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Renewing and improving the environmental risk assessment of chemicals

John P. Sumpter [a,*], Andrew C Johnson [b], Tamsin J. Runnalls [a]

[a] Institute of Environment, Health and Societies, College of Health, Medicine and Life Sciences, Brunel University London, Uxbridge, Middlesex UB8 3PH, United Kingdom
[b] UK Centre for Ecology & Hydrology, Maclean Building, Benson Lane, Crowmarsh Gifford, Wallingford, Oxfordshire OX10 8BB, United Kingdom.

HIGHLIGHTS

- Can the environmental risk assessment (ERA) of chemicals be improved?
- Experts from around the world were asked to suggest improvements.
- Many different suggestions for improvement to the ERA were made.
- It is concluded that environmental risk assessments of chemicals can be improved.

GRAPHICAL ABSTRACT

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ABSTRACT

The processes underpinning the environmental risk assessment (ERA) of chemicals have not changed appreciably in the last 30 years. It is unclear how successful these processes are in protecting the environment from any adverse effects of chemicals. To ascertain if the current methodology can be improved, and if so, how, we invited experts to suggest how the current ERA process could be improved. They were not asked to select from a list of suggestions. The 36 experts made 109 suggestions for improvement, which could be grouped into 33 categories. The category that received the most support, from 12 experts, was to utilise a broader range of scientific information, including all up-to-date information, in ERAs. The second most popular category, supported by 10 experts, was the suggestion to regulate mixtures of chemicals; the current regulatory process involves chemical-by-chemical assessment. Two quite radical proposals were suggested. One was to replace the regulator with artificial intelligence. The other was to establish a new competent authority that would appoint groups of experts, each including representatives of the range of stakeholders, to decide which studies were required, commission those studies, then conduct the ERA based on the results of those studies. These two radical proposals, which the authors support strongly, are not necessarily mutually exclusive. We conclude that the present ERA process could be improved to better protect the environment from the myriad of chemicals in use.

1. Introduction

It is now widely accepted that all habitats across the entire world, as well as the wildlife living in them, are contaminated by anthropogenic chemicals that were not present a century or more ago (in most instances we use the word contamination, rather than pollution, in order not to imply that all the chemicals currently present in the environment are causing adverse effects). This realisation, coupled with the fact that some chemicals (e.g. pesticides, also called plant protection products) are inherently toxic, has led to chemical contamination being described as one of the nine planetary boundaries driving global environmental change (Rockström et al., 2009). Despite subsequently updating the concept of planetary boundaries (Steffen et al., 2015), the planetary boundary covering chemical contamination - now termed 'Introduction of novel entities' - is not yet sufficiently quantified, due to lack of knowledge on

* Corresponding author at: Institute of Environment, Health and Societies, College of Health, Medicine and Life Sciences, Brunel University London, Uxbridge, Middlesex UB8 3PH, United Kingdom.
E-mail address: john.sumpter@brunel.ac.uk (J.P. Sumpter).

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the severity of the effects of contamination on both human health and the health of the environment. This is especially true in the less developed parts of the world. In addition, the International Science-Policy Platform on Biodiversity and Ecosystem Services (IPBES) identified chemical pollution on a global scale as one of the five main drivers of biodiversity loss (IPBES, 2019). Based on concerns such as these, the European Union now has a 'Zero-pollution ambition' (European Commission, 2019). Its zero-pollution vision for 2050 is for air, water and soil pollution to be reduced to levels no longer considered harmful to human health and natural ecosystems.

These various 'high level' concerns about the adverse consequences of chemical contamination have, understandably, led to calls to make chemical regulation more stringent than it is presently. Concern about adverse effects of chemicals on the living environment arose as a consequence of Rachel Carson's ground-breaking book 'Silent Spring' (Carson, 1962). In the 1980s and 1990s, discussions took place in both Europe and America on how best to determine the environmental risks posed by the use of toxic chemicals (reviewed in Syberg and Hansen, 2016). These discussions laid the foundations of the current chemical risk assessment process for both humans and the environment. In the case of environmental risk assessment (ERA), the process is based on comparing likely hazard of a chemical with the degree of exposure to that chemical. To do this, the four steps involved in ERA need to be completed: hazard identification, dose-response assessment, exposure quantification and risk assessment. Sometimes a fifth step, agreeing a 'Protection Goal', is also included in the ERA. Because nowadays chemicals have to be registered before their use is permitted, it is necessary to estimate (i.e. predict) parameters such as the concentration of a chemical below which adverse effects are unlikely and the maximum concentration likely to be present in the environment. This has led to the final step in the ERA process, namely risk assessment, being a comparison of the predicted exposure concentration (PEC) with the predicted-no-effect-concentration (PNEC), so that a PEC/PNEC ratio can be obtained. A PEC/PNEC ratio of one or above signifies that a chemical might adversely affect the environment.

