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van den Brink, Paul J., Boxall, Alistair B A [orcid.org/0000-0003-3823-7516](https://orcid.org/0000-0003-3823-7516), Maltby, Lorraine et al. (38 more authors) (2018) *Toward sustainable environmental quality: Priority research questions for Europe*. *Environmental Toxicology and Chemistry*. ISSN 1552-8618

<https://doi.org/10.1002/etc.4205>

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# 1 Towards Sustainable Environmental Quality: Priority Research

## 2 Questions for Europe

3 *Paul J. Van den Brink<sup>1,2</sup>, Alistair B.A. Boxall<sup>3\*</sup>, Lorraine Maltby<sup>4</sup>, Bryan W. Brooks<sup>5</sup>, Murray*  
4 *A. Rudd<sup>6</sup>, Thomas Backhaus<sup>7</sup>, David Spurgeon<sup>8</sup>, Violaine Verougstraete<sup>9</sup>, Charmaine Ajao<sup>10#</sup>*  
5 *Gerald T. Ankley<sup>11</sup>, Sabine E. Apitz<sup>12</sup>, Kathryn Arnold<sup>4</sup>, Tomas Brodin<sup>13</sup>, Miguel Cañedo-*  
6 *Argüelles<sup>14,15</sup>, Jennifer Chapman<sup>3</sup>, Jone Corrales<sup>5</sup>, Marie-Agnès Coutellec<sup>16</sup>, Teresa F.*  
7 *Fernandes<sup>17</sup>, Jerker Fick<sup>18</sup>, Alex T. Ford<sup>19</sup>, Gemma Giménez Papiol<sup>20</sup>, Ksenia J. Groh<sup>21</sup>, Thomas*  
8 *H. Hutchinson<sup>22</sup>, Hank Kruger<sup>23</sup>, Jussi V.K. Kukkonen<sup>24</sup>, Stefania Loutseti<sup>25</sup>, Stuart Marshall<sup>26</sup>,*  
9 *Derek Muir<sup>27</sup>, Manuel E. Ortiz-Santaliestra<sup>28</sup>, Kai B. Paul<sup>29</sup>, Andreu Rico<sup>30</sup>, Ismael Rodea-*  
10 *Palomares<sup>31</sup>, Jörg Römbke<sup>32</sup>, Tomas Rydberg<sup>33</sup>, Helmut Segner<sup>34</sup>, Mathijs Smit<sup>35</sup>, Cornelis*  
11 *A.M. van Gestel<sup>36</sup>, Marco Vighi<sup>30</sup>, Inge Werner<sup>37</sup>, Elke I. Zimmer<sup>38</sup> and Joke van Wensem<sup>39</sup>*

12 <sup>1</sup> Department of Aquatic Ecology and Water Quality Management, Wageningen University,  
13 P.O. Box 47, 6700 AA Wageningen, The Netherlands.

14 <sup>2</sup> Wageningen Environmental Research (Alterra), P.O. Box 47, 6700 AA Wageningen, The  
15 Netherlands.

16 <sup>3</sup> Environment Department, University of York, Heslington, York, YO10 5NG, UK

17 <sup>4</sup> Department of Animal and Plant Sciences, The University of Sheffield, Western Bank,  
18 Sheffield, S10 2TN, UK

19 <sup>5</sup> Department of Environmental Science, Baylor University, Waco, Texas, USA.

20 <sup>6</sup> World Maritime University, Malmo, Sweden.

21 <sup>7</sup> Department of Biological and Environmental Sciences, University of Gothenburg, Carl  
22 Skottsbergs Gata 22 B, 40530 Gothenburg, Sweden

23 <sup>8</sup> Centre for Ecology and Hydrology, MacLean Building, Benson Lane, Wallingford, Oxon, OX10  
24 8BB, UK.

25 <sup>9</sup> Eurometaux, 12 avenue de Broqueville, 1150 Brussels, Belgium.

26 <sup>10</sup> European Chemicals Agency (ECHA), Annankatu 18, 00120 Helsinki, Finland

27 <sup>11</sup> US Environmental Protection Agency, 6201 Congdon Blvd, Duluth, MN, 55804, USA

28 <sup>12</sup> SEA Environmental Decisions, Ltd., 1 South Cottages, The Ford; Little Hadham, Hertfordshire  
29 SG11 2AT, UK

30 <sup>13</sup> Department of Ecology and Environmental Science, Umeå University, 90187 Umeå, Sweden.

