



EUROPEAN COMMISSION  
HEALTH & CONSUMER PROTECTION DIRECTORATE-GENERAL  
Directorate C - Scientific Opinions  
**C1 - Follow-up and dissemination of scientific opinions**

**PRELIMINARY REPORT ON  
THE ECOLOGICAL RISK ASSESSMENT OF CHEMICALS**

**DISCUSSED BY THE SCIENTIFIC STEERING COMMITTEE  
AT ITS MEETING OF 7-8 NOVEMBER 2002**

NOTE :

This report was discussed by the SSC on 7-8 November 2002 as a preliminary document. It is based on data published in scientific journals or available from ongoing research projects. Other relevant information may, however, be available from other sources that do not commonly report on scientific or technical press. Scientists, industrial associations, research institutes, veterinary pathology laboratories, etc... are therefore invited to comment on the attached documents and, if appropriate, provide additional information. These contributions should be sent **before 3 January 2003** to the secretariat of the SSC. The SSC will, if appropriate, integrate them in its final opinion. The industry is invited to, as far as possible, coordinate its comments and channel them through existing associations. Individual comments are, however, also welcomed.

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**TASK FORCE ON HARMONISATION OF RISK ASSESSMENT**

**WORKING GROUP ON THE ENVIRONMENT**

**REPORT ON A HARMONISED APPROACH TO  
THE ECOLOGICAL RISK ASSESSMENT OF  
CHEMICALS**

**1. INTRODUCTION**

Several SANCO Scientific Committees are involved in the environmental (ecological) risk assessment of chemicals. Other Scientific Committees outside SANCO are also involved.

Basically the task can be divided in two main activities:

1. Revision of comprehensive (in-depth, holistic) risk assessment prepared by MS for registration, authorisation, etc.
- Comprehensive risk assessment of High Production Volume Chemicals. Related to Commission Regulation (EC) 1488/94 this includes a full risk assessment of the whole life cycle of certain priority chemicals. The assessments cover local, regional and continental scenarios and try, whenever possible, to use real emission data and to establish comparisons between predicted and observed level. The CSTEE has produced opinions on several comprehensive risk assessments.
- Risk Assessment for new and existing plant protection products (pesticides and biocides). In principle this a type of targeted risk assessment to address the risks associated with the specific use of plant protection products by the farmers under Directive 91/414/EEC. The outcome of this risk assessment is the inclusion of the active substance on a positive list (Annex I) of substances that can be used in plant protection products, with or without restrictions, or the total ban of the substance. Monitoring data are essential for proper identifications of the properties of the substance. Risk Assessment for New Pesticides. In principle this is a type of targeted risk assessment to address the risks associated with the specific use of plant protection products by the farmers under Directive 91/414/EEC. The outcome of this risk assessment is the inclusion of the active substance in a positive list (Annex I) of substances that can be used in plant protection products when a “safe use” is identified under the Uniform Principles.

- Predictive risk assessment of new notified substances. Related to Commission Directive 93/67/EEC this constitutes a pre-requisite for the production-import-commercialisation of substances that are not currently on the EU market. It represents a predictive approach for a holistic risk assessment of all potential risks associated with the life cycle of the substance.
  - Risk Assessment for Veterinary Medicines. Under Directive 2001/82/EEC the environmental risk of new veterinary medicines must be assessed before their commercialisation. It is a type of targeted risk assessment for the inclusion in a positive list. It mostly focuses on local scenarios for national and central marketing authorisations.
  - Risk Assessment for Human Medicines. Under Directive 2001/83/EEC the environmental risk of new medicines must be assessed before their commercialisation. It is a type of targeted risk assessment mostly focusing on local scenarios for national and central marketing authorisations. No formal guidance documents have been made available yet.
  - Risk Assessment for Biocides. Regulated by Directive 98/8/EC this also represents a targeted risk assessment for inclusion of biologically active chemicals in a positive 1A-1B low risk list. Nevertheless, this regulation presents a much larger variability on intended uses than those related to pesticides or veterinary medicine and therefore, a larger diversity of scenarios both local and regional should be required. The Directive is currently under implementation and the opinion of the CSTEE on the technical guidance document has been requested.
  - Risk assessment for feed additives. Regulated by Directive 2001/79/EC the assessment of additives in animal nutrition includes the specific requirement of environmental impact. The guidelines were drafted by the SCAN and submitted to the Commission for adoption. The basic principles are equivalent to those for veterinary medicines.
  - Risk assessment of food additives, packaging materials and cosmetics. No environmental assessment is currently conducted in the case of additives for human nutrition, packaging materials nor cosmetics.
2. Review of risk assessment conducted for specific targets as supporting scientific evidence for particular decisions. These risk assessments are basically produced by consultants, contracted ad-hoc for each particular assessment.
- Targeted risk assessment of problematic substances/uses. These represent a shortened version of the previous type concentrated on certain specific uses of dangerous chemicals, trying to support decisions on specific bans or restrictions. They do not cover the whole life-cycle of the chemical but certain aspects of it, and mostly focus on local or regional scenarios. The use of real emission/exposure data is crucial for a proper decision and in most cases includes a comparative study with those other substances/technologies considered as proper alternatives for the studied chemical.

The CSTEE has produced several opinions on targeted risk assessment prepared by consultants contracted by DG Enterprise.

- Risk assessments as part of other regulatory decisions. In addition to specific risk assessment studies such as those presented above, risk assessment also constitutes the basis for several decision-makings in the related areas. To give an example relevant for the CSTEE work, risk assessment decisions are incorporated in the Water Framework Directive to give guidance on prioritisation of pollutants and to set Environmental Quality Standards.

An additional distinction can be made according to the marketed situation of the chemicals already on the market or submitted for authorisation. Obviously, this situation will determine the type of risk assessment to be conducted. If the chemical is already on the market, the evaluation of real exposure levels and environmental problems could be possible. For risks assessments conducted prior to the authorisation of the product, the assessment must depend exclusively on modelled predictions and default estimations.

Currently, the market situation has also legal consequences on the need for conducting the risk assessment and the availability of information. However, this situation is expected to change with the implementation of the recommendations of the White Paper on the Future Chemicals Strategy adopted in February 2001.

## **2. THE ROLE OF DG SANCO SCIENTIFIC COMMITTEES IN COMPREHENSIVE/IN DEPTH ENVIRONMENTAL RISK ASSESSMENTS**

Basically, the SC is responsible for an independent evaluation of the scientific basis of the final conclusions adopted by the technical experts of the Commission and MS, or of the dossier submitted by the applicant through the Commission. The structure is represented in Figure 1.

# THE RISK ASSESSMENT PROCESS

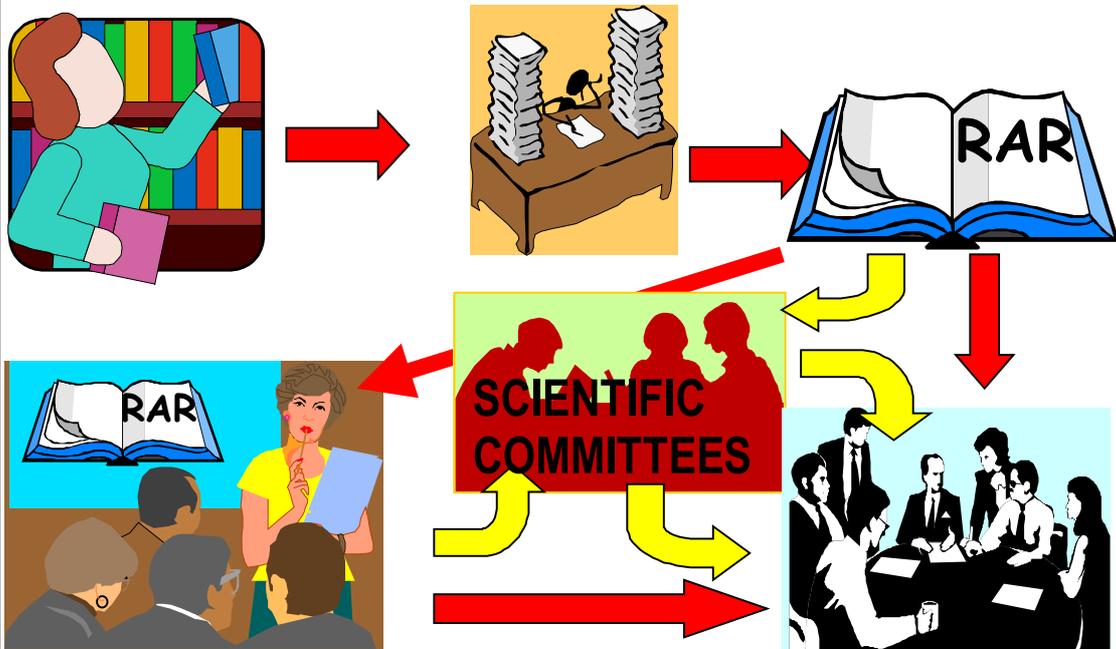


Figure 1: Schematic representation of the risk assessment process. The assessment of the available information concludes with the production of a risk assessment report (RAR) or dossier summary produced by the rapporteur MS, the applicant or a contracted consultant. The opinion of the SCs can be requested either at this stage or after and in-depth consideration by experts groups from the Commission services and experts from all MSs. Then, the report and the opinion of the responsible SC are submitted to decision makers. The opinions of the SCs become publicly available through Internet.

The SCP and the CSTEE are Committees with most experience in these assessments. The SCAN is involved in the assessment of feed additives, the guidelines for which are largely similar as those for veterinary medicines; the latter are assessed outside SANCO by the EMEA

A main difference concerns the terms of reference for the consultation:

- For the SCP / SCAN opinion is requested on specific questions from the Commission regarding the evaluation of each pesticide / feed additive in the context of the Council Directives 91/414/EEC and 2001/79/EC, respectively.
- For the CSTEE opinion is requested in general terms related to the quality of the risk assessment reports produced for priority chemicals under Regulation 793/93 and scientific basis of the conclusions, using the following general questions:

*In the context of Regulation 793/93 (Existing Substances Regulation), and on the basis of the examination of the Risk Assessment Report the CSTEE is invited to examine the following issues:*

- 1. Does the CSTEE agree with the conclusions of the Risk Assessment Report?*
- 2. If the CSTEE disagrees with such conclusions, the CSTEE is invited to elaborate on the reasons for this divergence of opinion.*

In addition, the SCP opinions are requested for both, new and existing pesticides, while the CSTEE opinion is requested only on existing chemicals but not on new (notified) substances which are treated confidentially.

### **3. DESCRIPTION OF ENVIRONMENTAL RISK ASSESSMENT PROCEDURES**

Although environmental risk is defined as the probability of observing/producing adverse environmental/ecological effects, European legislation of environmental risk assessments includes in all cases a low tier assessment based on a deterministic approach: if the exposure is clearly below the concentrations found toxic in laboratory studies, the environmental risk is expected to be low enough to be accepted.

Each piece of legislation sets specific methods for risk characterisation (PEC/PNEC; TER; etc.) but in the deterministic approach the whole assessment is reduced to the

acceptability of certain ratios between the expected exposure and the observed toxicity, defined by a set of application/uncertainty factors.

The CSTEE opinion on risk assessment for terrestrial ecosystems identified clear inconsistencies among the margins of safety recommended for general chemicals, pesticides or veterinary medicines, particularly in the terrestrial assessment. The new proposal for the revision of the TGD, if finally accepted, will extrapolate these inconsistencies to aquatic compartments.