Although the basic methodology of the ERA of chemicals is consistent across all chemicals, subtle differences in what and how much information is required in order to conduct an ERA have developed, depending on the type of chemical. For example, in the E.U. there are presently different regulatory frameworks for biocides, industrial chemicals, pesticides, human medicines, and veterinary medicines (see van Dijk et al., 2021, for details). This fragmentation of the risk assessment and registration of chemicals into silos is common across the world. In addition, environmental risk assessment is usually conducted completely separately from human health risk assessment of chemicals. And to add even further complexity to the risk assessment of chemicals, individual countries (or occasionally blocks of countries, such as the European Union) have their own regulations and legislation (Lee and Choi, 2019), although these frameworks are often complemented by international agreements covering specific groups of chemicals, particularly those that undergo long-range transport (e.g. the Stockholm Convention covering persistent organic pollutants (POPs)).

During the time that the existing ERA process has been at the heart of protecting the environment from adverse impacts of chemicals (about 30 years), the number of chemicals in everyday use worldwide, as well as the amounts of most chemicals, have increased dramatically. The most recent estimate (Wang et al., 2020) is that at least 350,000 chemicals are registered for use. The majority of these chemicals will not have undergone an ERA. We accept, however, that the ERA process has not stood still in the last 30 years. For example, registration requirements for some chemicals (e.g. pesticides) have increased very significantly, necessitating testing on many more species, both in the laboratory and the field.

It is difficult, if not impossible, to determine how successful the ERA of chemicals has been at protecting the environment. On the one hand, it is possible to argue that, as relatively few examples are well documented in which chemicals reaching the environment caused significant, widespread, adverse effects (reviewed in Johnson et al., 2020), the ERA process is, generally, working reasonably well, although this conclusion ignores any long-term, insidious effects of chemical pollution, which could be significant. On the other hand, it can be argued that many more adverse effects have likely occurred, but that these have gone unnoticed and/or unrecorded. In addition, the cumulative effects of exposure to complex mixtures of chemicals might be significant (Malaj et al., 2014); a situation that would not be considered by the current processes, because ERAs are usually conducted on individual chemicals, not mixtures of chemicals.

There is now a widespread view that the current processes involved in the regulation of chemicals may be insufficiently protective of the environment, and hence they need to be improved (reviewed in Johnson et al., 2021; Wang et al., 2021). Yet, surprisingly, relatively little appears to have been written in the open scientific literature on how the current ERA process could be improved (some suggestions on specific aspects of the ERA can be found in, for example, Kortenkamp and Faust, 2018; LaLone et al., 2021; Syberg and Hansen, 2016; van Dijk et al., 2021). We are not aware of any study that has addressed any potential improvements that could be made to the ERA process by seeking the opinions of a relatively large group of experts possessing very considerable expertise in environmental risk assessment. Yet with so much experience of the ERA process available - particularly in regulatory organisations and the chemical industry in its widest sense - it seemed sensible to us to seek opinions from a hopefully fairly representative, and relatively large, group of these experts, in order to obtain a unique, original set of recommendations on how the ERA process might be improved. We realise that with many different regulatory jurisdictions in existence, both with regard to geography (i.e. many countries have their own, unique, regulatory regimes) and chemical groups (i.e. separate regulatory processes for different groups of chemicals), environmental risk assessment of chemicals is presently a very long way from the theoretically ideal 'one substance, one assessment' approach sometimes advocated. Thus, it is easy to be pessimistic about the objective of the piece of work reported here. We understand that pessimism. Nevertheless, we conducted the research described in this paper not with the aim of mandating how the ERA process should be improved, but instead with the more modest aim of stimulating discussion in this area, in order to take things forward.

