted risk assessment may comprise for example the risk for consumers during paint use. The advantage of targeted risk assessments is beyond doubt that in most cases it will take less time to complete them. The other side is, however, that there is a serious chance of 'missing' other critical endpoints. This is clearly demonstrated in this study by the relatively high number of unexpected results. It is of course a policy decision what is to be preferred.

3.4 Scope of risks (Industry and Use Categories)

Is there consistency in the industry types or use types that are mostly associated with a potential concern for chemicals? A great number of chemicals are mostly used within a particular Industry Category (IC) and by only focussing on individual chemicals no picture can be obtained on the general 'performance' of that IC. If an IC would happen to be linked with many conclusions i) or iii), extra attention should be paid to such IC's in future.
Figure 3 gives the results of the screening on the relation between the various types of IC's and the number of conclusions i) or iii) for environment. This figure clearly illustrates that conclusions i) or iii) are drawn for a broad spectrum of ICs. The RARs ended up with a potential risk or need for additional data for 15 out of 16 defined ICs. The IC's 'Polymers', 'Basic chemicals' and 'Chemical synthesis' showed the highest number of conclusions i) or iii). As stated in section 2.4 no further, detailed subdivision is made between the various Use Categories (UC) within an IC. But as an example the various UC's for the IC Polymers industry are given that resulted in a conclusion i) or iii). The chemicals acrylic acid, methyl methacrylate and toluene are used in the polymer industry as an intermediate (UC33). Dibutylphthalate, diethylhexylphthalate and C10-13 chloroalkanes are used as a plasticizer (UC47). Pentabromodiphenylether is used in the polymer industry as flame retardant (UC22) and nonylphenol as cleaning/washing agent (UC9). The potential risks or data needs related to the polymer industry are thus found to be associated with eight different chemicals and four different UC's.
Hydrogen fluoride, 4,4'-methylenedianiline, aniline, toluene, nonylphenol and 1,2,4'-trichlorobenzene are all chemicals that are used as intermediates in the chemical industry (synthesis) (IC3/UC33). For this use of these chemicals a conclusion i) or iii) was drawn in the corresponding risk assessments. This may be seen as a somewhat unexpected result as the IC/UC combination 3/33 is often claimed to be characterized by closed systems with hardly any or even no environmental releases.
On average the same result is observed for human health (Figure 4). The RARs ended up with a potential risk or need for additional data for all 16 defined ICs. And also for human health the highest number of conclusions i) or iii) is unexpectedly associated with the IC 'Chemical synthesis".
It can be concluded that both the environmental and human health conclusions i) or iii) may occur for a wide range of Industry categories. No industry category can in advance be excluded from performing risk assessments. The IC's with a potential risk or need for data are made up of several Use categories, as was illustrated with the example of the Polymer industry.

3.5 Additional testing

A prerequisite for performing a risk assessment within EC regulation 793/93 is that the minimum data requirements is complied with. For many EU HPVCs this minimum set of data on physicochemical and (eco)toxicological properties is accompanied by a large amount of additional information (the so-called 'data rich' chemicals). Despite this abundance of data it was shown that for both environment and human health many additional tests (base-set and post base-set) had to or still must be carried out before completion of the risk assessment (see Figure 5). Table 3 and Figure 7 present the numbers and types of additional tests for human health and environment, respectively.

For human health, additional testing primarily concerned base-set testing, either because for a specific endpoint no base-set data were available, or available base-set data were considered

insufficient/inadequate to meet the requirements. This was especially the case for the endpoint reproductive toxicity, where a test conducted according to OECD Guideline 421 (Reproduction/Developmental Toxicity Screening Test) was the most frequently requested test to meet the minimum requirement. A possible explanation might be that the minimum requirement for reproductive toxicity (i.e. 'screening' information should be available) is rather vague, and that apparently the guidance given in the TGD on how to interpret this is not effective/adequate. It is noteworthy that this issue has recently been point of discussion in the TGD revision process. The TGD Revision Sub-group on Reproductive Toxicity has proposed that, in order to fully assess the various endpoints covered by the term reproductive toxicity (and to be in line with the data requirements for new substances and biocides), the minimum data requirements for reproductive toxicity should be changed to a two-generation study (OECD TG 416 or corresponding Annex V method) and prenatal developmental toxicity studies in two species (OECD TG 414 or corresponding Annex V method).