However, the SCs have recognised that the criteria for acceptability are political, not scientific, decisions, and, therefore, have focused their opinions on the availability of scientific sound information for supporting the conclusions of low risk based on existing regulatory decisions (i.e., the Uniform Principles for pesticides, the TGD for general chemicals).

A description of the ERA procedures for different types of chemicals is included below.

## **3.1 RISK ASSESSMENT OF INDUSTRIAL CHEMICALS**

### **INTRODUCTION**

This is concerned with assessing likelihood of adverse effects from industrial chemicals – existing (on the market) and new (before market) - on ecosystems in general. This involves comparing likely exposure concentrations with no-effect concentrations. The process is described in the Technical Guidance Document in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94 on risk assessment for existing substances (EC, 1996) or TGD.

### **EXPOSURE**

For new substances, usually no relevant measured data are available. Therefore, concentrations of a substance in the environment must be estimated. Unlike for new substances, the exposure assessment of existing substances does not always depend upon modeling. Data on measured levels in various environmental compartments have been gathered for a number of substances.

In many cases a range of concentrations from measured data or modelling is obtained. This range can reflect different conditions during manufacturing and use of the substance, or may be due to assumptions in or limitations of the modeling or measurement procedures. Measured concentrations can also have a considerable uncertainty associated with them, due to temporal and spatial variations.

For existing chemicals, the rapporteur initially makes the generic “reasonable worst case” exposure assessment based on modeling, to derive an environmental concentration.

The subsequent step is to estimate the substance’s release rate based upon its use pattern. All potential emission sources are analysed from production and formulation to use and disposal, and the receiving environmental compartment(s) is/are identified. After assessing release, the fate of the substance once released to the environment is considered. This is estimated by considering likely routes of exposure and biotic and abiotic transformation processes. The quantification of distribution and degradation of the substance (as a function of time and space) leads to an estimate of  $PEC_{local}$  and  $PEC_{regional}$ . The PEC calculation is not restricted to the primary compartments, surface water; soil and air, but also includes secondary compartments such as sediments and groundwater.

For the release estimation of substances, a distinction is usually made between substances that are emitted through point sources to which specific locations can be assigned and substances that enter the environment through diffuse releases.

Point source releases have a major impact on the environmental concentration on a local scale ( $PEC_{local}$ ) and contribute to the environmental concentrations on a larger scale ( $PEC_{regional}$ ).

$PEC_{local}$

The concentrations of substances released from point sources are assessed for a generic local environment. This is not an actual site, but a hypothetical site with predefined, agreed environmental characteristics, the so-called “standard environment”. These environmental conditions can be average values, or reasonable worst-case values, depending on the parameter in question. The scale is usually small and the targets are assumed to be exposed in, or at the border of, the area.

#### PEC<sub>regional</sub>

The concentrations of substances released from point and diffuse sources over a wider area are assessed for a generic regional environment. The PEC<sub>regional</sub> takes into account the further distribution and fate of the chemical upon release. It also provides a background concentration to be incorporated in the calculation of the PEC<sub>local</sub>. As with the local models, a generic standard environment is defined. The PEC<sub>regional</sub> is assumed to be a steady-state concentration of the substance.

For the chemical industry, two separate industrial categories exist: one for basic chemicals and another for chemicals used in synthesis. Basic chemicals are considered to comprise commonly used chemicals such as solvents and pH-regulating agents such as acids and alkalis. Also the primary chemicals from the oil refining process are considered as basic chemicals. Substances used in synthesis fall into one of two classes, namely intermediates (substances produced from a starting material to be converted in a subsequent reaction into a next substance) and other substances. These other substances consist mainly of ‘process-regulators’ (e.g. accelerators, inhibitors, indicators). For industrial category 5 (personal/domestic) the use and application of substances (as such or in formulations) is considered at the scale of households. The types of application are e.g. adhesives, cosmetics detergents, and pharmaceuticals. Some applications have been covered in other industrial categories at the stage of private use. These applications comprise fuels and fuel additives (mineral oil and fuel industry), paint products (paints, lacquer and varnishes industry) and photochemicals (photographic industry). For industrial category 6 (public domain), use and application at public buildings, streets, parks, offices, etc. is considered.

A standard table in the TGD provides the estimated total release fractions of the production volume (emission factors) to air, (waste) water and industrial soil during production, formulation, industrial/professional use, private use, and recover, according to their industrial category. The production volume is defined as the total tonnage of a substances brought to the European market in one year, i.e. the total volume produced in the EU plus the total amount imported into the EU, and minus the total volumes exported from the EU excluding the volumes of the substance present in products imported/exported. The total volume released is averaged over the year and used for the PEC<sub>regional</sub> calculation.

Other standard tables in the TGD are used for the determination of the releases from point sources for the evaluation of PEC<sub>local</sub>. They provide the fraction of the total volume released that can be assumed to be released through a single point source, and the number of days during which the substance is released, thus allowing the daily release rate at a main point source to be calculated.

If the major share of a substance placed on the market remains in chemical products or articles at their end of service life (releases during production, processing and use are

comparatively small), the waste life cycle stage of the substance will need particular attention. This refers e.g. to organic substances in landfills and metals in waste incineration processes. The underlying criterion for considering waste emissions in the risk assessment of substances, is that the waste stage will contribute significantly to the overall exposure or environmental concentration in comparison to the emissions from other parts of the life cycle of the substance (e.g. production and use stages).

Transport and transformation (“fate”) describe the distribution of a substance in the environment, or in organism, and how it changes with time (in concentration, chemical form, etc.), thus including both biotic and abiotic transformation processes. In general, the assessment of degradation processes is based on data, which reflect the environmental conditions as realistically as possible. Data from studies where degradation rates are measured under conditions that simulate the conditions in various environmental compartments are preferred. The applicability of such data, however, have to be judged in the light of any other degradation data including results from screening tests. Most emphasis is put on the simulation test results but in the absence of simulation test data, degradation rates and half-lives have to be estimated from screening test data.

A listing of various PECs is given in tables of the TGD (EC, 1996)

## **EFFECTS**

The effects assessment comprises the following steps:

- Hazard identification: which aims to identify the effects of concern. For existing substances the aim is also to review the classification of the substance while for new substances a proposal on classification is done;
- Dose (concentration) – response (effect) assessment: at this step the predicted no effect concentration (PNEC), shall, where possible, is determined.

The function of risk assessment is the overall protection of the environment. Certain assumptions are made concerning the aquatic environment which allow, however uncertain, an extrapolation to be made from single-species, short-term toxicity data to ecosystem effects. It is assumed that:

- Ecosystem sensitivity depends on the most sensitive species, and;
- Protecting ecosystem structure protects ecosystem processes.

If correct, these two assumptions have important consequences. By attempting establish which species is the most sensitive to the toxic effects of a chemical in the laboratory, extrapolation can in principle subsequently be based on the data from that species. Furthermore, the functioning of any ecosystem in which that species exists is protected provided the structure is not sufficiently distorted as to cause an imbalance. It is generally accepted that protection of the most sensitive species should protect structure, and hence ecosystem processes.

Currently, for new chemicals, the testing strategy is defined by the production/import tonnage. For existing chemicals, the ERA is based on a revision of the available

information conducted by the producer/importer. However, the White Paper on the future for a Chemical Strategy considers the harmonisation of procedures for both existing and new chemicals.

In any case, for all new substance the pool of data from which to predict ecosystem effects is very limited: only short-term data are available at the base-set. For most existing substances the situation is the same; in many cases, only short-term toxicity data are available. In these circumstances, it is recognized that, while not having a firm scientific validity, empirically derived assessment factors must be used. Assessment factors have also been proposed by the EPA and OECD. In applying such factors, the intention is to predict a concentration below which an unacceptable effect will most likely not occur.

In establishing the size of these assessment factors, a number of uncertainties must be addressed to extrapolate from single-species laboratory data to a multi-species ecosystem. These areas have been adequately discussed in other papers, and may best be summarized under the following headings:

- Intra- and inter-laboratory variation of toxicity data;
- Intra- and inter-species variations (biological variance);
- Short-term to long-term toxicity extrapolation;
- Laboratory data to field impact extrapolation. (Extrapolation is required from mono-species tests to ecosystem. Additive, synergistic and antagonistic effects arising from the presence of other substances may also play a role).

The proposed application factors are presented below.

AVAILABLE INFORMATION	APPLICATION FACTOR
Acute LC50 on three relevant taxa (Aquatic: Fish, invertebrates, algae) (Soil: Plant, earthworms, soil micro-organisms)	1000
Chronic NOEC on one taxonomic group	100
Chronic NOECs on two taxonomic groups	50
Chronic NOECs on three taxonomic groups	10
	Case-by-case

Reliable QSAR estimates for fish, daphnids and algal toxicity are available for chemicals with a non-specific mode of action. These estimates can be used to assist in data evaluation and/or to contribute to the decision making process whether further testing is necessary to clarify an endpoint of concern and if so, to optimise the testing strategy, where appropriate.

Substances that strongly absorb on to sediment particles or that bind chemically or via ion exchange to sediment components are candidates for performing an effects assessment for sediment organisms. For most chemicals the number of toxicity data on benthic organisms is limited. At the base-set level for new and existing substances there is no requirement for toxicity tests with sediment organisms. Therefore, as a screening approach the equilibrium partitioning method is proposed to compensate for this lack of toxicity data. This screening method triggers the implementation of whole-sediment tests with benthic organisms.

Chemicals can reach the soil via several routes: application of sewage sludge in agriculture, direct application of chemicals and deposition from the atmosphere. This means that the possibility of adverse effects for soil ecosystems has to be assessed. The proposed strategy focuses on effects of chemicals on soil organisms. At present no strategy is available to assess possible effects on soil processes like filtration, buffering capacity and metabolic capacity.

However, the terrestrial ecosystem comprises the above-ground community, a soil community and a groundwater community. Currently, only effects on soil organisms exposed directly via pore water /or soil are addressed. Reference is made to the strategy for air and for bioaccumulation and secondary poisoning of birds and mammals. So far, it is not possible to carry out effects assessment for the groundwater community because no toxicity data are made available.

There are several motivations for introducing the usage of “Species Sensitivity Distributions” (SSDs) into the PNEC derivation, but the main one is that they make use of all the available data when deriving a PNEC. Therefore taking into account the information concerning the interspecies variability will not lead to more stringent outcomes for substances with larger databases.

However, such methods can also be criticised. The most common drawback is that risk assessment based on SSDs (or probabilistic assessment in general) is more complex than the deterministic approach and requires additional (loss of transparency). Complexity could lead to confusion, or to lack of confidence, or to increase the potential for generating mathematical artefacts. Some of the other drawbacks like the question of the representativeness of selected test species; the comparability of different endpoints and the arbitrary choice of trigger values (fixed value of 10 or a specific percentile and/or a statistical confidence level) are also applicable to the deterministic risk assessment.

The methodology used for effects assessment (and therefore the risk characterisation) of chemicals in water and soil cannot be applied yet in the same manner to the atmosphere. Methods for the determination of effects of chemicals on species arising from atmospheric contamination have not yet been fully developed, except for inhalation studies with mammals.

The TGD does not include guidance on a quantitative characterization of risk by comparison of the  $PEC_{air}$  to  $PNEC_{air}$ , only a qualitative assessment for air is feasible. However, in certain cases, the rapporteur MSs have conducted a quantitative evaluation of the available information, establishing comparisons among the relevance of the available information and the required application factor for a PNEC derivation, or estimating the margin of safety provided by the ratio between the exposure estimation and the measured toxicity on plants or foliar/ground invertebrates.

