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Review

Ecotoxicology: The Challenges for the 21st Century

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Abstract: The usual procedures for ecological risk assessment (ERA) have been based for decades on simplified approaches in order to provide basic information on the huge amount of chemicals introduced into the environment. These approaches allowed the development of international regulatory tools capable of substantially reducing the adverse effects on ecosystems in developed countries. Nevertheless, these approaches suffer from a lack of ecological realism and are poorly suitable for understanding the actual consequences for ecosystem health. The need for more ecologically-based approaches is now recognized by the scientific community and has been highlighted by a recent document of the European Commission. In this paper, a synthesis is presented of the most important issues and the need for research to improve the ecological realism of exposure and effect assessment and the tools that should be developed to reach this objective. In particular, the major challenges are the following: the effects of variable exposure patterns; the vulnerability of ecosystems; the indirect ecological effects; the responses to multiple stress factors; the improvement of ecological modeling. The possibilities for using new scientific achievements in regulatory ERA are also discussed.

Keywords: ecotoxicology; ecological risk assessment; exposure assessment; effect assessment; ecological modeling; European Commission

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1. Introduction: A Short History of Ecological Risk Assessment and Environmental Protection

To better understand why an in-depth discussion on the future development of ecotoxicology and of ecological risk assessment (ERA) is nowadays a prime issue, it could be useful to draw a short history of this relatively young science.

Although the negative impact of human activities on the environment started at the beginning of cultural development some thousands of years ago, public awareness about environmental damages is a recent event, starting in the middle of the 20th century. In particular, the significant impacts of exposure to potentially dangerous chemicals on the natural environment were recognized by public opinion only after the famous book "Silent Spring" [1].

The emissions of chemicals produced by human activities in ecosystems, especially in surface water, were likely to produce effects at the lethal and sub-lethal levels in populations. Therefore, ecotoxicology was developed with the aim of producing simple tools, capable of providing answers to several growing and well-identified problems, even using relatively scarce information. The currently used approaches for ERA represented the basis for the development of international regulations and are likely to be protective enough for ecosystems. These regulatory tools led to an increased level of chemical control and to an improvement of environmental quality [2]. Therefore, severe effects, frequent in the past, are now unlikely to occur; nevertheless, the effects of anthropogenic stress factors are still capable of producing serious damage to ecosystems.

An additional relevant change, from the old concept of environmental protection to the more recent approaches accepted by regulatory tools, refers to what has to be protected. The first definition of water quality criteria (WQC) was developed by the U.S. Environmental Protection Agency [3], to protect water bodies in order to allow for major uses of water resources (drinking, bathing, fisheries, agricultural and industrial uses) for man. A substantially different and more ecologically based approach was proposed many years later in Europe [4], stating that a water quality objective: "*should not produce conditions capable of altering the structure and functions of the aquatic ecosystem*".

A further important step has been addressed with the European Water Framework Directive (WFD) [5], which overcomes the traditional chemical-based concept of water quality assuming ecological effects as a basis of control. Therefore, the assessment of environmental quality must be defined in terms of the "structure and functioning of ecological systems", rather than be only based on chemical contamination. The evolution of the environmental quality concept and the requirements for a more site-specific and ecologically-based approach, to be implemented according to the Water Framework Directive, have been pointed out by Vighi *et al*. [6].

As a consequence, there is an increasing need for approaches capable of answering more complex questions than dose/concentration-response relationships can. To do this, it is essential to improve the predictive power of ecology and ecotoxicology for describing and modeling ecologically relevant effects at the hierarchical level of communities and to increase the ecological realism of ERA in order to better describe the actual consequences for ecosystems [7].

2. The Development of Ecotoxicological Approaches

In order to produce basic information on the adverse effects that may be determined by potentially dangerous chemicals on living organisms (other than man), testing methods on aquatic and terrestrial single species were developed and applied. A huge amount of data was produced in the second half of the last century. However, considering the enormous number of chemicals that may be introduced into the environment, information on many chemicals is still far from being complete, even for the base set.