For a few carcinogenic substances the minimum data requirements were not met. Although this formally would lead to a conclusion i (and was counted as such in this report), additional base-set testing was put on hold. This means that the need for these tests will be revisited in the light of the risk reduction strategy that is required for a carcinogenic substance.

In those cases that additional testing for human health meant post base-set testing this merely concerned in vivo mutagenicity testing and repeated dose toxicity testing via a route other than oral. In contrast to environment, the post base-set tests were not 'new' or could be ascribed to certain classes of chemicals, with possible exception of the brominated flame retardants. Given their persistent and bioaccumulative nature, as well as their occurrence in human breast milk at increasing levels, for brominated flame retardants information is needed on the effects of prolonged (e.g. lifetime) exposure and on the risks of feeding breast and cow's milk to infants. To address the effects of lifetime exposure, a (new) methodology should be developed, including data requirements that may be indicated for such a methodology. As it was recognized that it would take some considerable time to generate the methodology and to gather further information, it was also recommended to consider risk reduction measures at the same time.

For the additional tests for environment some further attention will be paid to the compartments water, atmosphere, soil and sediment. In contrast to human health, for environment the additional testing in most cases refers to post base-set testing rather than bringing an (original) base-set requirement to an acceptable level.
For water it mostly refers to chronic daphnid or chronic fish testing. Only short-term test results (=base-set) were mostly available and the PNEC water was subsequently based on these short term data. During the risk assessment the PEC/PNEC ratio turned out to be above 1 for one or more environmental exposure scenarios, thus indicating a potential risk for the aquatic compartment. An option then was to perform long term aquatic testing in order to refine the PNEC. The TGD gives guidance on the testing strategy to be followed in those cases. As the uncertainty is reduced by (an) additional long-term test(s) a lower assessment factor could be used. This results in most cases in less conservative PNECs and as a consequence there is a chance that PEC/PNEC ratios may then become lower than 1, indicating no risk. An example of such case was the chemical cumene.
For five chemicals, i.e. aniline, acroleine, acrylonitrile, dibutylphthalate (two test) and tetrachloroethylene, tests were (or have to be) carried out in which plants were exposed to the chemical via the airborne route. The exposure estimation for these chemicals indicated that concentrations in air may be substantial and on the effects side, literature data point to

potential hazard of the chemical for plants via air. Although the available studies could be used as a (qualitative) trigger for potential hazard, they were considered as an insufficient basis for the quantitative risk assessment. The relevance of plant testing via the airborne route is further underlined by the fact that for an additional chemical on the fourth P-list, butylbenzylphthalate, a plant fumigation test will soon be carried out as well (pers. comm. Norwegian-rapporteur). And in case of hydrogen fluoride the environmental conclusions iii) for atmosphere in the RAR were based on a PNEC for air based on toxicity to plants. The remarkable emergence of the atmosphere plant testing for a significant number of chemicals should be reflected in more clear guidelines on how to perform these types of test. Now the test protocols ranged from short term (a few weeks), laboratory testing with a few annuals to elaborate long term (six months) testing under field conditions with both annuals and several tree species. The latter type of testing was conducted for tetrachloroethylene in the so-called Open Top Chambers. The update of the TGD will pay more attention to the testing strategy for plant testing via air (tiered approach). Additionally, further standardization is needed for the different types of tests.