For the evaluation of an atmospheric risk, the following abiotic effects of a chemical on the atmosphere have to be considered:

- Global warming;
- Ozone depletion in the stratosphere;
- Ozone formation in the troposphere;
- Acidification.

If for a chemical there are indications that one or several of these effects occur, expert knowledge needs to be consulted. A proposed quantitative approach is described in De Leeuw (1993):

#### Global warming

The impact of a substance on global warming depends on its IR absorption characteristics and its atmospheric lifetime. A potential greenhouse gas shows absorption bands in the so-called atmospheric window (800-1200nm).

#### Stratospheric ozone

A substance may have an effect on stratospheric ozone if e.g.

- the atmospheric lifetime is long enough to allow for transport to the stratosphere, and;
- it contains one or more Cl or Br substituents.

In general, ozone depletion potential values approach zero for molecules with atmospheric lifetimes less than one year.

#### Tropospheric ozone

The generation of tropospheric ozone depends on a number of factors:

- the reactivity of the substance and the degradation pathway;
- the meteorological conditions (the highest ozone concentrations are expected at high temperatures, high levels of solar radiation and low wind speeds);
- the concentration of other air pollutants (the concentration of nitrogen oxides have to exceed several ppb).

#### Acidification

During the oxidation of substances containing Cl, F, N or S substituents, acidifying components (e.g. HCl, HF, NO<sub>2</sub> and HNO<sub>3</sub>, SO<sub>2</sub> and H<sub>2</sub>SO<sub>4</sub>) may be formed. After deposition, these oxidation products will lead to acidification of the receiving soil or surface water.

### RISK ASSESSMENT

This is most often carried out by comparing PECs with appropriate PNECs to give a variety of ratios (ie.  $PEC/PNEC = RQs$  cf. TER or PPPs). Values of less than one are generally deemed to be acceptable and no further action is taken. Values greater than one either require reconsideration (refinement of PECs and/or PNECs) or suggest the need for action.

Typical PEC refinement options are based on use of real emissions instead of the default values included in the TGD. The refinement of the PNEC value can be conducted by incorporating additional chronic toxicity data or moving to higher tier assays such as mesocosms or field studies. However, this second option, while common for plant protection products, is rarely considered in the case of industrial chemicals.

## 3.2 PESTICIDES: ACTIVE SUBSTANCES FOR PLANT PROTECTION PRODUCTS

### GENERAL

The detailed evaluation and decision making criteria are laid down in **Annex VI** (uniform principles) to the Directive 91/414/EEC. Thus this Annex may be considered as a structured guidance for risk and benefit analyses of plant protection products (PPP). Additional technical guidance is presented in Guidance Documents (e.g. DG SANCO, 2000a; 2000b; 2001ab; 2002; FOCUS 2000; 2001).

*General evaluation principles* are that all normal conditions under which the PPP may be used (regarding plant health, principles of integrated control, purpose of use, dose, frequency and timing of applications, agricultural practice, environmental conditions including climate) as well as the consequences of its use must be taken into account. The evaluation in the first step is based on the best available data but in a second step also takes account of potential uncertainties in the data and the range of use conditions that are likely to occur (realistic worst case approach), to determine whether the results could differ significantly.

The environmental assessment comprises both the hazard identification and risk assessment. For a hazard identification, for example persistence and bioconcentration in aquatic and soil organisms are considered as inherent properties. The approach to handle these as independent parameters is not dealt with in this chapter, but persistence is used as a property to trigger the performance of selected effect studies for risk assessment.

With respect to the *fate, distribution and unwanted impacts* of the active substance, i.e. the potential risk, no authorization of a PPP for the evaluated conditions of use can be granted, if – inter alia - the following are observed:

- Concentrations in **groundwater** are expected to exceed the lowest of the following limit values :
- 1) Maximum concentration set in Council Directive 80/778/EEC related to the quality of water intended for human consumption, or the maximum concentration laid down by the Commission when including the active substance in Annex I.

No authorisation shall be granted if the concentration of the active substance or of relevant metabolites, degradation or reaction products in groundwater, may be expected to exceed, as a result of use of the plant protection product under the proposed conditions of use, the lower of the following limit values :

- i. The maximum permissible concentration laid by Council Directive 80/778/EEC <sup>1</sup> of 15 July 1980 relating to the quality of water intended for human consumption, or
- ii. The maximum concentration laid down by the Commission when including the active substance in Annex I, on the basis of appropriate data, in particular toxicological data, or, where that concentration has not been laid down, the concentration corresponding to one tenth of the ADI laid down when the active

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<sup>1</sup> OJ L 229,30. 8. 1980, p. 11. Directive as last amended by Directive 91/692/EEC (OJ L 377, 31. 12. 1991, p. 48).

substance was included in Annex I unless it is scientifically demonstrated that under relevant field conditions the lower concentration is not exceeded.

No authorisation shall be granted if the concentration of the active substance or of the relevant metabolites, breakdown or reaction products to be expected after use of the plant protection product under the proposed conditions of use in surface water :

- Exceeds, where the surface of the water in or from the area of envisaged use is intended for the abstraction of drinking water, the values fixed by Council Directive 75/440/EEC of 16 June 1975 concerning the quality required of surface water intended for abstraction of drinking water in the Member States<sup>2</sup>, or
- Has an impact deemed unacceptable on non-target species, including animals, according to the relevant requirements provided for in point 2).

The proposed instructions for use of the plant protection product, including procedures for cleaning application equipment, must be such that the likelihood of accidental contamination of surface water is reduced to a minimum.

No authorisation shall be granted if the airborne concentration of the active substance under the proposed conditions of use is such that either the AOEL or the limit values for operators, bystanders or workers are exceeded.

When that concentration has not been laid down, the concentration corresponding to one tenth of the ADI laid down in Annex I, unless it is scientifically demonstrated that under relevant field conditions the lower concentration is not exceeded.

## 2) As regards **impact on non-target species** :

- Where there is a possibility of birds and other non-target vertebrates being exposed, **no** authorisation shall be granted if :
  - The acute and short-term toxicity/exposure ratio for birds and other non-target terrestrial vertebrates is less than 10 on the basis of LD50 or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact occurs after use of the plant protection product according to the proposed conditions of use ;
  - The bioconcentration factor (BCF, related to fat tissue) is greater than 1, unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable effect occur – directly or indirectly – after use of the plant protection product according to the proposed conditions of use.
- Where there is a possibility of aquatic organisms being exposed, **no** authorisation shall be granted if :
  - The toxicity/exposure ratio for fish and Daphnia is less than 100 for acute exposure and less than 10 for long-term exposure, or
  - The algal growth inhibition/exposure ratio is less than 10, or

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<sup>2</sup> OJ No L 194, 25. 7. 1975, p. 34. Directive as last amended by Directive 91/692/EEC (OJ No L 377, 31. 12. 1991, p. 48).

- The maximum bio concentration factor (BCF) is greater than 1000 for plant protection products containing active substances which are readily biodegradable or greater than 100 for those which are not readily biodegradable,

Unless it is clearly established through an appropriate risk assessment that under field conditions no unacceptable impact on the viability of exposed species (predators) occurs – directly or indirectly – after use of the plant protection product according to the proposed conditions of use.

- Where there is a possibility of honeybees being exposed, no authorisation shall be granted if the hazard quotients for oral or contact exposure of honeybees are greater than 50, unless it is clearly established through an appropriate risk assessment that under field conditions there are no unacceptable effects on honeybee laevae, honeybee behaviour, or colony survival and development after use of the plant protection product according to the proposed conditions of use.
- Where there is a possibility of beneficial arthropods other than honeybees being exposed, no authorisation shall be granted if more than 30% of the test organisms are affected in lethal or sublethal laboratory tests conducted at the maximum proposed application rate, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on those organisms after the use of the plant protection product according to the proposed conditions of use. Any claims for selectivity and proposals for use in integrated pest management systems shall be substantiated by appropriate data.
- Where there is a possibility of earthworms being exposed, no authorisation shall be granted if the acute toxicity/exposure ratio for earthworms is less than 10 or the long-term toxicity/exposure ratio is less than 5, unless it is clearly established through an appropriate risk assessment that under field conditions earthworm populations are not at risk after use of the plant protection product according to the proposed conditions of use.
- Where there is a possibility of non-target soil micro-organisms being exposed, no authorisation shall be granted if the nitrogen or carbon mineralisation processes in laboratory studies are affected by more than 25% after 100 days, unless it is clearly established through an appropriate risk assessment that under field conditions there is no unacceptable impact on microbial activity after use of the plant protection product according to the proposed conditions of use, taking account of the ability of micro-organisms to multiply.

<b>Species</b>	<b>short-term TER Based on acute toxicity data</b>	<b>Long-term TER Based on chronic data</b>
<b>Terrestrial organisms (BCF &gt;1)</b>		
Birds	<10	<5
Vertebrates	<10	<5
Earthworms (representative for soil organisms)	<10	<5
Bees	Alternative method ( a hazard ratio value must be below 50 to be acceptable)	
Non-target arthropods (tests to be carried out with two standard species as surrogates and two crop specific species)	Alternative method (Decision based on effect level instead of TER) (>30% lethal)	
Soil micro-organisms	Alternative method (Decision based on effect level instead of TER) (>25% lethal)	
Further non-target organisms	test procedures and assessment be discussed on a case-by-case basis	
- Soil macro-fauna (e.g. Collembola or gamasid mite; reproduction or litter bag) (for persistent substances only=DT90>100 days)		
- Other flora and fauna believed to be at risk (assessment scheme to be developed)	BCF <100 or <1000 depending on biodegradation potential	
- Secondary poisoning		
<b>Aquatic organisms</b>		
Fish	<100	<10
Daphnia	<100	<10
Algae	<10*	
Bioconcentration : BCF	>1000 for degradable	>100 for non degradable

\* Algal growth inhibition test for 72 h. Since algae go through several cell division cycles during the exposure time, the test can be considered as algae lifecycle test (long term exposure), however, the acute endpoint (EC50) is used.

## **DETAILS ON ENVIRONMENTAL EXPOSURE AND RISK ASSESSMENT**

### **GROUNDWATER**

Residues which enter **groundwater** may cause exposure to the consumer of drinking water. Risk Assessment on Groundwater is performed by a tiered approach comprising modelling, laboratory studies, lysimeter studies and – if needed – field testing. Proceeding from one Tier to another is triggered by fixed concentrations.

Vulnerability of ground water to contamination resulting from the use of an active substance is addressed by nine realistic worst-case scenarios. Collectively, these represent agriculture across Europe, for the purposes of an initial screening (**Tier 1**) EU-level assessment of leaching potential. The scenarios do not mimic specific fields, and nor are they necessarily representative of the agriculture at the location after which they are named or in the Member States where they are located.

The purpose of the standard scenarios is to assist in establishing if “safe” scenarios exist which are relevant for use of a substance. Since they form Tier 1 of the assessment, they have been defined to represent a realistic worst case.