2. Materials and methods

The aim of this project was to determine if the current environmental risk assessment methodology for chemicals could be improved, and if so, how. To achieve that aim the opinions of experienced, appropriately knowledgeable, scientists (hereafter termed experts) were sought via an e-mail invitation to provide input (see Supplementary Information Fig. 1). A conscious attempt was made to obtain opinions from experts who worked in different types of organisation (e.g. academia, regulatory bodies, industry, environmental consultancies; Table 1) and who worked in different countries (Fig. 1). However, intentionally we did not invite an equal number of experts from the various professions to participate. Instead, we invited a predominance of regulators (15), on the basis that this group would probably be more experienced and knowledgeable about the ERA process than any other groups of experts, and scientists working in industry (10), because they too were very experienced in conducting ERAs on their companies products.

Table 1
Number of experts involved in the review by profession. We have included within the category 'Regulatory Authority' research scientists who conduct regulatory-relevant research within a regulatory agency.

Sector	Number
Academia	5
Consultancy	3
Industry	10
NGO	4
Regulatory Authority	14

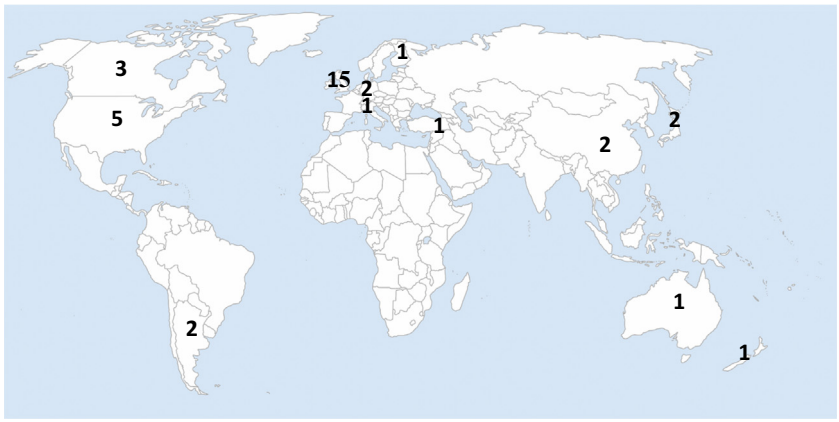

Fig. 1. Location of the 36 experts who provided suggestions for improvements to the existing environmental risk assessment process for chemicals.

It is realised that our choice of experts covers only a very small proportion of the many people and many organisations currently involved in ERAs in one way or another. For example, many countries that have their own regulatory processes in place are not represented. Nor are many regulatory agencies. Nevertheless, we selected our experts on the basis that collectively we considered them to be capable of providing a balanced, international perspective on the ERA of chemicals.

Most experts had 30, or more, years of relevant experience. The expertise of some experts was limited to a single class of chemicals (e.g. pesticides, pharmaceuticals), whereas other experts had more wide-ranging expertise. When invited to participate, experts were not told the names of anyone else whom we had invited to contribute suggestions; this was done to prevent any collusion between experts. Most experts provided their own personal opinions, rather than those of their organisations (many explicitly stated this), although a few (we believe less than 5) consulted colleagues working in their organisations before providing a collective list of suggestions. We accept that our experts, like everyone, might have their own biases; we discuss the issue of potential bias in the Discussion.

Nearly all experts who were approached replied (36), and provided suggestions for improvement to the current ERA process (see Supplementary Information Table 1 for the names and organisations of the experts). The experts each provided between 1 and 7 suggestions for improvement to the current ERA process; in total, 107 suggestions were received. The respondents were not asked how any of their suggestions might be achieved. Some experts stated their suggestions in no more than a sentence or two (e.g. "use up-to-date scientific information"), whereas others expanded to varying degrees on their suggestions (e.g. they specifically suggested including omics information within up-to-date information). Recommendations were then firstly sorted into categories according to whether they were identical or similar. For example, one category was labelled 'Regulate Mixtures', and received all suggestions covering the need to conduct risk assessments based not only on single chemicals (as now), but also on environmentally-realistic mixtures of chemicals. Then an attempt was made to group at least some of these categories under broader headings; for example, several categories are concerned with incorporating recent scientific knowledge and advances into the ERA, and hence could be grouped under 'Utilise Modern Approaches'.

3. Results

No expert stated that he/she thought that the existing ERA process was as good as it could be; all experts considered that the current process could, and should, be improved.