For simplified ERA, there was the need to estimate safe concentrations for ecosystems, *i.e.*, at least ideally, concentrations that would not produce adverse effects on any of the components of the biological communities at whatever exposure time (e.g., PNECs: predicted no effect concentrations). This led to the development of simplified approaches described in international guidelines, such as the Technical Guidance Document (TGD) on risk assessment of the European Commission [8]. These approaches are based on the assumption that a PNEC may be estimated from a few ecotoxicological data produced on a reduced number of selected test organisms, assumed as representative of the different trophic roles of ecosystems (e.g., algae, *Daphnia* and fish for aquatic ecosystems). The level of uncertainty of the approach is covered by the use of assessment factors decreasing with the increase in available information.

The extreme simplification of the approach makes it difficult to possibly extrapolate the results in predicting the actual consequences on the structure and functions of the natural ecosystems:

- the standard conditions of laboratory tests may not reproduce the variability of physical, chemical and biological parameters of aquatic and terrestrial ecosystems;
- the sensitivity of a few selected test species may not be representative of the distribution of sensitivity among the species of complex biological communities;
- the possible interactions among various stress factors of different origin that may affect the ecosystem are not accounted for;
- single species tests cannot account for the interactions and indirect effects that regulate the functioning of biological communities.

Nevertheless, in spite of these limitations, traditional ecotoxicological tests and procedures for estimating PNECs still represent an irreplaceable tool, at least for comparative and screening estimation of the adverse effects of potentially dangerous chemicals, realistically applicable with moderate effort to a large number of substances. Moreover, the standard experimental conditions are generally set in order to maximize the toxic effects (worst-case conditions); many of the selected species are generally sensitive, and the assessment factors are quite conservative. Therefore, experimental evidence supports the hypothesis that traditional approaches for estimating PNECs may be considered protective enough for the environment [9,10], even if large margins of uncertainty exist. Finally, one must be aware that the suitability of the approach should also be related to the objective of the protection. In this sense, a difference exists between the concept of PNEC and those of RAC (regulatory acceptable concentration), applied mainly to plant protection products, which accept a moderate effect on ecosystems when exposure cannot be completely avoided.

More advanced approaches may be used, and some of them are suggested by the TGD. The species sensitivity distribution (SSD) approach [11–14] allows for moving from the traditional deterministic procedure to a probabilistic one capable of evaluating the probability of a species being affected by a given concentration of a toxic substance. SSD allows estimating which fraction of the biodiversity of an ecosystem may be affected (PAF: potentially affected fraction) [15], providing information on possible changes in the structure of the biological community and representing a substantial improvement of the traditional procedures. Obviously, it requires much more information on a suitable number of species that should cover a substantial part of the range of variability of sensitivity to the considered chemicals. Two major limitations may be envisaged. First, the definition of the PAF that may be accepted as protective for the ecosystem is controversial. According to the original proposal of the Dutch school [16], the TGD proposes HC5 (hazardous concentration 5%) as a safe level for ecosystems, *i.e.*, the concentration at which 5% of the species may be adversely affected. An application factor (AF) ranging from five to one should be applied as a function of the uncertainty of the HC5 assessment. It is assumed that the ecosystem is protected if at least 95% of the species of the community are protected. This assumption may be acceptable in the case of specific ecosystems at the local scale in areas subject to high human pressure. On a wider scale (regional, continental), the loss of 5% of biodiversity is unacceptable. Second, the method is still based on simple laboratory tests on single species. Just setting a HC5 cannot account for more complex issues, such as secondary effects and interactions between the species of a community. In particular, several relevant questions need to be answered:

- How is the fraction of affected species distributed within trophic levels?
- Are all the levels of the food chain adequately protected?
- Is the biodiversity within the different trophic levels adequately protected?
- Are "keystone" species included within PAF?
- Does the loss of the species included within PAF substantially damage the structure and function of the ecosystem?
- Can the levels of primary and secondary productivity be adequately maintained?