From this first Tier assessment there are three possible outcomes

1. The critical model output for a substance may exceed 0.1 µg/l for all relevant scenarios
  2. It may be less than 0.1 µg/l for all relevant scenarios
  3. It may exceed 0.1µg/l for some relevant scenarios and be less than 0.1µg/l for others
- If a substance exceeds 0.1µg/l for all relevant scenarios, then Annex 1 inclusion would not be possible unless convincing higher Tier data (e.g. studies, monitoring or more refined modelling) were available to over-ride the modelling results.
  - If a substance occurs at less than 0.1µg/l for all relevant scenarios, then the choice of a realistic worst-case definition for the scenarios means that there can be confidence that the substance is unlikely to cause harm in the great majority of situations in the EU. This does not exclude the possibility of leaching in highly vulnerable local situations within specific Member States, but such situations should not be widespread and can be assessed at the Member State level.
  - If a substance occurs at less than 0.1µg/l for at least one but not for all relevant scenarios, then in principle the substance can be included on Annex 1 with respect to leaching to groundwater. The scenarios represent major agricultural areas of the EU, so this would indicate that uses unlikely to cause harm have been identified, which are significant in terms of agriculture in the EU. The scenarios which gave results less than 0.1µg/l, along with the results of any higher Tier studies which already exist, help to indicate the extent of the acceptable uses which exist for the substance. These higher Tier studies could include lysimeter or field leaching studies, monitoring and more refined modelling. The results of the entire leaching assessment at the EU level could then be used to guide local assessments of leaching at the Member State level.” (FOCUS, 2000).

## **SURFACE WATER**

Risk Assessment on Surface water also is performed using a tiered approach. Depending on the results of the initial risk assessment, more detailed data relating to environmental exposure or hazard may be required to clarify the environmental risk. Such data are generated from an increasingly comprehensive series of studies (higher tiered studies). At each Tier a relevant comparison has to take place between the estimated exposure and the estimated hazard and there are thus separate Tiers for both exposure and hazard estimation. This includes fate modelling and laboratory fate studies (for the exposure assessment) as well as laboratory acute and chronic single

species testing on the lower Tier and – as higher Tier testing – full life cycle tests and aquatic microcosms (for the hazard assessment). Ecological monitoring is a further promising tool for risk assessment of existing plant protection products.

PEC-calculations are performed using mathematical simulation models that need environmental and chemical input data (FOCUS, 2001). “The first step in the Tiered approach is to estimate surface water exposure based on a putative extreme worst case loading scenario. However, it has been pointed out, that the proposed conditions do not necessarily represents worst-case conditions in all cases, and are particularly problematic for the Mediterranean area (Ramos et al., 2000). The estimated exposure may be compared to the relevant toxicity concentrations, the lethal or effect concentration, L(E)C50, or the No-effect concentration, NOEC, of the water organisms investigated. If, at this early stage, the use is considered safe no further surface water risk assessment is required. If however, the result indicates that use is not safe, it is necessary to proceed to a Tier 2 exposure assessment.”

The use is not considered safe in case the TERs are below the triggers already given in the first paragraph of this chapter.

### **TERRESTRIAL COMPARTMENT**

For the terrestrial compartment only a preliminary tiered assessment scheme has been developed (SCP, 2000), a Guidance document is available DG SANCO 2002.

“In the terrestrial compartment, several sub-compartments and various exposure routes must be distinguished:

- within the soil
- on the soil surface
- on plants

When a PPP is applied, terrestrial organisms can be exposed depending on where they live:

- within the soil, via soil particles with absorbed PPP (contact, oral uptake)
- on the soil surface, via soil particles or plants (contact, oral uptake) and by direct contact/uptake (spray liquid, granules)
- on plants, via contact and oral uptake of plant material or other animals, or by direct contact/uptake (spray liquid, granules).

This multitude of cases has to be addressed in different ways.

For non-target arthropods other than bees and soil micro-organisms, the exposure is not assessed separately from the effects but is included in the effects testing in a quantity and way that mimics more or less closely the worst cases of the intended use conditions (e.g., the PPP is mixed into soil, or onto a surface, which is then used directly in a toxicity test). Thus, the effect of the combined, overall exposure is often measured directly, without quantifying the respective contributions of the different exposure routes. In addition, effects of direct application of spraying liquid to the arthropods are often measured. However, this situation is expected to change shortly after the outcome of a second topic workshop for discussing the risk assessment protocol for these non-target arthropods (Candolfi et al, 2001). The new proposal includes an initial tier assessment based on dose-response toxicity tests on two selected species. The results

are presented as the standard LD50, where the dose is expressed as the application rate. These values are then compared with the expected exposure level, represented by overspray for in-crop populations and spray drift in the case of off-crop populations. Results of field trials and laboratory assays are compared for selecting the extrapolation factors that should be applied to the laboratory LD50s, and, considering that a similar approach was used for bees, the workshop conclusions recommended the use of Hazard Quotients for expressing the risk characterisation. These conclusions are currently under debate for their incorporation in the regulatory protocol.

For birds and mammals, earthworms and bees, however, the assessment includes an exposure estimation and the effect prediction based on dose-response tests. Exposure is estimated as the residue levels in/on food items (treated plants, granules, drops of spraying liquid) and estimations of daily food uptake (from general biological/ecological data); PECsoil, or the direct application rate, for vertebrates, earthworms and bees respectively (of DG SANCO, 2002).

## **HIGHER TIER RISK ASSESSMENT**

### **Plant Protection Products: Environmental risk assessment procedures and scenarios**

#### **GROUNDWATER**

Tier 1 assessment results in three possible outcomes: i.e. the model output may exceed 0.1 µg/l for all relevant scenarios, it may be less than 0.1 µg/l for all relevant scenarios, or it may exceed 0.1µg/l for some relevant scenarios and be less than 0.1µg/l for others. Both, the first and the last mentioned possibility can, nevertheless, result in the inclusion of the substance in Annex 1 if convincing higher Tier assessments results demonstrate acceptable use. The higher Tier assessment comprises both, the use of specific scenarios / site specific data and data from lysimeter studies or field testing as model input. As for Tier 1, no comparison with effect data is needed since groundwater as such is to be protected. The Tier 2 and 3 can be summarized as given in the annexed scheme (DG AGRICULTURE, 1995).

#### **SURFACE WATER**

The general concept of higher Tier exposure assessment for surface water is given for Tier 2 – 4 in the scheme (modified from reference 2). The scheme has been proposed by the FOCUS group on surface water and is - so far – not adopted by the Scientific Committee on Plants.

“Tier 2 assumes surface water loading based on sequential application patterns taking into account the degradation of the substance between successive applications. Again the PECs are calculated and may be compared to the same and/or different toxicity levels for aquatic organisms. As with Tier 1, if the use is considered acceptable at this stage, no further risk assessment is required whereas an unacceptable assessment necessitates further work using a Tier 3 calculation. In Tier 3, more sophisticated modelling estimations of exposure are undertaken using a set of 10 scenarios .... representing ‘realistic worst-case’ situations for surface water within Europe. At this

stage, the calculated PECs for each scenario are compared with relevant toxicity data and a decision made as to whether it is necessary to proceed to Tier 4 exposure estimation. Risk assessments using Tier 3 exposure estimation may incorporate higher-Tier toxicity data generated from micro- or mesocosm studies.

The final ... Tier 4 can be regarded as a higher-Tier exposure assessment step. This may include a variety of refinement options of different degrees of complexity covering, for example refinement of fate input parameters, or regional and landscape-level approaches. By its nature, Tier 4 will be a 'case-by-case' process, depending on the properties of the compound, its use pattern, and the areas of potential concern identified in the lower Tier assessments. As such, it is not appropriate to make specific recommendations for the Tier 4 process. Rather, some guidance on the sorts of approaches that may be applied has been developed. It is conceivable that Tier 4 approaches would be used both for Annex 1 listing and for national registration purposes. For certain specific uses, Tier 4 approaches could also be useful for identifying safe uses at Member State level, for example if certain local or regional considerations mean that the lower-Tier, EU level assessments were overly conservative.“<sup>2</sup>

### **TERRESTRIAL COMPARTMENT**

As for the aquatic compartment, TER-values (see first para for figures) are used as triggers to proceed to further options that are refined exposure estimates, higher-tier-studies or re-evaluation of the risk considering magnitude, probability and ecological significance of the effects. (Recently, probabilistic approaches are being put forward especially focused on birds and mammals. These include the use of field observations on the time spent for foraging in treated crops/orchards, in order to specify the likelihood, type and duration of exposure (SSC, 2000). The higher-tier-studies aim at (DGSANCO, 2002):

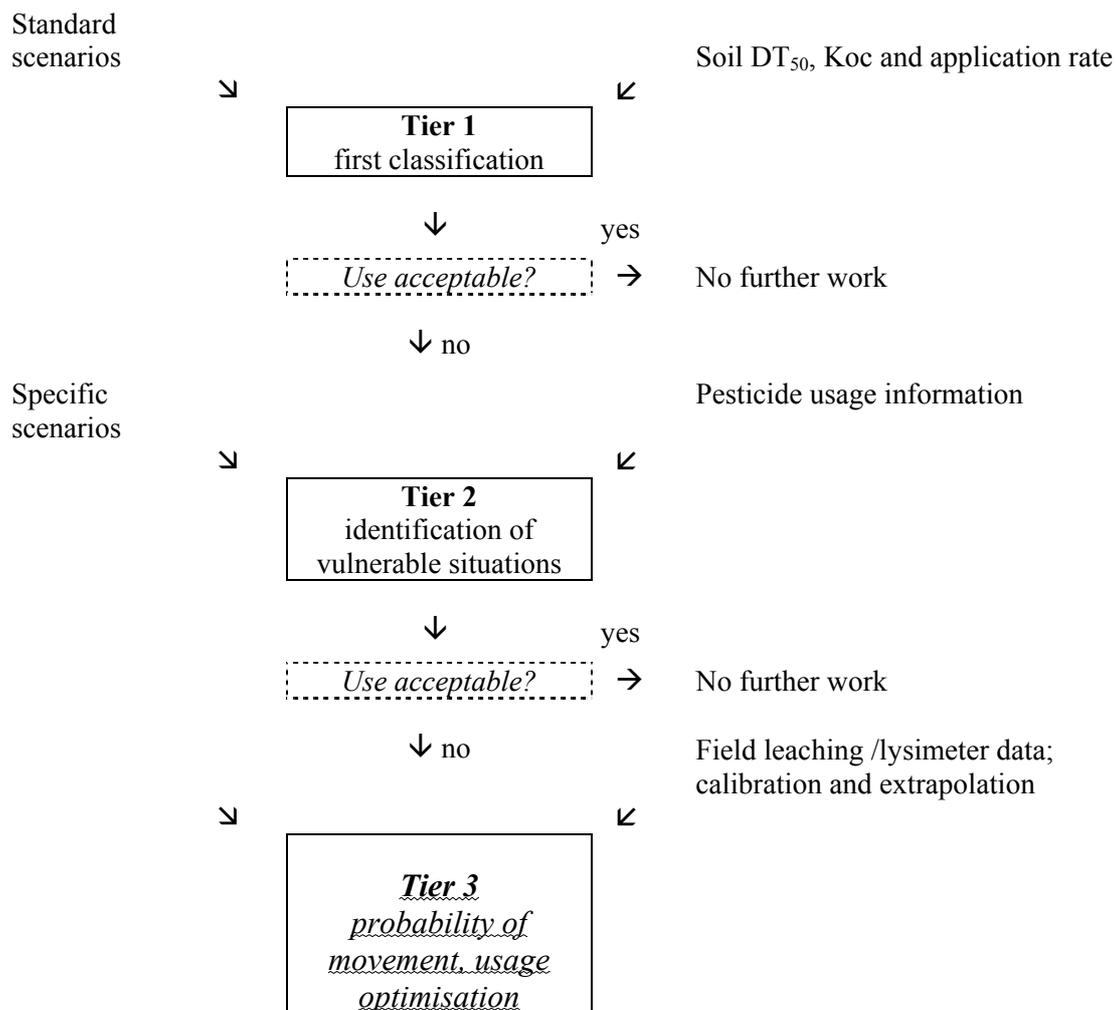
- generation of information on certain parameters of the risk assessment (e.g.: an avian acceptance test gives information on the palatability of potential food items which is used to refine the food consumption rate and thus the exposure estimate)
- investigate effects under more realistic conditions
- produce effects data for a wider range of species and cover inter-species interactions (example: model ecosystems or soil community tests in the field).