Figure 7 illustrates that most additional tests were (or will be) performed for sediment and soil. It must be noted that, in contrast to the post base-set testing for e.g. water and atmosphere, in many cases more than one soil or sediment test per chemical is performed. For example for 3,4-dichloroaniline both Lumbriculus and Chironomus testing was performed. It should also be stated, however, that for some chemicals the PEC/PNEC ratios for sediment and/or soil appeared to be above 1, indicating a potential concern for these compartments, but the RARs did not conclude that additional testing was needed (yet). This despite the fact that no actual data on either soil or sediment toxicity was available and the PNECs were derived with the equilibrium partitioning method from the PNEC water. This is for example the case for sediment for the chemicals naphthalene and nonylphenol. The argumentation is that the requirement for further testing should await the outcome of the risk reduction strategy for the aquatic (surface water) compartment, since the sediment PECs will be directly affected by any measures to reduce concentrations in water. Such ‘if, then’ additional testing needs were recorded as ‘unspecified’ in our specification of post base-set tests for soil and sediment (Figure 8 and Figure 9).

Three situations can be distinguished with regard to the obvious need for additional soil and sediment testing. (Prerequisite is of course that the exposure assessment indicates that the soil/sediment is a relevant compartment for that particular chemical). Firstly, the predictive value of the equilibrium partitioning method is rather low for a number of chemicals. This because for those chemicals the K_{ow}, being the basis for the equilibrium partitioning approach, is in general not a good descriptor for the binding of the chemical to the particulate sediment or soil organic carbon (K_{oc}). This is true for compounds for which sorption does not depend on hydrophobic interactions, but where others modes of sorption, e.g. ionic or ligand exchange exchange interactions, can be assumed. Secondly, when the initial PEC/PNEC ratio indicates a potential concern for sediment and soil and the PNEC was based on the equilibrium partitioning method, further testing will reduce the uncertainty. Thirdly, if the PEC/PNEC is > 1 and the PNEC is based on one soil/sediment test, additional soil/sediment testing will also further reduce the uncertainty. The combination of wide dispersive use and strong binding capacities to soil/sediment particles, irrespective of the mode of sorption, clearly triggers the need for a good set of experimental data. If such data are lacking, additional testing is unavoidable. Within the group of completed EU chemicals this was found for among others the phthalate ester DEHP, the flame retardants penta- and octa-bromodiphenylether and aniline. For new chemicals with a production volume between 100 and 1000 tonnes/year the notifier has to submit terrestrial ecotoxicity data (Annex VIII). This study clearly demonstrates that the absence of such base-set requirement for existing

chemicals, in particular HPVCs, sooner or later causes difficulties for chemicals with substantial emissions to soil.
The spin-off of all post base-set testing for soil and sediment performed within the frame work of EC Regulation 793/93 to general test development should not be ignored. Especially in the rather new field of sediment testing, the need for experimental data for a number of EU-chemicals has been a stimulus for further test development. The current state-of-the-art on the testing strategy for sediment will be included in the update of the TGD.

In general it can be concluded that many high quality data are (or will be) generated on a number of important HPVCs. Furthermore, post base-set testing turns out to be always needed for specific classes of chemicals and use patterns. A discussion may be needed for the adequacy of the current base-set for HPVCs. For human health more thought is needed on the compliance of base-set requirement (esp. reproductive toxicity).
The availability of high quality and up-to-date international review reports on major priority chemicals has proven to be also very useful for several adjacent working areas, both nationally and internationally (e.g. setting of water quality standards or soil sanitation limits).

3.6 Limitations of evaluation

Finally, we should also face the limitations of this evaluation. First of all we should realize that the group of evaluated chemicals is relatively small (n=41). One should be careful therefore with generalizing from this limited group. On top of that, the group is also not a random selection of the approximately 2000 HPVCs, and definitely not of the ca. 100,000 EINECs chemicals. In the preparatory discussions on the first three P-lists, Member States mostly brought forward chemicals with already a clear national or international ‘history’. It is logical that this previous history increases the chance of concluding the risk assessment with potential concern for one or more endpoints. Further no distinction is made in this evaluation between the different types of conclusions i) or iii). For example the difference between local and regional risks for the environment. It is obvious that there is a disparity between a potential risk occurring ‘only’ at the sewage treatment plant of one production or processing site and a potential risk in surface water for an entire region. We also did not discriminate between conclusions i) or iii) that were based on (partly) generic exposure scenarios and those based on more realistic site-specific data. The latter being preferably measured data. Although in most cases all efforts are made to limit the number of generic exposure assessments in the final, decisive RAR, they still occur (especially for workers).