The ecological realism of the effect of the assessment might be substantially improved by the use of higher tier testing methods, such as model ecosystems, field and semi-field studies, micro- and meso-cosms. These approaches, too, are suggested as a possible alternative to traditional laboratory tests by the old TGD, as well as by many other more recent guidance [17–19]. Therefore, their use in ERA is rapidly growing. They represent a powerful tool for improving the understanding of the responses to stress factors at a higher hierarchical level. However, for a better use in ERA, some problems need to be solved:

- improving the methodological standardization for a better comparison and reproducibility of the results;
- improving the capability to extrapolate from specific test conditions to the variability of the characteristics of natural ecosystems;
- improving the transparency of the procedures to estimate a safe concentration from mesocosm results.

A different approach that for a long time received much attention in ecotoxicology is the use of sub-individual end points (e.g., biomarkers, omics, *etc*.). The first applications of biomarkers in ecotoxicology appeared in the late 1970s [20–22]. More recently, in the late 1990s, there was a rapid increase of the application of the omics (proteomics, metabolomics and genomics) approaches [23]. It has been proven that these approaches may represent excellent early-warning indicators of exposure to stress factors, but the real meaning in terms of potential effects on population dynamics or community structure and function is largely unknown. There is the need for a better understanding of the relationships between sub-individual effects and ecologically relevant endpoints and of how molecular markers relate to one another to produce phenotypic effects [23,24]. Therefore, at present, the use of these approaches in ERA is strongly controversial. Many practical and conceptual challenges remain to be solved [25].

3. Assessing Exposure

Unlike human risk assessment, which is mainly hazard-driven, ERA is exposure-driven, and exposure assessment is a key issue, such as effect assessment. Exposure assessment is usually based on a combination of monitoring and modeling approaches. However, modeling is to be considered the most powerful approach for at least two reasons: first, reliable and extensive monitoring data are available for a relatively small number of chemicals; second, monitoring is an *a posteriori* approach, while modeling allows assessing exposure *a priori*, before a chemical has been introduced into the environment, and therefore, it is the only possibility for prevention.

Fugacity-based multimedia models represent, since the late 1970s, the best tool for predicting the environmental distribution of chemicals [26]. A huge amount of models have been produced, applicable from the local to the global scale and at different levels of complexity. However, the same need for simplification, highlighted above for effect assessment, is also applicable to exposure assessment. Therefore, the usual ERA approaches for exposure prediction are based on modeling the application to simplified standardized scenarios with generic environmental characteristics (compartments size, temperature, organic carbon, *etc*.) and does not allow for evaluating the complexity of spatially and temporally varying environmental scenarios and discharges. For example, the European TGD proposes a scenario assumed as being representative of local, regional and continental European conditions (e.g., [8]); and the FOCUS Group (FOrum for Co-ordination of pesticide fate models and their Use) describes a series of selected climatic and agronomic conditions (e.g., [27]). As for effect assessment, these procedures require relatively low efforts and allow for estimating PECs (predicted environmental concentrations) that represent the basic requirement for comparative and screening estimation of exposure to chemicals in different environmental compartments (water, soil, air). However, they suffer from a lack of ecological realism and do not cover the complexity and variability of realistic natural scenarios. Therefore, current approaches cannot be applied for site-specific risk assessment as required by a proper management of environmental quality.

4. Characterizing Risk

The results of simplified approaches for exposure and effect assessment are two simple numbers (PEC and PNEC) that may be compared for risk characterization. If we assume that, for regulatory purposes, defining a precise numerical threshold is a necessary requirement, a PEC/PNEC ratio is a suitable tool. However, nobody knows what really happens to the structure and functioning of natural ecosystems if a PEC/PNEC of one is exceeded. Whatever the procedure for determining a PNEC that has been adopted (deterministic application of assessment factors to single species tests, probabilistic assessment using SSD and HC5), one must be aware that the characteristics of a community are regulated by emergent properties that cannot be easily described and predicted from lower hierarchical levels. Therefore, a number of questions remain to be answered:

- Is the natural homeostatic capability of the ecosystem sufficient to counteract the effect of stress factors?
- How relevant are indirect ecological effects (competition, predation, *etc*.) for enhancing or reducing the effect of a stressor?
- How much time is required for a complete recovery of the community (resilience) if the stress factor is not continuous?