31 <sup>14</sup> Freshwater Ecology and Management (FEM) Research Group, Departament de Biologia  
32 Evolutiva, Ecologia i Ciències Ambientals, Institut de Recerca de l'Aigua (IdRA), Universitat de  
33 Barcelona (UB), Diagonal 643, 08028 Barcelona, Catalonia, Spain.

34 <sup>15</sup> Aquatic Ecology Group, BETA Tecnio Centre, University of Vic - Central University of  
35 Catalonia, Vic, Catalonia, Spain.

36 <sup>16</sup> ESE, Ecology and Ecosystem Health, INRA, Agrocampus Ouest, 35042 Rennes, France.

37 <sup>17</sup> Institute of Life and Earth Sciences, Heriot-Watt University, Edinburgh EH14 4AS, UK

38 <sup>18</sup> Department of Chemistry, Umeå University, 90187 Umeå, Sweden.

39 <sup>19</sup> Institute of Marine Sciences, University of Portsmouth, Ferry Road, Portsmouth, England,  
40 PO4 9LY, UK

41 <sup>20</sup> Environmental Engineering Laboratory, Chemical Engineering Department, Universitat  
42 Rovira i Virgili, Av. Països Catalans 26, Tarragona, Spain

43 <sup>21</sup> Eawag, Swiss Federal Institute of Aquatic Science and Technology, 8600 Dübendorf  
44 Switzerland

45 <sup>22</sup> School of Geography, Earth & Environmental Sciences, University of Plymouth, Plymouth  
46 PL4 8AA, United Kingdom

47 <sup>23</sup> Wildlife International Ltd., Easton, Maryland, USA

48 <sup>24</sup> Department of Biological and Environmental Science, P.O. Box 35, FI-40014 University of  
49 Jyväskylä, Jyväskylä, Finland

50 <sup>25</sup> DuPont De Nemours, Agriculture & Nutrition Crop Protection, Hellas S.A. Halandri Ydras 2&  
51 Kifisias Avenue 280r. 15232 Athens, Greece

52 <sup>26</sup> Unilever, Safety & Environmental Assurance Centre, Colworth Science Park, Sharnbrook,  
53 MK441LQ, UK. (Retired)

54 <sup>27</sup> Aquatic Contaminants Research Division, Water Science Technology Directorate,  
55 Environment and Climate Change Canada, 867 Lakeshore Road, Burlington, Ontario L7S 1A1  
56 Canada

57 <sup>28</sup> Spanish Institute of Game and Wildlife Resources (IREC) CSIC-UCLM-JCCM. Ronda de Toledo  
58 12, 13005 Ciudad Real, Spain

59 <sup>29</sup> Blue Frog Scientific Limited, Quantum House, 91 George St., EH2 3ES, Edinburgh, UK

60 <sup>30</sup> IMDEA Water Institute, Science and Technology Campus of the University of Alcalá, Avenida  
61 Punto Com 2, 28805 Alcalá de Henares, Madrid, Spain

62 <sup>31</sup> Department of Agricultural and Biological Engineering, University of Florida, Gainesville, FL  
63 32611, USA

64 <sup>32</sup> ECT Oekotoxikologie GmbH, Böttgerstrasse 2-14, D-65439 Flörsheim, Germany

65 <sup>33</sup> IVL Swedish Environmental Research Institute, PO Box 5302, 40014 Göteborg, Sweden

66 <sup>34</sup> Centre for Fish and Wildlife Health, University of Bern, 3012 Bern, Switzerland

67 <sup>35</sup> Shell Global Solutions, Carel van Bylandtlaan 30, 2596 HR The Hague, The Netherlands

68 <sup>36</sup> Department of Ecological Science, Faculty of Science, Vrije Universiteit, De Boelelaan 1085,  
69 1081 HV Amsterdam, The Netherlands

70 <sup>37</sup> Swiss Centre for Applied Ecotoxicology, Ueberlandstrasse 133, 8600 Dübendorf, Switzerland

71 <sup>38</sup> ibacon GmbH, Roßdorf, Germany

72 <sup>39</sup> Ministry of Infrastructure and the Environment, P.O. Box 20901, 2500 EX The Hague, The  
73 Netherlands

74 \* - Corresponding author: Email [Alistair.boxall@york.ac.uk](mailto:Alistair.boxall@york.ac.uk)

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76 opinions expressed in this article represent exclusively the personal ideas of the author and  
77 do not represent the official position of the Agency.