3.7 Final conclusions

Despite the above-mentioned limitations we feel that this study provides a number of very useful points of departure for further discussions on risk assessment for chemicals and must play a part in the discussions on the implementation of the ‘White Paper’. For example down-stream users are apportioned to get a more prominent role in the future risk assessment of chemicals. The importance of getting detailed information from down-stream users early in the risk assessment process evidently emerged from our evaluation as a result of the high number of unforeseen consumer applications. In addition this study clearly demonstrates that for certain chemicals the Annex VIIA base-set will undoubtedly be insufficient. Additional testing has to be anticipated as much as possible in order to avoid a long-term process.

As stated in section 1.2 the work on EC Regulation 793/93 has been a target of criticism for several years now. A number of drastic alterations are being suggested in the Commission's White paper on the Future Chemicals Policy. One should of course always be receptive to improvements and new concepts, but after the results of the current evaluation study we would like to conclude with (the translation of) an old, wise Dutch saying: "Don't throw away your old shoes, before you have new".

References

EEC, 1993. Council Regulation 793/93/EEC of March 1993 on the evaluation and control of risks of existing substances. Off. J. Eur. Communities, L48/1.

NL, 2001. The Use of Targeted Risk Assessments in the EU. NL-document prepared for EU Existing Chemicals CA Meeting. January, 2001.

UN, 1992. United Nations. Environmentally sound management of toxic chemicals including prevention of illegal international traffic in toxic and dangerous products. Agenda 21, chapter 19. United Nations Conference on Environment and Development, Rio de Janeiro, Brazil.

White Paper, 2001. White Paper Strategy for a Future Chemicals Policy. Eur. Commission. COM (2001) 88- C5- 0258/2001. Brussels.

Appendix 1. Questionnaire (template)

rivm
research for man and environment

EUROPEAN COMMISSION
DIRECTORATE GENERAL JRC
JOINT RESEARCH CENTRE
Institute for Health and Consumer Protection
Unit: Toxicology and Chemical Substances
European Chemicals Bureau

Evaluation of EU-HPVC risk assessments

Showing the benefits of EC Regulation 793/93

II. Questionnaire

Notes:
1. Please use for each finalised chemical a separate questionnaire.
2. Please submit only one questionnaire for each chemical (if environment and human health are both finalised, please combine)
3. Deadline for submission is **1 March 2001**.
4. Please return questionnaires by e-mail to charles.bodar@rivm.nl

1	Chemical name: CAS number: Rapporteur: Contact person:
2	*Question:* For which sections of RAR agreement was reached at TM level? *Answer:* (tick where appropriate; Note: combination of answers is possible) ❑ environment ❑ human health, consumers ❑ human health, man indirectly exposed

	❑ human health, workers
3	*Question:* What was the reason for placing the chemical on EU Priority List? *Answer:* (tick where appropriate; Note: combination of answers is possible) ❑ environment ❑ human health, consumers ❑ human health, man indirectly exposed ❑ human health, workers Please specify below reason(s) as much as possible?
4	*Question:* Was additional, beyond base-set, (eco) toxicity or fate testing being asked for during the risk assessment process? *Answer:* (tick where appropriate; environment <u>and</u> human health combined) ❑ yes ❑ no If yes, please specify type of test(s) below?
5A	*Question:* What are the final conclusions, in terms of conclusion i), ii) or iii), of the RAR? *Answer:* *(*tick where appropriate; Note: combination of answers is possible) …… 5A1. <u>Environment</u>: ❑ i) ❑ iii) ❑ all ii) …… 5A2. <u>Human health, man indirectly exposed:</u>