Even if higher tier assessment is used (e.g., mesocosms), answering these questions is not easy, because mesocosm studies are performed on specific communities under specific environmental conditions. Extrapolating the results to different kinds of ecosystems and conditions may be problematic.

5. The Need for More Ecologically-Based Approaches

Assuming that the aim of environmental protection is to preserve biologic communities and ecosystems, both in their functional and structural features, it follows that optimal ecotoxicological endpoints should be capable of providing quantitative answers to a number of questions; for example:

- What is the probability of the loss of a population?
- How much will the biodiversity change?
- Is the structure of the food-web protected?
- How much will productivity decrease?

The direct answer to these questions needs complex approaches. Therefore, the best ecotoxicological endpoints should be those that can be linked directly to community-level effects [28]. Anyway, it is questionable if most commonly used endpoints are suitable for covering this objective. Current procedures required by chemical regulations only achieve a small part of these goals [29]. We must be aware that the complexity of the problem is two-fold:

1. The complexity of biological communities: the characteristics of a community are not just the sum of the characteristics of individual populations; the structure and function of the community is regulated by emergent properties that are not easy to be described and predicted at lower hierarchical levels;
2. The complexity of stress factors: toxic agents are only a component of the potential stress factors that may alter the behavior of natural populations and communities; the combination of multiple stress factors (anthropogenic and natural, such as temperature, oxygen depletion in water, water shortage in soil, *etc*.) needs to be taken into account for explaining environmental changes.

Van Straalen [7] pointed out that the consequence of multivariate stress on a community is a deviation from the normal operating range (NOR) of the system. The NOR itself is defined as a multidimensional space, describing the structure and functions of the community in the absence of stress [30]. Another problem is the recovery capability of the system. For a population, recovery capability is a function of many factors, such as:

- the reproductive strategy and the potential growth rate ® that allows for, for "r" strategist populations, a more rapid re-colonization if the stress pressure ends or an easier genetic adaptation if the stress pressure continues;
- the presence of less sensitive resting larval stages;
- the dispersal capability.

In a community, recovery should be intended as the restoring of NOR. In particular cases, a change of NOR due to pollution-induced community tolerance (PICT) may be accepted. It can be produced by changes in community structure, increasing the dominance of less sensitive populations [31]. However, this kind of change is more related to the concept of RAC than to that of PNEC.

6. The Activity of the European Commission

The European regulatory framework for environmental protection is not limited to legal acts focused on chemicals and on their authorization to be commercialized and used, such as REACH [32], the pesticides directive [33] and the biocides directive [34]. Many important European directives are clearly focused on ecosystems, such as the Water Framework Directive [5], the Marine Strategy Framework Directive [35] and the forthcoming Soil Framework Directive; others are focused on the protection of habitats and biodiversity, such as the Birds Directive [36] and the Habitats Directive [37]. These regulatory acts require site-specific approaches, capable of protecting specific ecosystems, and tools that can describe the complex interactions among ecological (biotic and abiotic) factors that may influence the effect of specific stressors.

In this context, some specific objectives for an improved ecological risks assessment can be identified:

- to develop tools that go beyond the classical concept of PEC and that are capable of describing more realistic exposure patterns for single chemicals and mixtures;
- to increase the ecological realism of effects assessment by improving the use of higher tier and field or semi-field data and of methods that can predict or assess ecological processes;
- to define good practices for ecological modeling and agree on scenarios and ecological endpoints, so that models can be used to assess ecological risks for a wide range of species, regions and environmental conditions;
- to improve the development of site-specific assessments, taking into account the characteristics of exposed ecosystems;
- to account for the complexity of real ecosystems, considering the effects of biotic and abiotic interactions at community and ecosystem levels.