In general, the higher-tier-studies provide information on the exposure effects under more realistic conditions as compared to the laboratory studies, i.e. semi-field or field-tests. Some tests on the terrestrial compartment are standardized – such as the bee field tests. Most tests have to be planned on a case-by-case basis. Usually, the results of the basic tests together with the background information are used to define the design and objective of the higher-tier-study.

As compared to the surface water, exposure pathways are more complex and multiple, and thus the procedure to proceed from one tier to another has to be more flexible in considering different aspects. As a consequence, “linear” tiered assessment schemes comparable to those elaborated are not sufficient.

## Tiered assessment schemes: groundwater and surface water

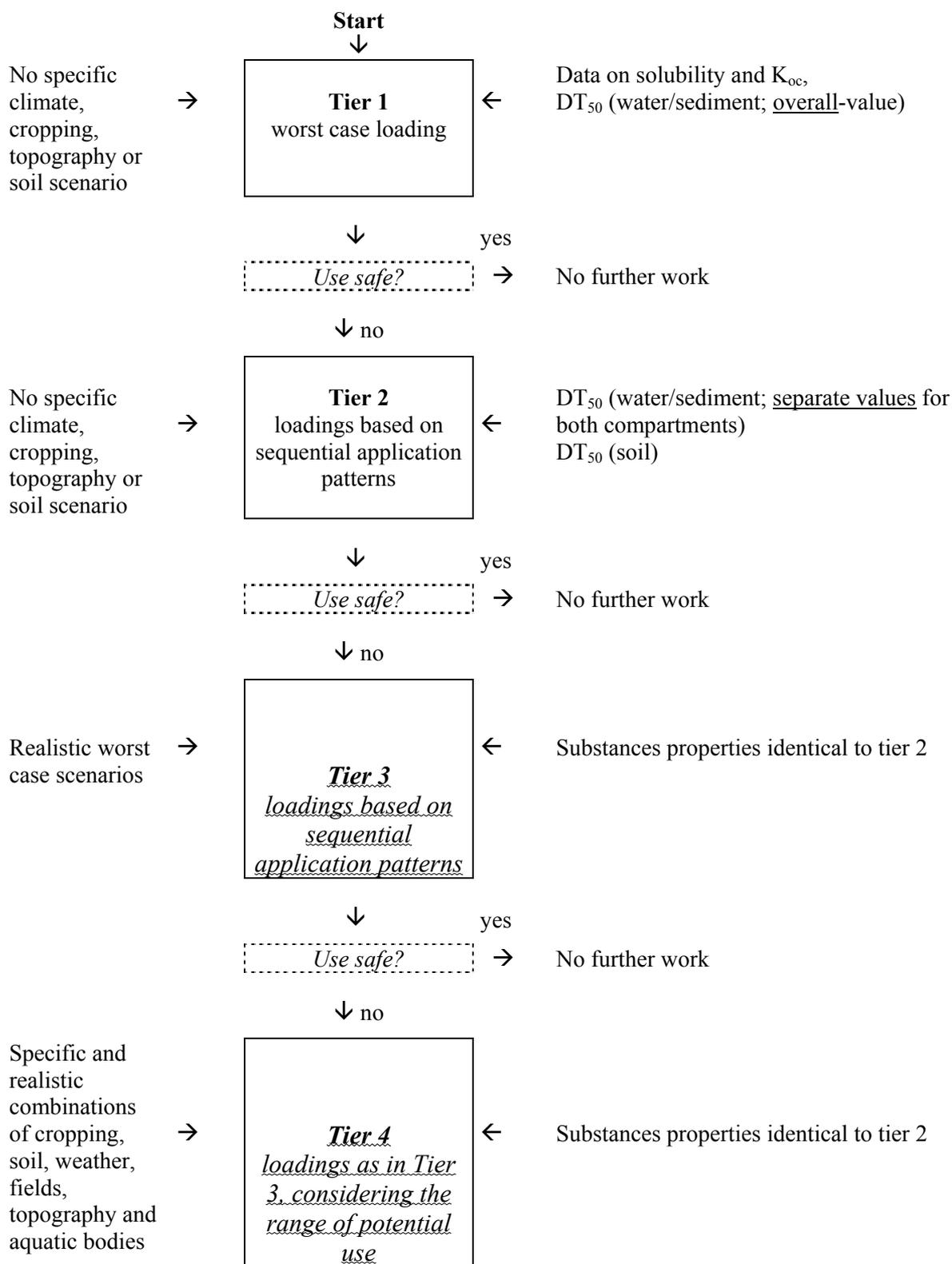
### 1. Groundwater



#### References:

1. FOCUS (2000) "FOCUS groundwater scenarios in the EU plant protection product review process" Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference Sanco/321/2000, 197pp
2. Modelling environmental fate of plant protection products in the context of their Authorization within the European Union, Document 1694/VI/95, DG Agriculture

## 2. Surface Waters



### References:

1. FOCUS (2001): FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC“. Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.0.xxxpp

### **3.3. PHARMACOLOGICAL VETERINARY MEDICINES.**

DG Enterprise is responsible for the European legislation on the registration of medicinal products. The registration process is mandated to the 'European Medicines Evaluation Agency' (EMA). Within EMA, scientific committees advise on the requests for marketing authorisation with respect to quality, efficacy and safety of the products. These committees are the CVMP for veterinary medicines and the CPMP for human (proprietary) medicines. Member states appoint two independent experts to both the CVMP and CPMP, that can be regarded as a "Scientific Board for Registration" and as 'Scientific Committees'; although, the appointment follows different rules than those used for the DG SANCO SCs. The Scientific Committees may rely on registered experts for additional expertise.

Member States are involved in the registration process through their formal representatives in the Standing Committees (SC) and Pharmaceutical Committee (PhC). The SC, as part of the DG Enterprise, decides on the proposals of the CVMP/CPMP and turns them into binding law. DG Enterprise has the PhC at its disposal, which was installed by Directive 75/320, for advice on interpretation of the directives, compulsory consultation when changing directives, and other issues.

The assessment of veterinary medicines is required by the Directive 2001/82/EC. Veterinary products notified under article 13 of the 2001/82 Directive are not required to be assessed on environmental risks according to Annex V of the directive; only the UK and NL assess 'old products'.

The EMA published guidance on the environmental risk assessment of veterinary pharmaceuticals (EMA, 1997). The assessment for veterinary products was initiated in 1997. The assessment scheme for veterinary medicines takes the use of the product and the properties of the products (anthelmintic or not) into account in determining the scope of the assessment (phase I or II), the emission routes (slurry-soil; water; pasture) and data requirements.

The assessment targets the parent drug by following a total residue approach. The identification of metabolites as substances of concern is not embedded in the assessment scheme; there are no compulsory data on degradation rate and route in any compartment.

A limited assessment is foreseen for substances with a generally accepted low hazard (vitamins, electrolytes), and with a presumed negligible emission and exposure levels. In fact, the exposure level that is considered irrelevant is quantified both for water and soil for antibiotics: 1 µg/L and 100 µg/kg, respectively. These triggers are substantiated with an assessment of a dataset of toxicity values of several antibiotics. The approach as such, i.e. determining the level of toxicity that will have a very small likelihood of being present in a product, and thus the level of exposure that can be considered an acceptable risk considering all products, is assumed to be equivalent to the practice in the exposure assessment, where the 'insignificant' emission routes are not considered in view of all emission routes. However, the assessment to determine an acceptable level is of poor quality from an ecotoxicological point of view (Knecht and Montforts, 2001). The soil trigger for feed additives is, on the contrary, 10 µg/kg in the 2001/79 directive. Furthermore, EMA points out that endo- and ectoparasiticides were not included in the aquatic database and that the trigger value should not apply for these compounds. The same holds true for the terrestrial database, but the soil trigger does apply for parasiticides spread through manure from stabled animals. For exposure of veterinary

medicines in water the trigger is 1 µg/L; while the trigger suggested for human medicines in the draft proposal currently under discussion is 0.01 µg/L (EMEA, 2000), based on the same dataset.

The CSTEED has questioned both, the use of exposure triggers without ecotoxicological information and the trigger values proposed in the guidance document (CSTEED, 2001).

In the guidance, emission is limited to four routes: no emission, emission to water, emission to soil and direct emission into the environment (pasture animals). Emission to water and groundwater via soil and direct emission at application are not considered. Emission in the waste-stage of the product is not included in the guidance, although it should be part of the assessment as mentioned in 2001/82. The burden of proof as to what the emission routes actually are at and after administration is for every application with the applicant, and the management decision is with the assessor, but without terms of reference to decide on the absence of emission.

Further assessment in Phase II, as published by EMEA (1997), consists of the hazard quotient approach, where predicted exposure and effect are combined. Several risk characterization methods are used, risk ratio triggers (e.g. PEC/EC50), effect levels for non dose-response tests (e.g. dung fauna) or the PEC/PNEC ratio for aquatic organisms). Breaching acceptability triggers leads to refinement of the assessment and inclusion of field studies. The assessment factors do not follow the TGD for existing substances. The guidance is ambiguous on the decision schemes in lines of: what compartments have to be assessed (e.g.: surface water and groundwater are not assessed directly in Phase I: do they have to be assessed in Phase II)? What data are compulsory, what exposure models and effect models must be used, and how should field studies be designed; should do persistence and accumulation come to expression in exposure modelling and effect assessment? Methodological problems resulting from the guidance have been addressed in Halling-Sorensen, Jensen et al. (2001); Montforts (2001); Montforts, Kalf et al. (1999).

If the standards in Phase II are not met, a higher Tier assessment is possible, starting at refining exposure and effect modelling and ending in field studies, not necessarily on a local scale. The guidance does not address to the disposal of waste products.

There are several discrepancies between a proper assessment and the guidance available (Montforts and De Knecht, 2002).

- decision making criteria are not clearly defined
- exposure triggers are used to estimate low risk without any ecotoxicity data
- there are no clear standards expressing acceptability
- the methodology has not been elaborated to a satisfactory extent
- justification of the trigger values is scientifically unsound
- the ERA does not protect the desired environmental quality
- insufficient data are collected (no clear data requirements)
- testing protocols are lacking.

### **3.4 FEED ADDITIVES**

The environmental risk assessment of feed additives includes a tiered approach, based on two phases, that are closely related to the assessment of veterinary medicines.

Phase I is described in Commission Directive 2001/79/EC as a screening assessment of existing information with the purpose of determining whether or not a significant

environmental effect is likely. However, this whole step focuses on exposure assessment, without consideration of data on the toxicity. Use patterns, and expected concentrations in manure, soil and groundwater determine the need for conducting Phase II assessment.