	❑ i) ❑ iii) ❑ iiia) ❑ iiib) ❑ all ii) ……. 5A3. Human health, consumers: ❑ i) ❑ iii) ❑ iiia) ❑ iiib) ❑ all ii) ……. 5A4. Human health, workers: ❑ i) ❑ iii) ❑ iiia) ❑ iiib) ❑ all ii)
5B	In case of conclusion(s) i) or iii(b)) for '**environment**' and '**human health, man indirect exposed**' under item 5A, please answer questions 5B1-5B4. ……. *Question 5B1*. Are the conclusion(s) i) or iii(b)) related to a local or a regional problem? *Answer:* *(*tick where appropriate; Note: combination of answers is possible) ❑ local (further questions: see *Question 5B2*) ❑ regional (further questions: see *Question 5B3*) ……. *Question 5B2*. The local conclusion(s) i) or iii(b)) are related to: - which life cycle stage of the chemical? - which main category (MC) and industry (IC) and use categories (UC)? - which compartment? - a generic (default) exposure scenario(s) or to (a) scenario(s) based on (site-) specific data? Or to measured data? *Answer (see options below table):*

	Life cycle stage[1)]	MC[2)]	IC[3)]	UC[3)]	Compartment[4)]	Generic, site-specific or measured [5)]	Concl i) or iii(b))[6)]

	…. …. ….	… … …	.. .. ..	.. .. ..	…. …. ….	…. …. ….	…. … ….

1) options: **prod**uction, **for**mulation, **proc**essing, **pri**vate use or **dis**posal
2) options: Ia, Ib, Ic, II, III or IV
3) give appropriate IC or UC number
4) options: **aqu**atic, **sed**iment, **ter**restrial, **atm**ospheric, **sec**ondary poisoning or **man** indirect
5) options: **gen**eric, **sit**e-spec. or **mea**sured
6) options: i or iii(b)

……

Question 5B3. The regional conclusion(s) i) or iii(b)) are related to:
- which compartment?
- a generic (default) exposure scenario(s) or to (a) scenario(s) based on (site-) specific data? Or to measured data?

Answer (options see below table):

Compartment[1)]	Generic, site-specific or measured[2)]	Concl i) or iii(b))[3)]
…..	….	….

1) options: **aqu**atic, **sed**iment, **ter**restrial, **atm**ospheric, **sec**ondary poisoning or **man** indirect
2) options: **gen**eric, **sit**e-spec. or **mea**sured
3) options: i or iii(b)

……

Question 5B4. Are the conclusion(s) i) or iii(b)) related to unintentional emission sources?

Answer:

- ❑ Yes
- ❑ No

If yes, please specify below?

5C

Question 5C1: In case of conclusion(s) i) or iii(b) for '**human health, consumer'** under item 5A, these conclusion(s) are related to which specific products?

Answer:
(please specify type of product)

……

Question 5C2. Are the conclusions i) or iii(b)) related to modelled (e.g. CONSEXPO) or measured exposure data?

<table>
<tr><td></td><td colspan="3">Answer:

❑ exposure model
❑ measured data</td></tr>
<tr><td>5D</td><td colspan="3">Question 5D1: In case of conclusion(s) i) or iii(b)) for '<u>human health, worker'</u> under item 5A, these conclusion(s) are related to:
- which exposure scenario (incl. specification of life cycle stage) of the chemical?
- modelled (e.g. EASE) or measured exposure scenario(s)?

Answer (see options below table):</td></tr>
<tr><td></td><td>Scenario[1)]</td><td>Model or measured[2)]</td><td>Concl. i) or iii(b))[3)]?</td></tr>
<tr><td></td><td>…… …..</td><td>….</td><td>….</td></tr>
<tr><td></td><td colspan="3">1) please shortly describe exposure scenario (incl. life cycle stage, e.g. production or formulation)
2) options:exposure model or measured
3) options: i or iii(b)</td></tr>
<tr><td>6</td><td colspan="3"><u>Additional remarks from Rapporteur</u></td></tr>
</table>

Many thanks for your cooperation!