The need for the development of tools that can increase the ecological realism of exposure and effect assessment, taking into account the properties and the complexity of potentially exposed ecosystems, has been recognized by the European Commission, which recently developed an opinion on "Addressing the New Challenges for Risk Assessment" [38]. The ecological section of the document reports a synthesis of the major issues that have been recognized as relevant towards improving the ecological realism of ERA considering the characteristics of natural ecosystems that are potentially exposed. The report describes the most important processes that need to be better known and suggests some tools that may be used to achieve the goal. It also evaluates the science that is still available behind them, their practical usefulness in ERA and highlighted the need for future research. A short synthesis of the main issues addressed in the document is given below.

6.1. Challenges in Exposure Assessment

A number of relevant issues that require investigation in order to improve the reliability of experimental and predictive approaches for exposure assessment have been listed and discussed [39].

6.1.1. Better Use of Monitoring Data and Databases

The huge amount of national and international monitoring data available is often useless in ERA, due to a lack of methodological uniformity, insufficient metadata, *etc*. There is the need for criteria and protocols for obtaining and comparing monitoring data in risk assessment. In this frame, there is also the need to verify and harmonize the information that may be obtained in the REACH regulation according to the internationally recognized data quality requirements [32], not only on monitoring, but also on physical-chemical data.

6.1.2. Improvement of Modeling Approaches

A number of effective models are now available for predicting the distribution and fate of chemicals. However, some important issues need to be covered:

- modeling the fate of polar and ionized chemicals, as well as nanomaterials;
- developing models capable of predicting time and space variability for a realistic exposure assessment;
- developing ecologically realistic scenarios accounting for the variability of environmental characteristics;
- developing models capable of describing the food web path of chemicals and also determining specific organism parameters to extend the applicability of bioaccumulation models;
- assessing the role of vegetation uptake in regulating the input to the food chain and the organic carbon cycle.

6.1.3. Sorption and Bioavailability

The bioavailability of chemicals is a key issue to assess their biologically active exposure. Tools are available to assess the bioavailability for non-polar organic chemicals and metals and their sorption on soil and sediments. However, these tools are not always used in ERA. Moreover, polar and ionized chemicals are generally soluble, but with highly variable solubility and solubility rates, making predictions sometimes difficult.

6.2. Challenges in Effect Assessment

Protecting the structure and functions of ecosystems would require a deeper knowledge of ecological processes. Describing and predicting the effects that may be determined by stress factors at higher hierarchical level and expressing them in quantitative terms, for the needs of regulatory ERA, would require the development of specific methods and tools [40,41]. Some of them already have sound scientific basis and may be practically applied, even if large margins for improvement still exist. In other cases, the present level of knowledge is not deep enough, and suitable tools are not sufficiently developed for a practical application in risk assessment.

6.2.1. Issues to Be Accounted for

6.2.1.1. Effect Assessment for Complex Exposure Patterns

Natural ecosystems are seldom exposed to constant concentrations of toxicants, as in usual testing procedures. Usually, exposure patterns are variable and difficult to predict, as occurs for pesticides that reach water via pathways driven by rainfall events [42]. Such complex exposure patterns may be reproduced using specific experimental design or described by modeling [43]. The advantage of modeling is the possibility of extrapolation to a wide range of field exposure scenarios [42,44]. Toxicokinetic/toxicodynamic (TK/TD) models describe the processes that link exposure to effects in an organism [44,45]. For assessing the effects of variable exposures, TK/TD models seem to be a suitable tool to improve [46].

6.2.1.2. Effect Assessment at Low Hierarchical Level

At present, the relationship between molecular effects and responses at higher hierarchical levels (population, community) is largely unknown. Therefore, the usefulness of molecular approaches in ecological risk assessment remains to be established. The capability of sub-individual endpoints to predict ecologically relevant effects must be improved.

6.2.1.3. Ecosystem Vulnerability

Vulnerability is a function of three factors: susceptibility to exposure, sensitivity and recovery capability [47]. The concept may be applied at different hierarchical levels (population, community) and is not accounted for in current ERA procedures, mainly because current assessments are generally non site-specific (chemical-oriented instead of ecosystem-oriented). Assessing vulnerability is a key issue for the protection of specific ecosystem. For a practical application in ERA, the vulnerability concept should be expressed in quantitative terms. Some tools capable of quantifying the vulnerability to specific stress factors have already been developed and proposed, particularly for freshwater ecosystems [48,49]. The development, application and validation of methods capable of assessing the vulnerability of aquatic and terrestrial ecosystems to different kinds of stressors is a priority for research.