Phase II is sub-divided in two steps. Phase II-A is a lower tier assessment based on short-term data. Both aquatic and terrestrial compartments are considered, using three taxonomic groups for each compartment, fish, *daphnia* and algae for the aquatic; terrestrial plants, earthworms and soil micro-organisms for the terrestrial. It is assumed that the risk for terrestrial vertebrates is covered by the assessment of efficacy and risk for the target farm species. The toxicological information for the key species within each compartment is analysed and a PNEC value is derived by applying a safety factor to the most sensitive species. The recommended factor is 100 for both, aquatic and terrestrial organisms. Risk characterisation follows the PEC/PNEC comparison. The suggested acceptable levels for this comparisons range between 1 and 0.1, depending on the nature of the test result.

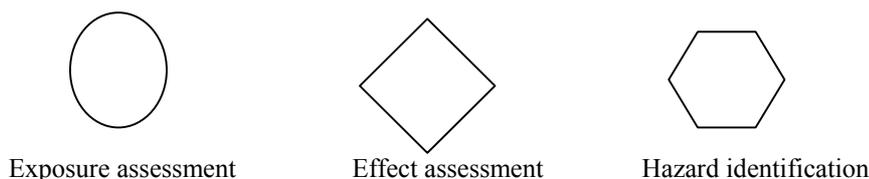
This phase also includes some hazard identification steps, particularly for bioaccumulation and persistence in soil. If a hazard is identified, Phase II-B evaluation must be conducted independently of the PEC/PNEC estimations.

Phase II-B requires sublethal long-term studies. No specific triggers or guidance for risk characterisation is currently applied.

## 4. SCHEMATIC REPRESENTATION OF THE RISK ASSESSMENT PROCEDURES AND DECISION TREES

The conceptual model, analysis plan, and decision strategy for each group of chemicals is summarised in the following figures.

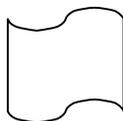
The following conventions have been used: Basic geometric figures represent the data inputs, establishing distinctions between exposure, effect and hazard identification data:



In the case of hazard identification, the information can be specifically related to exposure or to effect conditions, and therefore, two symbols can be used to present a single data input step.

In addition, exposure assessment can be conducted at different levels within a single step, i.e., the general release on the environment (covering all compartments) is followed by specific assessment for soils, surface water, groundwater, etc. These cases are represented by a large circle/ellipse with several small circles inside is presented

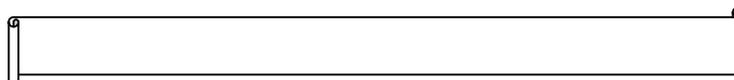
True risk characterisations, as comparisons of exposure levels and expected effects, are presented by the following symbol:



The terminology employed for the characterisation, as well as the covered risk, is presented. Standard terms include:

- PEC: Predicted Environmental Concentration
- PNEC: Predicted No Effect Concentration
- TER: Toxicity Exposure Ratio
- HQ: Hazard Quotient
- EL: Effect Level

Decision steps are represented by the following symbol:



These decision steps appear at different point within the process. If conditions for acceptability are fulfilled, the process stops at this point. Therefore, the steps included under each decision step will only be conducted when the outcome of the decision is than an unacceptable risk cannot be excluded.

Higher tier assessment, based mostly on case-by-case evaluation without specific guidance or recommendations are represented by the following symbol:



It can cover exposure and/or effect refinement, higher tier studies including mesocosms or field studies as well as risk reduction measures.

Figures are presented in annex 1.

## 5. HIGHER TIER RISK ASSESSMENT

The current regulatory arena does not present clear guidance on acceptability in the case of environmental risk assessment conducted on the basis of higher tier information.

Both, the SCP and the CSTEE have acknowledged the use of higher tier assessments, either based on probabilistic exposure and/or effect estimations, or on the use of microcosms/mesocosms/field studies.

The use of species-distribution curves for the derivation of PNEC values and the use of probabilistic risk assessment have been considered valid and scientifically sound (i.e. **CSTEE Opinion on Cadmium. The Final Report by WS Atkins International Ltd. Based on: The Final Report (September 1998) & Additional Assessment September 1998): "Assessment of the risks to health and to the environment of Cadmium contained in certain products and of the effects of further restrictions on their marketing and use"**).

The use of an uncertainty factor of 1 for field studies has been considered acceptable when the available information was considered to cover the most sensitive species/systems. (**CSTEE Opinion on "Risk assessment underpinning new standards and thresholds in the proposal for a daughter directive for tropospheric ozone"**). Specific factors for covering the remaining uncertainty should be applied if the available information does not cover all potential possibilities.

The need for a higher tier risk assessment has been identified in certain cases (**CSTEE Opinion on the results of the Risk Assessment of HYDROGEN FLUORIDE**). The SCs have welcomed the application of case-specific assessments for analysing risks not covered by the guidance documents when the assessments were scientifically sound and presented in a transparent way, and have concluded that the lack of guidance in the technical documents cannot be used to justify that an assessment which is considered relevant is not conducted.

In the absence of clear regulatory guidance on acceptability, the SCs have adopted opinions based on the realistic risk: probability for adverse environmental effects.

## 6. UNCERTAINTY ASSESSMENT

Most environmental risk assessment procedures are based on quantitative comparisons between toxicity data and expected exposure levels. For lower tier assessment, regulations include the acceptability trigger, and therefore the uncertainty assessment is limited to consider the data reliability, model uncertainty when relevant and the appropriateness of the proposed assessment factor. In fact the use of larger or smaller application factors than those proposed, although allowed by most procedures, is rarely applied.

The exposure assessment is based on scenarios and models. For generic assessments, standard scenarios based on a set of assumptions are usually proposed. Screening scenarios usually represent worst-case conditions, while higher tier assessments present trends to more realistic evaluations. A similar situation is observed for models. The regulatory goals of model predictions are diverse and three groups of models are

discerned based on their applicability: screening, primary and secondary models; or on their scale: local, regional or continental. Models are also classified according to their algorithmic design. Mathematical modelling approaches for estimating mass transfer and concentration in environmental compartments can be either deterministic or stochastic, and are either mechanistic (rate models) or functional/empirical (capacity models). Some characteristics are presented below:

- Screening models should be used to provide rapid prediction of the potential environmental fate of a compound. Primary models should provide a standardized approach to characterise substance behaviour and should permit rapid review of modelling submissions by regulators and help to ensure consistent regulatory decision making. Secondary models are appropriate for chemical and site-specific predictions. Secondary models might be applicable for higher tier assessments and will require calibration.
- A deterministic model uses a single set of assumed conditions taken from the range of conditions that can be present in reality. The practical use of the predictions depends on the nature and extent of the variability within the actual system. Several parameter values in current exposure models are selected from the stochastic distributions, e.g. pesticide residues on feed and drift values for repeated applications of pesticides.
- Stochastic models take the complete distribution of parameter values into account. With this probabilistic approach the full range of the resulting outcomes and the main sources of uncertainty are available for decision-makers. It is claimed that this approach may be useful for management purposes as it shows the information needed to refine the (deterministic) risk assessment.. These models are however not yet fully integrated in the regulatory risk approach for products: the acceptability of risk for pesticides, biocides, chemicals, medicines and feed additives is expressed in risk thresholds where safety factors account for uncertainty. The acceptability of risk is not (yet) expressed in the probability of exceeding a certain threshold, in which case the uncertainty would be placed in the distribution,
- All models operate within certain dimensions (time units, distances and areas) on which the parameter values depend, and the type of model is not necessarily related to the spatial scale of the simulation. Local, regional and continental scales are complementary to each other, as different processes can be modelled. However, within several frameworks only one scale of modelling is applied and comparative situations are handled differently (e.g. exposure of agricultural soil by fertilisers, veterinary medicines, feed additives, biocides, pesticides and sewage sludge).
- For diffuse non-point source emissions continental and regional modelling is warranted (e.g. chemicals and biocides), for foreseeable point-source emissions local modelling is preferred (e.g. pesticides, feed additives, medicines), together with regional models for long-range transport processes.

Addressing the uncertainty and variability associated to the scenarios and models is not easy. The European environmental conditions cover several ecoregions, from the Northern latitudes to the temperate Mediterranean area; therefore, a large variability for most parameters should be expected.

The parameter values in a model are considered representative for the range of rates for the modelled process within the selected area and interval in space and time. In general the variability of input parameters increases with the size of the area or duration for which the prediction is made.

In lower tier estimations variability is usually reduced to a fixed standard scenario. The rationale for the selection of parameters representing “European” conditions should be transparent.

Uncertainty represents a lack of knowledge about specific factors or parameters that characterise the physical system that is being modelled. In fact, these parameter values are fixed, but the actual value (or expected distribution for the value) cannot be determined accurately. Uncertainty can lead to inaccurate or biased estimates and can be reduced through further measurements with for instance a larger sample size, or an unbiased sample design. The use of more sophisticated modelling and analysis tools can also reduce uncertainty. The use of field measurements is an option in all frameworks. The design of a representative monitoring strategy and the final selection of representative data is imperative in order to validate or falsify the model predictions. Only in case of the assessment of an ongoing activity, real-time measurements can replace model results.

- In exposure assessment uncertainty includes:
  - parameter uncertainty (e.g. measurement errors),
  - model uncertainty (e.g. uncertainty due to necessary simplifications or variability), and
  - scenario uncertainty (modelling scale, selection of emission and distribution routes, descriptive errors).

The comparison between the recommended application factors in the effect assessment for establishing a low risk assessment is not an easy task because the terminology and procedures varies for the different groups of chemicals.

Tables 1 and 2 present a summary of these comparisons, expressed as the margins of safety calculated for each assessment, provided in the CSTEE opinion on the terrestrial environment (CSTEE, 2000) with the additional inclusion of feed additives.

**Table 1. Comparison of the application factors or margins of safety (ratio between toxicity and the expected exposure level) for the protection of terrestrial organisms employed in the environmental risk assessment of feed additives, veterinary medicines, industrial chemicals and pesticides.**

Group	Exposure route	Timing	Margin of safety*			
			Feed Additives	Veterinary Medicines	Industrial chemicals	Pesticides
Vertebrates (birds and mammals)	Direct	Acute Chronic	Not considered	10 -	Not considered Not considered	10 5
	Secondary poisoning	Acute Chronic	Not considered	10 -	1000 100- <b>10</b>	10 5
Plants	Soil	Acute Chronic	100- >1000 -	10 -	1000 100- <b>10</b>	Not considered
Earthworms	Soil	Acute Chronic	100- >1000 -	10 or 100 depending on persistence in soil	1000 100- <b>10</b>	10 5
Bees	Oral Contact	Acute Acute	Not considered	Not considered	Not considered Not considered	5-17 5-1500
Other arthropods	Contact	Acute	Not considered	<1-1	Not considered	1-5

Soil micro-organisms	Soil	Acute Chronic	100- >1000 -	10 -	1000 100- <b>10</b>	1-5
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**Table 2. Comparison of the factors or margins of safety (ratio between toxicity and the expected exposure level) for the protection of aquatic organisms employed in the environmental risk assessment of feed additives, veterinary medicines, industrial chemicals and pesticides.**

Group	Exposure route	Timing	Margin of safety*			
			Feed Additives	Veterinary Medicines	Industrial chemicals	Pesticides
Fish	Water column	Acute	100- >1000	100	1000	100
		Chronic	-	-	100- <b>10</b>	10
Invertebrates (Daphnia)	Water column	Acute	100- >1000	100	1000	100
		Chronic	-	-	100- <b>10</b>	10
Algae	Water column	Acute	100- >1000	100	1000	10
		Chronic	-	-	100- <b>10</b>	10
Aquatic plants	Water column	Acute	Not considered	Not considered	1000	10
		Chronic	-	-	100- <b>10</b>	10

\*The term Margin of safety in Tables 1 and 2 is used by analogy with human risk assessment, representing the ratio between the toxicity endpoint (acute L(E)C50 or chronic NOEC) and the expected exposure level (short or long-term PEC). Numbers represents the values recommended for concluding low risk in the lower tier assessment.