As would be anticipated, suggestions for improvement to the ERA of chemicals were, to some degree, influenced by the background of the expert. Thus, an expert working for an agrochemical company was likely to suggest improvements particularly relevant to the ERA of pesticides, while an expert working for a pharmaceutical company was likely to suggest improvements to the current regulatory guidelines for medicines, such as those originating from the European Medicines Agency (EMA). Nevertheless, many of the suggestions provided were quite general, and hence would apply to the regulation of any group of chemicals (e.g. Increase flexibility; move away from the current 'box ticking'). Importantly, suggestions from different professions (e.g. academia, industry) were not obviously distinct; that is, for example, academics did not provide a unique set of suggestions that no other group of experts suggested.

The most common recommendations for improvement of the ERA are listed in Table 2. The single most recommended improvement was to utilise up-to-date scientific knowledge. Many experts commented, in various ways, that a wealth of new methodologies offered relevant information about the potential effects of chemicals on organisms had been obtained since the existing ERA guidelines were established, yet little, if any, of this information was presently utilised in the regulatory process. In particular, use of data obtained from omic studies was mentioned many times (omic studies assess changes in RNA transcript levels, protein levels, or metabolite levels). This desire to utilise up-to-date scientific knowledge in the ERA is even more apparent when grouping our existing categories

Table 2
The most common recommendations made by the experts for improvement to the existing ERA process for chemicals. It has been necessary to condense the often comprehensive comments made by some of the experts into a few words in order to produce this table.

Position	Category	Number of recommendations
1:	Utilise up-to-date scientific knowledge	12
2:	Regulate mixtures	10
3:	Improve fate and behaviour tests	7
4=:	Group similar chemicals (e.g. by mechanism of action)	6
4=:	Communicate uncertainty, including that ERAs may overestimate risk	6
4=:	Increase flexibility; move away from current 'box ticking'	6
7=:	Internationalize regulation	5
7=:	Improve training of regulators	5
9=:	Combine environmental and human health risk assessments	4
9=:	Include socioeconomic impact (i.e. risk/benefit analysis)	4
9=:	Establish regulations appropriate for developing countries	4
12=:	Include all stakeholders	3
12=:	Update ERAs regularly	3
12=:	Regulate based on risks, not hazards	3
12=:	Use data from non-animal methods (e.g. in vitro, in silico)	3
12=:	Develop toxicity tests for groups of organisms currently excluded (e.g. molluscs)	3

(as shown in Table 1). Our categories 'Utilise up-to-date scientific knowledge', 'Group similar chemicals', 'Use data from non-animal methods', 'Replace the regulator with artificial intelligence', and 'Utilise better extrapolation across species' could all be considered ways of using broader knowledge and approaches within the ERA of chemicals, and therefore could be grouped together under 'Utilise a broader range of modern approaches.

The second most common suggestion was to regulate mixtures. To some extent this is done already by the use of so-called 'assessment factors', but could, and probably should, be done in a scientifically more robust and defensible manner. Many experts expressed concerns that regulation based on individual chemicals was not representative of the 'real world', where exposure is most often to complex mixtures of chemicals. Other categories that received support from a good number of experts included grouping chemicals with similar structures and hence similar anticipated effects (doing so would decrease the number of ERAs needed), communicating the uncertainty inherent in the ERA process, internationalizing regulation (i.e. develop guidelines and conduct ERAs at the international, not national, level), and improve the training of regulators. The latter two suggestions, together with 'Include all stakeholders', can be considered linked, as they would all increase the pool of expertise available to conduct ERAs.

Twenty suggestions were made by only one or two experts; these are listed in Table 3. As with the more frequently suggested recommendations, these less common suggestions for improvement ranged from the very general (e.g. combine regulation of chemicals, products and waste; chemical regulation needs to be proportionate to the magnitude of other stressors) to the specific (e.g. scrap trigger values; do not utilise species-sensitivity distributions).

Two particularly radical proposals were submitted. One was to replace the regulator with artificial intelligence (A.I.). The other was to establish a completely different regulatory system. That system would involve setting up a 'department' which decided which studies were required for the ERA of a particular chemical, and would have the power to mandate their commission, the results of which would be assessed by a group of environmental experts, which could include members of all stakeholders. These two radical proposals are discussed below.