6.2.1.4. Endocrine Disrupting Effects

Endocrine disrupting chemicals (EDCs) may produce ecologically relevant effects affecting population dynamics. Present knowledge is mainly focused on vertebrates, particularly mammals. Considering the complexity of the issue and the relevance of endocrine disruption for ecosystem protection, the knowledge of endocrine systems in invertebrates and the development of procedures for assessing endocrine disrupting effects must be improved.

6.2.1.5. Indirect Ecological Effects

Indirect effects due to ecological interactions strongly affect the actual consequences of stress factors at the ecosystem level. They can override direct effects and can mitigate, but also exacerbate, them. Experiments and community models have demonstrated the importance of indirect effects, but overall knowledge is still poor, particularly for use in ERA [50]. The development of more comprehensive studies, based on experiments and ecological modeling, is a key issue for assessing effects at an ecosystem level.

6.2.1.6. Assessing Effects of Mixtures of Chemicals and Stressors

Chemical regulatory tools are mainly based on individual substances, while ecosystems are usually exposed to multiple stressors. The combination of several chemicals at concentrations far below a no-effect level may produce significant additive effects [51]. The knowledge of the combined effect of chemical mixtures is nowadays sufficient for the development of regulatory proposals, and the issue is under specific consideration by the European Commission [52]. However, the science on the toxicity of chemical mixtures focuses primarily on the effects of mixtures at an individual level [53]. The few studies available at higher hierarchical levels are mainly oriented toward communities of algae and microorganisms [54,55]. Efforts to understand how a complex ecosystem may respond to mixtures of chemicals with different modes of action on the different taxonomic groups of living organisms are still lacking [50]. Moreover, the interactions between the combined effects of toxic chemicals and other stress factors or variable environmental parameters (e.g., temperature, pH, oxygen depletion in water, water shortage in soil, *etc.*) or, more in general, their dependence upon environmental factors is largely unknown [50]. Some effective approaches, such as the Biotic Ligand Model (BLM) [56,57], which allows for predicting the effects of some water characteristics on toxicity, are of limited applicability (e.g., metals).

6.2.2. Tools to Be Better Developed or Improved

6.2.2.1. Higher Tier Effect Assessment

A relevant problem for the use of higher tier approaches (micro- and meso-cosms, field and semi-field studies) in regulatory assessment is the improvement of transparency in the evaluation of the results, reducing the need for expert judgment. In particular, a priority for research is the development of statistically-based tools capable of quantitatively assessing uncertainties and to improve the transparent use of these approaches.

6.2.2.2. Trait-Based Risk Assessment

Trait-based approaches represent a promising tool capable of complementing taxonomically-based assessments with functionally-based assessment [58]. At present, they represent a tool for the analysis of population vulnerability and for many other approaches relevant for ERA [59]. One of the bottlenecks for the development and application of the approach is the lack of data for the precise characterization of suitable traits, particularly for traits describing detailed anatomic characteristics, as well as physiologic or metabolic patterns. The development of tools and databases for improving the application of trait-based ecological risk assessment represents a priority need for research.

6.2.2.3. Ecological Modeling

Ecological models are the most promising way to fully take into account ecology in risk assessment. However, current modeling practice is not yet ready for regulatory ERA, even if promising proposals have been made [60,61]. To make full use of the potential of ecological models, concerted action is needed, to agree on standard scenarios, ecologically relevant test species and endpoints, the acceptance criteria of ecological models and to develop well-tested, flexible models that are both routinely used and improved. Substantial progress has been determined by the results of the EU-funded CREAM (Mechanistic Effect Models for Ecological Risk Assessment of Chemicals) Ecological Modeling Project [62].