It is clear that large differences between the margins of safety can be found among the different chemicals, particularly in the terrestrial compartment.

In order to address the uncertainty of the process, in addition to the margin of safety, the amount and quality of the data must be considered. It is clear that the lowest margins of safety are requested for pesticides, but it is also clear that the standard testing requirements for pesticides are much higher than for any other group of chemicals. Acute and chronic data on several taxonomic groups, requiring in some cases several species within the group, are basic requirements for pesticides. The opposite situation can be observed for veterinary medicines, where the ecotoxicity test are required only if the exposure triggers are exceeded, and even in these cases test requirements for the initial assessment are low.

In these lower tier assessments, the protocols also present different approaches for covering the uncertainty assessment related to data quality.

The least flexibility can be found in the assessment of pesticides. Both data requirements (a set of standard test, which must be conducted under established protocols and GLPs) and acceptability triggers are fixed, and therefore the decision on acceptability is straightforward.

The greatest requirements for a transparent uncertainty assessment are observed for feed additives, where the acceptability trigger is expressed as a range instead as a single value. This situation forces the risk assessor to conduct a proper uncertainty assessment when the risk estimate falls within the range.

Industrial chemicals can be considered in-between these approaches. Data availability and quality are not so well established, and use of the PNEC approach obliges risk

assessors to consider an overall picture of the toxicological profile of the molecule. However, once a PNEC has been established, clear acceptability triggers are imposed.

The SCs have considered that the uncertainty assessment is a key element in the process even if the guidance includes specific triggers, and the level of uncertainty in the assessment should be presented in a transparent way.

The uncertainty analysis becomes the key issue in higher tier risk assessment. Although several workshops have been organised, the final conclusions still indicate the need for a case-by-case assessment. Two aspects require special attention within the uncertainty analysis: uncertainty on the ecological relevance of the observed effects, and uncertainty on the capability of the study(ies) to cover all relevant European conditions. Some proposals for addressing these issue are available. For example, Tarazona (1998) proposed to establish three main sources or types of uncertainty in ecological risk assessment. The epistemological uncertainty associated with the lack of knowledge on ecological functions and roles; the methodological uncertainty associated with the limitations in the available sources for producing relevant information; and the technical uncertainty associated with the reliability of the data.

Sources of uncertainty in the threshold assessment and potential solutions. From Tarazona (1998)

SOURCES	CLASSICAL SOLUTIONS	OTHER SOLUTIONS
CONCEPTS: lack of definition on ecotoxicological criteria and/or on the relevance of ecological endpoints	Safety factors Field studies and validations	Probabilistic approaches. "Mode of Action" biomarkers Prediction+Monitoring Assessment
METHODS: limitations in: Test species Endpoints	selection of "target" taxa  multispecies tests	Δ number of test species Δ number of exposure route Cost/effective tests Multivariate analysis Biomarker-based endpoints
TECHNIQUES: Problems of: Reproducibility Data analysis	Standardisation GLP, intercalibration  EC50, NOEC, LOEC	Biotechnological Applications Statistical improvement Time-concentration-effect assessments Modelling

Several proposals for evaluating the uncertainty in risk assessment are available (e.g. Helton and Davis, 2002; Pate-Cornell, 2002) which obviously may also be suitable for risk associated to environmental issues (von Stackelberg, 2002; Johnston, 2002).

The adoption of procedures for expressing the uncertainty in the risk assessment is strongly recommended.

## 7. OPINIONS ON GENERAL GUIDANCE DOCUMENTS

Several Scientific Committees, including SCP, SCAN and CSTEE have adopted several opinions on guidance documents related to environmental risk assessment of pesticides, general chemicals, feed additives, biocides and pharmaceuticals.

The request from the Commission services has not been consistent, and therefore, it is not easy to synthesize the set of general conclusions from these requests.

The SCP and the CSTEЕ have been requested to produce opinions on the scientific basis of the proposals presented to them. However, the SCAN was requested to produce a guidance document on the risk assessment of feed additives, which was subsequently submitted to the Commission for adoption.

Co-operation among the different Scientific Committees, through the participation of members of one Committee as external experts in Working Groups created under the umbrella of a different Committee, is being used in various cases, particularly to cover environmental issues. The CSTEЕ activities have covered a broad spectrum of chemicals, either directly, through consultations on guidance documents on environmental risk assessment of industrial (general) chemicals, biocides and human pharmaceuticals, or in co-operation with SCP and SCAN working groups covering pesticides and feed additives. In addition, an internal initiative from the CSTEЕ produced an opinion on the effect and risk assessment for terrestrial environments, which started with a comparison among procedures for different groups of chemicals.

Three main conclusions can be made from an epistemological assessment of the opinions produced by the different committees.

1. There is a general agreement for considering that the environmental exposure assessment must be related to the use pattern and possibilities for environmental releases during the life cycle of the substance. Distinctions among intended and non-intended releases are obvious, but not sufficient for a proper assessment of the environmental exposure. The need for specific scenarios for different groups of chemicals and even for different uses within the same category should be supported. However, it has also been recognised that the scenarios should be harmonised for related uses among different chemical categories: a good example are environmental releases of veterinary medicines, feed additives and some biocides associated to the use of contaminated sludge as soil fertilizer.
2. The use of environmental exposure triggers, currently accepted for veterinary medicines and feed additives and proposed for human pharmaceuticals, as well as for the groundwater risk assessment in the case of pesticides, has been strongly criticized by some committees. The problem arises from the assumption of the equivalence between low exposure level and low risk, when there is no information on the ecotoxicity of the substance. There is evidence that certain substances can be highly toxic to different species at concentrations clearly below the proposed exposure triggers, and therefore this approach is not justified.
3. The lack of harmonization among protocols is particularly significant for the terrestrial environment. The WG realises that, this fact has been already addressed in a specific CSTEЕ opinion, and therefore will not be subjected to an in-depth discussion in this general paper.

## **8. PROPOSALS FOR HARMONISATION.**

The protocols for environmental risk assessment do not have the advantage of the large experience associated to Human Health risk assessment. Nevertheless, they suffer from the same problem of a lack of harmonisation at the regulatory and scientific levels.

The WG considers that the need for specific guidance and scenarios required for certain assessments should not be used to justify the lack of harmonization. Efforts for harmonizing the protocols and the opinions of the scientific committees should be encouraged.

Two different groups of proposals are presented. The first group focuses on the scientific basis for the assessment. The second, on the format and terminology.

### **1. Harmonisation of the scientific basis of the environmental risk assessment**

Assessment of the current guidelines indicates the existence of large differences at all levels of the assessment, but particularly at the lower tier exercises.

- Exposure scenarios and models for the same compartment (e.g. agricultural soil exposed through the use of fertilizers) show large differences in both the definitions, and the default values.
- The effect assessment is probably the best harmonized, particularly regarding aquatic organisms. However, significant differences are observed in the use of QSARs, extrapolation of data, use of mammalian toxicity data (initially designed to support the Human Health assessment), or the terrestrial compartment in general. Certain assessments use toxicity tests designed on the basis of the expected level of exposure (e.g. the application rate). The WG strongly recommends moving to dose/response toxicity tests for all species.
- The risk characterization, at the lower tier level, is basically a risk quotient assessment based on the direct comparison between the toxicity observed in single-species laboratory tests and the expected environmental concentration. However, the margins of safety applied to these quotients can differ by orders of magnitude. The methodologies for the assessment also involve large differences, i.e., grouping or not the different taxonomic groups selected as key species for a particular compartment.
- The use of fixed exposure triggers is deployed for certain chemicals, but it cannot be supported from a scientific basis, as a risk assessment is in all cases a comparison of exposure and effects.

The WG suggests two different measures for reducing this lack of harmonization:

1. On the short term, an in-depth revision of the different protocols for environmental risk assessment.
2. On a medium term, more research on the scientific basis of environmental risk assessment is required.

## **2. Harmonisation of opinions: definitions, format, and structure of the conclusions.**

The WG has identified a number of differences that are not related to the scientific basis but to the procedure and regulatory definitions.

The WG considers that all these differences present a large obstacle for understanding the basic processes of environmental risk assessment. The transparency of the assessments, including the opinions of the scientific committees suffers from this lack of normalization. For example, the risk assessment based on PEC/PNEC ratios or on TERs has exactly the same meaning: acceptability is based on the use of a margin of safety for comparing toxicity versus expected exposure. However, the use of different terminology, trigger definitions, structure and format creates confusion among users of specific field when trying to understand the process described for other fields.

The WG considers that these aspects can be easily harmonized, both for the protocols and for their use by the scientific committees. This harmonization will increase the transparency and the feasibility for risk communication.

Some initiatives for harmonisation have been implemented already. A good example appears in the procedure for environmental risk assessment of feed additives. Although the basis for the protocol is the guidance document on veterinary medicines, a single methodology for risk characterisation is proposed. In fact, SCAN recommend use of the EMEA document on environmental risk assessment of veterinary medicines as the starting point for the proposal, but harmonising the procedures for risk characterization following the TGD for industrial chemicals. As a result, all risk characterizations for feed additives are based on the same approach PEC/PNEC ratios, providing a higher consistency than the assessment of pesticides or veterinary medicines which use at least three terms for risk characterisation.