Table 3
A list of the recommendations provided by one or two experts only.

Category	Number of recommendations
Untested chemicals should not be in use	2
Formalize how to conduct a Weight of Evidence assessment	2
Establish quality control standards for acceptable data	2
Replace the regulator with artificial intelligence (A.I.)	2
Chemical regulation needs to be proportionate to the magnitude of other stressors	2
Combine regulation of chemicals, products and waste	1
Improve enforcement of regulations	1
Products that only just receive approval should be subject to post-approval monitoring	1
Utilise better extrapolation across species	1
Scrap trigger values	1
'Regrettable' substitutions should be prohibited	1
Determine if some previous risk assessments provided reliable results	1
Utilise species-sensitivity distributions (SSDs) only when sufficient data are available	1
Do not introduce further, unrealistic, testing	1
Assess contaminants, especially the raw material used to produce the final product	1
Cease testing once a reasonable conclusion can be reached	1
Combine more endpoints into a single study	1
Establish a procedure to deal with unexpected toxicity of 'in use' chemicals	1
The regulatory system needs to facilitate innovation	1
Ban the most hazardous chemicals from all non-essential uses	1

4. Discussion

4.1. Involving all stakeholders

We want to emphasize that it was not our intention to criticise any one group of stakeholders. In particular, we are not suggesting that regulators are currently failing in their duty. They are not; they are doing a good job in applying, correctly and accurately, the guidelines laid down in the laws under which they operate. Nor is this paper only a critique of current ERA procedures. Instead, it is intended to stimulate a debate on whether, and how, the existing ERA procedures can be improved.

Given the absolutely crucial role that the ERA plays in protecting the environment from any adverse effects likely to be caused by the use of chemicals, it is very surprising that so little appears to have been written about how successful, or not, the current process is, and how it might be improved, to better protect the environment. The most likely explanation for this situation is that most of the open, easily accessed, scientific literature is produced by academic scientists who rarely actively engage in ERA, whereas regulators who conduct ERAs do not, in general, consider publication in the open scientific literature as an important component of their job (see below for further discussion of silos), although ERAs are usually published by governments on government websites. Many industries involved in the ERA process do not publish their results - some are considered confidential - although this situation may be changing; the pharmaceutical industry, for example, has recently published a considerable amount in the open scientific literature (e.g. Straub, 2009; Zeilinger et al., 2009). We acknowledge that this is a generalisation, which is perhaps best illustrated by the fact that some scientists working in the U.S. Environmental Protection Agency (EPA) are very prolific research scientists, whose published research is very influential. It is also true that a few academic scientists conduct, and publish, comprehensive ERAs (see, for example, Sumpter et al., 2021), and some companies (e.g. pharmaceutical and agrochemical companies) do both research and conduct comprehensive ERAs on their products. In addition, even if regulators publish relatively little original research, they can contribute very significantly to the improvement of original research (e.g. Moermond et al., 2016), in order that basic research is made more useful to the work of regulators.

4.2. The potential impact of bias

One distinctly possible outcome of our survey was that experts from one type of organisation might suggest one suite of improvements, whereas another group of experts might strongly favour a quite different suite of improvements. For example, research scientists might have suggested the inclusion of data derived from modern techniques (e.g. transcriptomics) in ERA, whereas industry experts might have favoured simplifying the ERA in various ways. However, an analysis of the results shows that no such segregation took place. All recommendations for improvement of the ERA that were provided by 3 or more experts (those listed in Table 1) came from at least two types of organisations, with just one exception out of the 16 recommendations. Thus, for example, the most commonly provided recommendation, namely utilise up-to-date scientific knowledge, was suggested by 3 of the 5 groups of experts (6 regulators, 5 industry scientists, and 1 consultant), and the second most commonly provided recommendation, regulate mixtures, was cited by 4 of the 5 groups of experts (6 regulators, 2 research scientists, one member of an NGO, and 1 consultant). It is thus possible to conclude not only that all experts consider that the ERA process could be improved, but also that there is a high degree of unanimity in the nature of those improvements. The single exception was the suggestion to regulate based on risk, not hazard; this recommendation was made by 3 experts, all of whom work in industry. Hazard-based ERAs are attractive because they are simpler and will probably be protective, but they can hinder development and use of newer chemicals that might be more environmentally friendly.