6.3. Ecologically-Based Risk Characterization

In current ERA procedures, risk characterization is usually represented by a simple number (PEC/PNEC or TER, Toxicity Exposure Ratio), which represents a threshold that must not be exceeded to avoid adverse effects to ecosystems (Figure 1). The pragmatic advantage of this approach, particularly for regulatory purposes, is the possibility to quantitatively express the risk with a relatively small amount of information by applying a simple and transparent procedure. Therefore, the usefulness of such a simplified procedure would remain irreplaceable for preliminary risk assessment for regulatory purposes.

However, the actual consequences on the health of natural ecosystems produced by a PEC/PNEC higher than one are unknown. It follows that effective risk management requires being able to calibrate changes in adverse effects with changes in chemical exposure, and assessments based on thresholds of effects are not helpful for risk management. This is particularly relevant if one considers that one of the aims of ERA is to provide a basis for interventions that relate to effects that should be weighed against the costs of mitigation approaches [63].

Therefore, an “ecologically”-based ERA, performed using more extensive information on ecologically relevant endpoints and ecologically realistic exposure assessment, should be based on a probabilistic assessment of the likelihood of a given adverse effect to occur, developing sound statistic approaches to quantify variability and uncertainty (Figure 2). In this procedure, the risk characterization will not be expressed by a simple numerical threshold.

Figure 1. Simplified scheme of the procedure for ecological risk assessment. PEC, predicted environmental concentrations; PNEC, predicted no effect concentration.

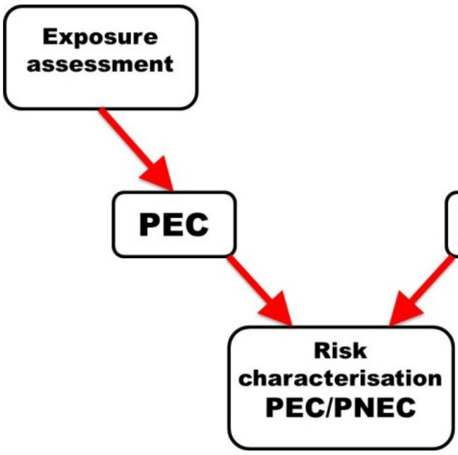
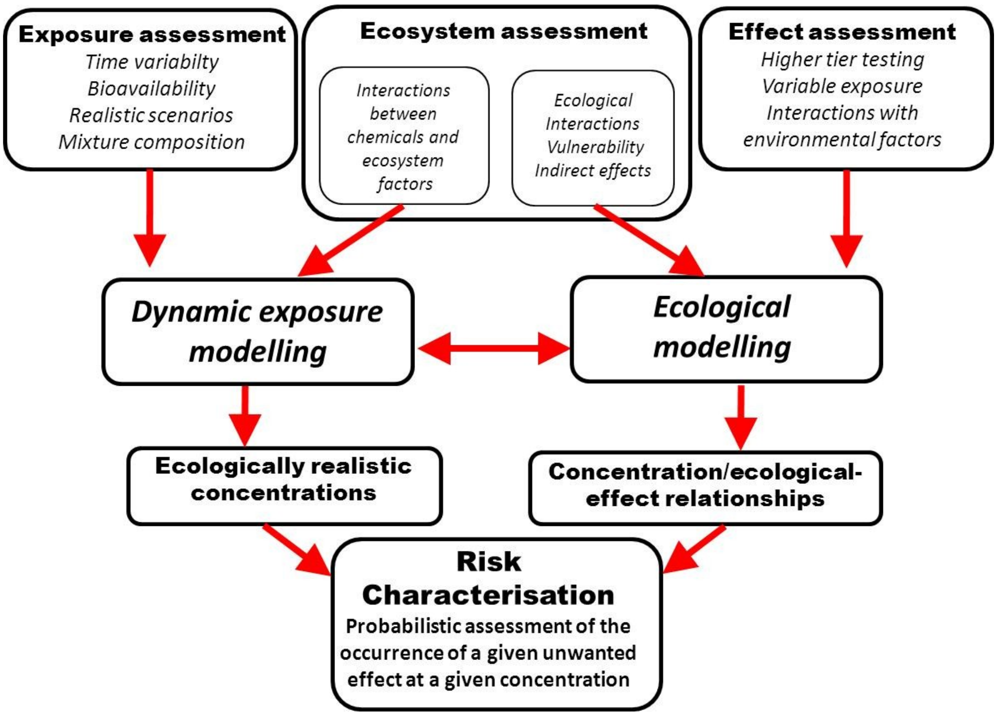


Figure 2. A proposal for a more ecologically-based procedure for ecological risk assessment (modified after [38]).