Appendix 2. Table 1: overview of the results

(Note that this overview reflects the situation of spring 2001. Afterwards changes may have occurred).

Explanation:
Column numbers 3, 4 and 5A/5B refer to question numbers in questionnaire (Appendix 1).
3: Reason for placing the chemical on the P-list.
4: Additional beyond base-set testing? (h: human health; e: environment; h/e: human health and environment). Types of tests are given in the last four columns where distinction is made between testing carried out during RA and testing as a result of conclusion i). Note that in the evaluation report the data are combined.
5A: Final conclusions of the RAR for env, man indirect, consumers and workers.
5B: IC/UC associated with conclusion i) or iii) for env or man indirect.

Substance	3	4	5A				5B	Env testing during RA	H h testing during RA	Env testing concl. i)	H h testing concl i)
			env	man in	cons	work					
HF	env	no	i	i	iii	i	3/33				
			iii	iii		iii					
DEGME	work	yes(h)	ii	ii	iii	iii			sensitization test		
1,4-dioxane	cons	no	ii	ii	ii	iii					
dms	work	no	ii	i	iiia	iii	unint.				
				iiia							
acroleine	man in	no	i	i	ii	iii	unint.			plant fumigation	
DEGBE	work	no	ii	ii	iii	iii					

DBP	env	yes (h/e)	i	ii	ii	iii	12/48 11/47	plant fumigation	28 day inhalation test	plant fumigation (2nd tier)	
MDA	env	no	i	iiia	i	i	3/33			long term sediment Lumbriculus	reproductive toxicity
	work			i	iiib	iii					
						iiib					
ethylacet	cons	yes(h)	ii	ii	ii	ii			repro/develop screening 421		
	work										
mma	env	yes (e)	iii	ii	ii	iii	11/33	algae test (new)			
	cons							chronic daphnia			
	work										
aa	env	no	i	ii	ii	iii	11/33 unint.			integrity of native ciliate populations in sewage	
	work		iii								
maa	env	no	iii	ii	ii	iii	unint.				
	cons										
	work										
DODMAC	env	yes(h/e)	ii	ii	ii	ii		28d sediment (Lumbriculus and Tunbifex)	repro/develop screening 421		
	cons										
	work										
methyl acetate	work	no	ii	ii	ii	iii					

aniline	env	yes (e)	i	iii	iii	iii	3/33 unint.	nitrification inhibition industrial STP		soil testing	
	cons		iii							sediment testing	
	work									plant fumigation	
										bioaccumulation soil and sediment	
1,4-dichloroben zene	env	no	ii	ii	ii	iii					
	cons										
	work										
cyclohexan e	cons	no	ii	ii	iii	iii					
	work										
DIDP	env	yes (e/h)	ii	ii	ii	ii		earthworm (14 d)	two-generation reprotox		
	cons							lettuce and grass			
								long term fish			
DINP	env	yes (e)	ii	ii	ii	ii		long term fish			
	cons							act. sludge (new)			
								lettuce (short term and long term)			
								grass			
								micro-org. soil and earthworm			
H2O2	env	no	iii	ii	iii	i	2/35 3/37				90 day inhalation study rats
						iii					
MTBE	env	no	i	iii	ii	iii				information/testing avoidance behavior wildlife	

	cons		iii								
	man in										
	work										
LAB	env	no	ii	ii	ii	ii					
acetonitrile	env	yes (h)	iii	ii	ii	iii	2/48		sensitization test		
									acute oral and inhalation in mice		
									acute dermal, skin irritation and eye irritation in rabbits		
cumene	env	yes (e)	ii	ii	ii	ii		chronic daphnia (+ algae?)			
DEHP	env	yes (e)	i	iii	iii	iii	2/47 11/47 16/47 14/47 16/52 12/48 15/55	sediment frog eggs		multi-gen fish study	
PCOC	env	yes (h/e)	ii	ii	ii	ii		chronic daphnia	micronucleus test (i.p. route)		
	cons										
	man in										
	work										
toluene	env	no	iii	ii	i	iii	3/33 2/48 9/48 11/33 14/48 13/48 unint.				additional information on repro effects and exposure time
	cons				iii						