A possible concern of any survey, including this one, is that the respondents (our 'experts') are biased, and hence the results of the survey may not

be representative of the general view. We do not know how representative our panel of 36 experts was. It is possible that a different set of 36 experts would have provided somewhat different opinions regarding how the ERA process could be improved. All scientists, and all people more generally, are probably biased to different degrees in different ways (see the discussion on how bias in scientists can distort scientific integrity in (Mebane et al., 2019). However, we attempted to minimise any bias by seeking the opinions of a relatively large number of established scientists, who were based in different organisations with different remits, in different countries. However, even if a different set of experts would have provided a somewhat different set of recommendations on how the ERA process could be improved, that would not have detracted from the main message of this paper. That is because this paper is not intended to be a manual for how to improve the ERA process. Instead, it is aimed at stimulating a debate, open to all scientists, on how to improve the ERA process, to make it both more efficient and more protective of the environment.

Many of the proposed improvements in the ERA process would likely lead to increased costs. Increasing the complexity, and hence costs, of the ERA can have both positive and negative consequences. On the positive side, it has led to the loss of many older chemicals, particularly pesticides, once their adverse effects were recognised, but on the negative side it has deterred investment in the development of newer, safer, ones.

4.3. The most radical proposals

Although the overwhelming majority of the recommendations for improvement to the ERA process could be considered as either adding additional complexity to the existing methodology (e.g. Develop toxicity tests for groups of organisms currently excluded; Include a socioeconomic impact) or improving existing aspects (e.g. Improve fate and behaviour tests; Increase flexibility – move away from current 'box ticking'), two recommendations were quite radical, and although very different, would, if enacted, both lead to a very different ERA process. One radical proposal was to replace the existing ERA process with predictions obtained using artificial intelligence (A.I.). Such a proposal has recently been recommended in the open scientific literature (e.g. Miller et al., 2018; Owen and Snape, 2021)). Doing so would, of course, take time, in order to advance knowledge in a number of areas (e.g. toxicokinetics, transformation in the environment), but it would address a number of the current concerns about the existing ERA process. These would include removing the need to use animals when determining the (eco)toxicity of chemicals, training of regulators could be simplified, uncertainty could be reduced, the ERA process would speed up considerably, allowing legacy chemicals in use but for which no ERA exist to be addressed, and the same technology and outputs could be applied internationally. Given that current regulatory practices cannot keep up with the speed of introduction of new chemicals, better predictive tools, such as A.I., must be the way forward.

The other radical proposal was to scrap the existing ERA process, in which industry obtain and provide the data to regulators to assess and reach decisions on, and replace it with a process involving a much wider range of stakeholders who are involved throughout the process. The actual process suggested was to establish a competent authority whose first job, once approached, would be to appoint, for each ERA, a group of appropriate experts who would conduct the ERA in its entirety. These expert groups would comprise of environmental experts covering the entire range of relevant stakeholders (i.e. the experts could come from industry, academia, or even the public). Each expert group would decide what data were required for the ERA, and it would have the mandate to commission the studies necessary to obtain those data, directly and independently of applicants. This structure would be financed with fees from the applicants; thus companies would pay for the ERA tests, as they do presently. A central, transparent database would be maintained, open to all, from the beginning of the ERA process. There would therefore be no need for discussions about confidentiality anymore, because the studies would not belong to the applicant. That openness would reduce repetitive testing and the associated waste of resources (and, importantly, animals) that can occur presently. The OECD Mutual Acceptance of Data approach might be a potential model to work from. In the opinion of this paper's authors, this idea of a new Competent Authority with considerable powers is considered a very valuable suggestion, whilst recognising that issues will occur, and one we would like to see discussed further.

We are strong supporters of both radical suggestions, which are not necessarily independent of each other. Bringing more expertise into the ERA process as it slowly but steadily changes from the existing chemical by chemical in vivo exposure and assessment paradigm to in silico predictions of real-world effects occurring from exposure to highly complex mixtures of chemicals seems to be a sensible future strategy.