## **REFERENCES (TO BE COMPLETED)**

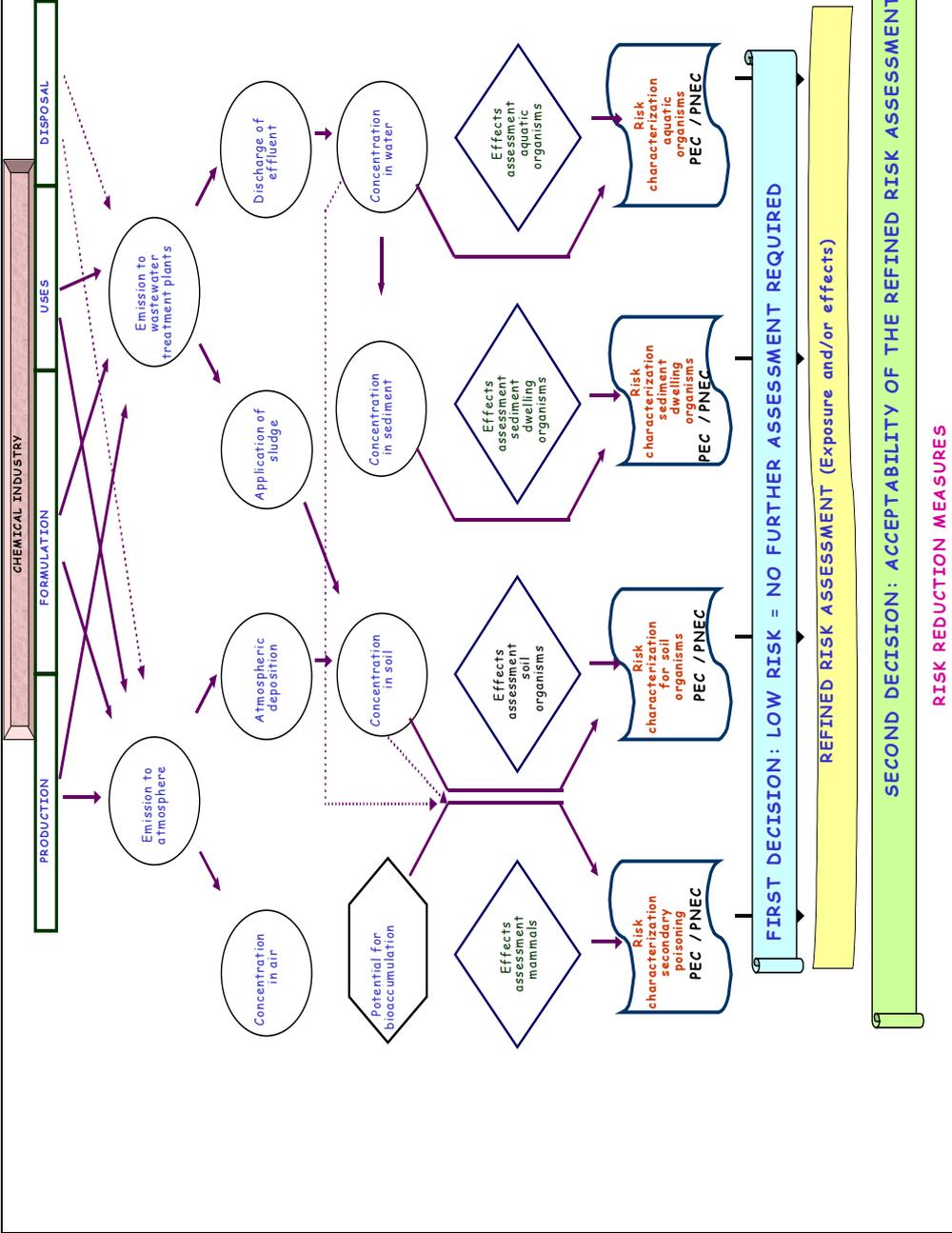
- Candolfi MP, Barrett KL, Campbell PJ, Forster R, Grandy N, Huet MC, Lewis G, Oomen PA, Schmuck R, Vogt H (eds) (2001): Guidance document on regulatory testing and risk assessment procedures for plant protection products with non-target arthropods. From the ESCORT 2 workshop. SETAC, Pensacola, 46 p.
- De Leeuw FAAM (1993) Assessment of the atmospheric hazards and risk of new chemicals. Procedures to estimate "hazard potentials". Chemosphere 27: 1313-1328.
- DG AGRICULTURE (1995) Modelling environmental fate of plant protection products in the context of their Authorization within the European Union, Document 1694/VI/95, DG Agriculture
- DGSANCO, 2000a. Working Document: Guidance Document on Terrestrial Ecotoxicology, DGSANCO, 2021/VI/98rev.7, 8.7.2000
- DGSANCO, 2000b. Working Document: Guidance Document on Persistence in Soil, DGSANCO, 9188/VI/97rev.8, 12.7.2000
- DGSANCO, 2001. Working Document: Guidance Document on Aquatic Ecotoxicology, DGSANCO, 3668/2001, 4.11.2001
- DGSANCO, 2002. Working Document: Guidance Document on Terrestrial Ecotoxicology Under Council Directive 91/414/EEC, 17.10.2002

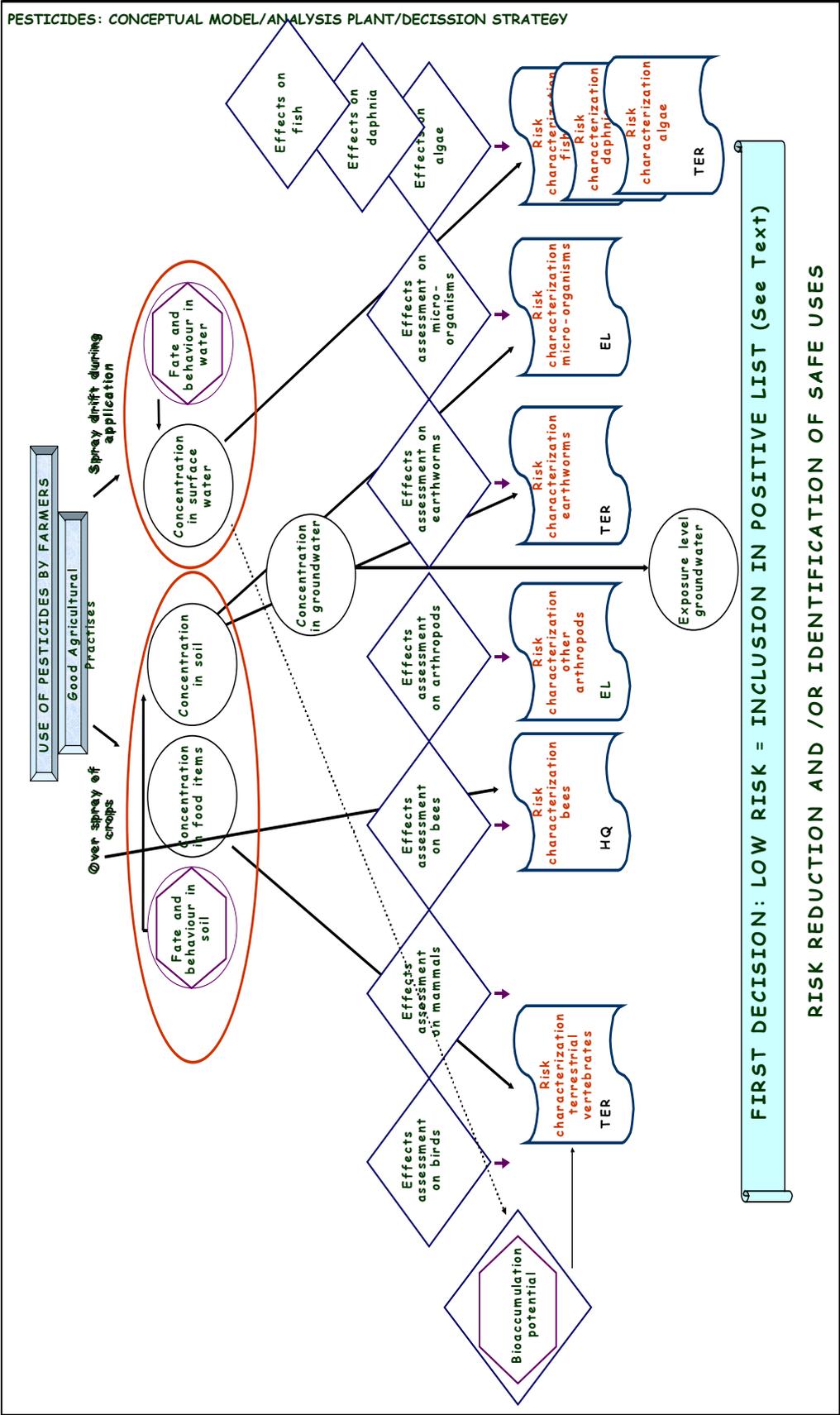
- EU (1996). Technical Guidance Document in support of Commission Directive 93/67/EEC on risk assessment for new notified substances and Commission Regulation (EC) 1488/94 on risk assessment for existing substances. PARTS I, II, III and IV. Document. ISBN 92-827-8011-2. Luxembourg: Office for Official Publications of the European Communities, 1996.
- EMA, 1997. Note for guidance: environmental risk assessment for veterinary medicinal products other than GMO-containing and immunological products. EMA/CVMP/055/96.
- EMA, 2000. Discussion Paper on Environmental Risk Assessments for Non-Genetically Modified Organism (non-GMO) Containing Medicinal Products for Human Use. ERA draft-dec2000.
- FOCUS (2000) "FOCUS groundwater scenarios in the EU plant protection product review process" Report of the FOCUS Groundwater Scenarios Workgroup, EC Document Reference Sanco/321/2000, 197pp
- FOCUS (2001): FOCUS Surface Water Scenarios in the EU Evaluation Process under 91/414/EEC". Report of the FOCUS Working Group on Surface Water Scenarios, EC Document Reference SANCO/4802/2001-rev.0.xxxpp
- Halling-Sorensen, B., Jensen, J., Tjørnelund, J., and Montforts, M. H. M. M. Worst-case estimations of predicted environmental soil concentrations (PEC) of selected veterinary antibiotics and residues in Danish agriculture. Kümmerer, K. Pharmaceuticals in the environment. 2001. Germany, Springer Verlag.
- Helton JC, Davis FJ. (2002) Illustration of sampling-based methods for uncertainty and sensitivity analysis. Risk Anal. 22:591-622.
- Johnston RK, Munns WR Jr, Tyler PL, Marajh-Whittemore P, Finkelstein K, Munney K, Short FT, Melville A, Hahn SP. (2002). Weighing the evidence of ecological risk from chemical contamination in the estuarine environment adjacent to the Portsmouth Naval Shipyard, Kittery, Maine, USA. Environ Toxicol Chem. 2002 21:182-94.
- Knecht, J.A. de., Montforts, M.H.M.M., 2001. Environmental risk assessment of veterinary medicine products: an evaluation of the registration procedure SETAC Globe 2, 29-31.
- Montforts, M. H. M. M. Regulatory and methodological aspects concerning the risk assessment of medicinal products. Kümmerer, K. Pharmaceuticals in the environment. 2001. Germany, Springer Verlag.
- Montforts, M.H.M.M., Kalf, D.F., Vlaardingen, P.L.A.v., Linders, J.B.H.J., 1999. The exposure assessment for veterinary medicinal products. Science of the Total Environment 225, 119-133.
- Montforts, M.H.M.M., De Knecht, J.A. (2002) European medicines and feed additives regulation are not in compliance with environmental legislation and policy. Toxicology Letters 131, 125-136.
- Pate-Cornell E. (2002) Risk and uncertainty analysis in government safety decisions. Risk Anal. 22:633-46.
- Ramos C, Carbonell G, Garcia Baudin JM, Tarazona (2000) Ecological risk assessment of pesticides in the Mediterranean region. The need for crop-specific scenarios. Sci Total Environ. 247:269-78.
- Tarazona J.V. (1998) Scientific concepts and uncertainties in the identification of ecotoxicological thresholds of acceptability and danger. The role of biological routes. In D.M. Pugh and J.V. Tarazona (editors) Regulation for Chemical Safety in Europe: Analysis, comment and criticism. Kluwer Academic Publishers. Dordrecht/Boston/London, pp 41-63.
- SCP, 2000. Opinion of the Scientific Steering Committee on Harmonisation of risk assessment procedures, adopted on 26-27 October, 2000, Appendix 2, Report on Exposure Assessment, p 25
- SSC, 2000. Opinion of the Scientific Steering Committee on Harmonisation of risk assessment procedures, adopted on 26-27 October, 2000, Appendix 2, Report on Exposure Assessment, p 26
- von Stackelberg KE, Burmistrov D, Vorhees DJ, Bridges TS, Linkov I. (2002) Importance of uncertainty and variability to predicted risks from trophic transfer of PCBs in dredged sediments. Risk Anal. 22:499-512.

## **ANNEX 1**

**ALSO USED FOR SETTING EQS UNDER THE WFD**

INDUSTRIAL CHEMICALS : CONCEPTUAL MODEL/ANALYSIS PLAN/DECISION STRATEGY





VETERINARY MEDICINES: CONCEPTUAL MODEL/ANALYSIS PLANT/DECISION STRATEGY