	man in										
	work										
1,2,4-trichlorob	env	yes (h)	iii	iii	iii	iii	13/43 3/33 2/48 0/43		Zymbal's Gland (supplemental histopath. examination)		
	man in										
acrylonitrile	env	yes (e)	iii	iiia	iiia	iii	3/33	biodegradation		plant fumigation	
	work		i								
o-anisidine	cons	no	ii	ii	iii	iii					
	work				iiia	iiia					
					iiib	iiib					
octa	env	no	i	i	ii	i	12/22			anaerobic degradation	90 d inhalation study (repr and immuno)
						iii				photodegradation	transthyretin-T4 competition
										28 d Lumbriculus	prolonged exposure effects
										plant growth and earthworm repr	information on excretion of substance in breast milk and cow's milk
										activated sludge	soil-plant transfer
C10-13 chloro	env	yes (e)	i	ii	ii	ii	8/35 7/47 11/47	Koc determination		soil unspec.	
			iii							sediment unspec.	
acrylamide	work	no	iii	iii	iiia	iii	16/13				
				iiia		iiib					
				iiib							

tri	work	yes (e)	i	iiia	iiib	iiib	3/33 2/48 8/9	plant fumigation (tetra)			
			iii								
nonylphenol	env	yes (e/h)	i		ii	iii	All (except 5 and 9)/9		dermal absorption information	sediment unspec.	
			iii								
bis penta	env	no	i		ii	i	12/22 13/22			anaerobic degradation	developmental toxicity
										photodegradation	
										28 d Lumbriculus	
										plant growth and earthworm repr	
										activated sludge	
penta	env	yes (e/h)	i		ii	i	11/22	ELS fish	multi-generation reproduction study with emphasis on exposure via breast milk		
			iii					long term Daphnia	studies on a.o. toxicokinetics, relative liver toxicity and behavioral effects in young (neonatal) and adults		
								Lumbriculus	dermal absorption		
								Hyalella			
								Chriornomus			
								six plant species soil			
								soil micro-organisms			
napthalene	env	yes (h)	iii		iii	iii	8/0		second in vivo	sediment unspec.	

									genotoxicity		
										soil unspec.	
methyloxi	work	no	ii		iiia	iiia					sensitisation test
					i	i					
but-2-yne-diol	cons	yes (h)	ii		ii	iii			28 day inhalation		
	man in								reproduction toxicity		
	work										
3,4-dichloroaniline	env	yes(e)	i		ii	iii	3/33 6/38	Lumbriculus sediment		earthworm test	
			iii					Chrinomus sediment		plant test soil	
										soil respiration	

Mailing list

1 Drs. A.W. van der Wielen, DGM/SAS
2 Ir. J. van der Kolk, DGM/SAS
3 Dr. D. Jung DGM/SAS
4 Mr. J. K. Kwisthout, DGM/SAS
5 Directie RIVM
6 - 10 Dr. B. Hansen (JRC/ECB, Italy)
11 OECD/EHS secretariat (Paris)
12 - 15 CEFIC secretariat (Brussels)
16 Dr. C. de Heer (TNO-Voeding Zeist)
17 Ir. A. Vijlbrief (SZW, Den Haag)
18 Dr. H. Roelfzema (VWS, Den Haag)
19 Dr. W. Slooff (CSR)
20 Drs. J.H. Canton (Laboratorium voor Ecotoxicologie)
21 Ir. P.T.J. van der Zandt (CSR)
22 Ir. J.M. M. Herremans (CSR)
23 Dr. D.T.H.M. Sijm (CSR)
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