4.4. The need to work together

One issue raised by quite a few experts was the issue of silos, of which there are various types. One type, mentioned in the Introduction, is that different classes of chemicals (e.g. biocides, pharmaceuticals, cosmetics) are risk assessed by different competent authorities; for example, the European Medicines Agency (EMA) conducts the ERAs for pharmaceuticals, but not any other class of chemicals. Another type of silo is created by there being different experts, often based in different organisations, involved in producing the information needed for an ERA and then assessing that information. These range from research scientists, often based in universities or research institutes, through to regulators based in the competent authorities, such as the EMA and European Chemicals Agency (ECHA) in Europe. Unfortunately, there is relatively little interaction or movement between staff working for these quite separate and distinct organisations (but see Martin et al., 2019, for a consensus on steps to improve the ecotoxicology utilised in the ERA). A further level of silo mentality is created by nationalism. The existence of independent regulatory jurisdictions (e.g. the European Union) often means that they conducts their own ERAs through the organisations they have established to do so. This can sometimes produce a great deal of repetition and redundancy at an international level: and sometimes contrasting decisions. Establishing some form of global organisation capable of assessing the risks posed by the use of chemicals would be very beneficial (Wang et al., 2021). Such an organisation would be particularly useful to the less developed world, which often does not have the expertise and structures necessary to conduct ERAs. We strongly support the establishment of a global registration and risk assessment process. In the interim, a quicker approach would be to improve co-ordination on the scientific aspects of assessment between different regulatory bodies.

4.5. Improving the quality of research

Perhaps surprisingly, few experts said that they thought improving the quality of research would be beneficial. Yet doing so is crucial, because it is widely accepted that a significant proportion of published research is not of sufficient quality to be used in an ERA (Hanson et al., 2017; Moermond et al., 2016). A recent publication illustrates this problem vividly; a very thoughtful and thorough analysis of the 8 research papers covering the (potential) effects of ultraviolet filters used in sunscreens on corals concluded that "none of the current studies on the toxicity of UV filters to corals are of potential regulatory or decision-making quality" (Burns and Davies, 2021). There is absolutely no point in utilising all up-to-date scientific information in the ERA process - the most common recommendation made by our experts - if those data are unreliable. Utilising unreliable information will lead to ERAs reaching incorrect decisions (see Burns and Davies, 2021). Doing so would also prolong any ERA, as applicants argued with regulators about the quality of data available to conduct the ERA.

4.6. Conclusions and cautions

In conclusion, there is very widespread agreement that the present ERA process for chemicals could, and should, be both updated and improved. Many different improvements could be made to the existing process.

These range from relatively minor changes to the current process to very radical approaches that would involve replacing the current process with a fundamentally different one. If the environment is to be protected from any harm caused by chemicals (see Collins et al., 2020, for a philosophical discussion on 'do no harm'), then change to the present system is required.

We recognize that many regulatory agencies are thinking along lines similar to us, and are aware of the need to update the ERA process. Some have, in fact, already incorporated some of the most popular improvements, such as utilising the most up-to-date science and accounting for mixtures, into their ERA processes. To provide just one example, the US EPA have similar goals regarding the use of New Approach Methodologies (NAMs) in chemical risk assessment (https://www.epa.gov/chemical-research/accelerating-pace-chemical-risk-assessment-apcra), as has Canada (Barton-Maclaren et al., 2022).

Finally, a word of caution is probably appropriate. Any new ERA process is unlikely to be perfect, just as the current process isn't (Johnson et al., 2021). One issue that could be particularly problematic is the toxicity not of the parent chemicals, but of any transformation products formed from them in the environment. The recent discovery that a transformation product of a chemical used in high amounts worldwide in the manufacture of car tyres is acutely toxic to adult salmon (Tian et al., 2021) illustrates this issue only too well.

However the ERA process is updated and improved, predicting which transformation products will be formed in the environment, then predicting their toxicity, will be challenging, although progress is being made in this area (see, for example, Maculewicz et al., 2022). In addition, more intelligently-applied environmental monitoring will be required, in order to detect any ERA failures (Collins et al., 2020). It is also worth keeping in mind that the ERA process is based upon assessing the toxicity of chemicals, whereas chemicals can pose risks by mechanisms other than toxicity, such as altering behaviour of organisms. But these are not reasons to postpone improvement of the ERA process.

CRediT authorship contribution statement

John P. Sumpter: Conceptualization, Methodology, Formal analysis, Investigation, Writing – original draft, Supervision. **A.C. Johnson:** Writing – review & editing, Funding acquisition. **Tamsin J. Runnalls:** Data curation, Writing – review & editing, Visualization, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Supplementary data

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