The type of damage to ecosystem health and its relevance should be expressed in terms of concentration-response relationships in order to provide answers useful for risk managers and decision makers, to better develop a socio-economic analysis and to evaluate the risks and benefits of management [64]. Therefore, the risk characterization, instead of a yes-or-no responses, will provide the quantification of the effects that may occur on a management-relevant endpoint (losses of biodiversity, reduction of ecosystem services, *etc*.) as a function of a likely exposure.

As a general approach, the scheme of Figure 1 could be assumed as a first tier risk assessment procedure, while Figure 2 represents the higher tier ERA, with complete management-relevant information.

7. Conclusions: Toward a New Paradigm in ERA

The need for a substantial shift in the current paradigm of ERA, moving from simplified tools (reductionist approach) toward an attempt at understanding the responses of complex ecological systems to the multitude of possible stress factors (holistic approach), has been recognized for a long time by the international scientific community. Indeed, the problem of putting more ecological realism into risk assessment was still highlighted in a classic article by Cairns [65].

However, one must be aware that the aim of ERA is to produce information in support of risk management and of political and regulatory choices. It is recognized that risk assessment makes little sense unless it is effectively informing the management process. In a recent European document developed by the scientific committees of DG SANCO (Directorate General for Health & Consumers), focused on "Making Risk Assessment More Relevant for Risk Management" [64], it is recommended to develop a system of dialogue that facilitates the exchange of information between risk assessors and risk managers, while ensuring the scientific integrity of the risk assessment.

As a consequence, an important question must be answered: will the increase in ecological complexity make this dialogue more difficult?

An example is the use of ecological modeling in ERA. Regulators are usually not trained to assess whether a model is appropriate for supporting their decisions. On the other hand, scientists may not be familiar with the requirements of regulatory risk assessment, so that even well-designed models could be of little use in a regulatory context, because, for example, they do not deliver appropriate risk characterization. Therefore, a regulatory use of ecological modeling may require a standardization process comparable to those developed for the standardized FOCUS scenarios and models [66] for assessing the fate of chemicals [61].

Another issue raised by the SANCO document is that, in order to be "management-relevant", risk assessments should produce information capable of helping cost/benefit analyses. A threshold-based risk assessment (like those based on simple numbers, such as PEC/PNEC) may be helpful for answering yes/no questions (e.g., pesticide registration), not for more complex risk management procedures, where it is required to express risk by an appropriate metric, in order to develop risk-benefit balance issues.

The two quoted European documents on "Addressing the New Challenges for Risk Assessment" [38] and on "Making Risk Assessment More Relevant for Risk Management" [64] do not provide the solutions to these complex issues, but indicate the direction that must be followed for solving them.

An interesting example of this trend is represented by a guidance document (GD) on aquatic risk for plant protection products developed by EFSA (European Food Safety Authority) [19]. This GD takes into account a number of issues that are not usually considered in traditional ERA procedures, such as refined exposure profiles, approaches for the appropriate designing of model ecosystem studies, assessment of ecological recovery, procedures for assessing uncertainties, *etc*. Moreover, the mandate of the panel that developed the GD also includes an opinion on the state-of-the-art of ecological modeling for the aquatic environment.

It may be concluded that new science is available or will be made available in the near future to address an ecological improvement of ERA. Not all is ready for use, and an effort is needed, by both the scientific and regulatory communities, for making the new scientific achievements realistically applicable. However, the right way has been traced, and it will represent a challenge for ecotoxicology in the 21st century.

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Conflicts of Interest

The authors declare no conflict of interest.

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