78

79 **ABSTRACT**

80 The United Nations Sustainability Development Goals (SDGs) have been established to end  
81 poverty, protect the planet and ensure prosperity for all. Delivery of the SDGs will require a  
82 healthy and productive environment. An understanding of the impacts of chemicals, which  
83 can negatively impact environmental health, is therefore essential to the delivery of the SDGs.  
84 However, current research on and regulation of chemicals in the environment tends to take a  
85 simplistic view and does not account for the complexity of the real world, which inhibits the  
86 way we manage chemicals. There is therefore an urgent need for a step-change in the way  
87 we study and communicate h the impacts and control of chemicals in the natural  
88 environment. To do this requires the major research questions to be identified so that  
89 resources are focused on questions that really matter. In this paper, we present the findings  
90 of a horizon scanning exercise to identify research priorities of the European environmental  
91 science community around chemicals in the environment. Using the key questions approach,  
92 we identified 22 questions of priority. These questions covered: overarching questions around  
93 which chemicals we should be most concerned about and where, impacts of global  
94 megatrends, protection goals and sustainability of chemicals; the development and  
95 parameterisation of assessment and management frameworks; and mechanisms to maximise  
96 the impact of the research. The research questions identified in this paper provide a first-step  
97 in the path forward for the research, regulatory and business communities to better assess  
98 and manage chemicals in the natural environment.

99 **Keywords:** key questions exercise, global megatrends, environmental risk assessment,  
100 chemical management, sustainability

101 **INTRODUCTION**

102 On 1 January 2016, the 2030 Agenda for Sustainable Development and its 17 Sustainable  
103 Development Goals (SDGs) came into force (UN, 2015). The aim of the SDGs is to end poverty,  
104 protect the planet and ensure prosperity for all, and their delivery depends on a healthy and  
105 productive environment. Europe, like many other parts of the world, is facing a number of  
106 major environmental challenges. These include habitat loss and degradation, climate change  
107 and associated extreme weather events, environmental contamination resulting from  
108 urbanization, agricultural intensification and increased per capita consumption of natural  
109 resources. These environmental challenges, which are a consequence of human activities, are  
110 resulting in biodiversity loss, increasing natural hazards, threatening food, water and energy  
111 security, impacting human health and degrading environmental quality (e.g., Leip et al., 2015;  
112 Civantos et al., 2012). The European Environment Agency (2015) has highlighted  
113 environmental impacts and health risks from chemicals and climate change as areas of major  
114 concern. It also states that, whereas industrial pollutant emissions in Europe have declined  
115 due to implementation of more stringent EU policies, they still cause considerable damage to  
116 the environment and human health (EEA, 2015).

117 However, our understanding of how chemicals impact the environment and human health is  
118 still poorly developed. For example, most research on and regulation of chemicals considers  
119 the impacts of individual substances yet in the real environment, chemicals will co-occur with  
120 100s or 1000s of other substances and stressors. Laboratory ecotoxicological studies, to  
121 support research and regulation, tend to explore impacts on single species rather than  
122 populations and communities. Variations in the nature of the environment in time and space,  
123 which will affect chemical impacts, are hardly accounted for in research and risk assessments.

124 In order to achieve the SDGs, a step-change is therefore needed in the way in which we study  
125 and regulate chemicals in the environment. However many questions that need to be  
126 addressed around the risks of chemicals in the environment and it will be impossible to tackle  
127 them all. There is therefore an urgent need to identify the research questions that matter  
128 most to the broad community across sectors and multiple disciplines so that research and  
129 regulatory efforts can be focused on the most pressing questions.

130 One approach to identifying key issues in a topic area is to perform horizon scanning exercises  
131 that promote engagement of researchers and stakeholders from a broad range of sectors  
132 (e.g., Fleishman et al. 2011; Rudd et al. 2011; Sutherland et al., 2011; Boxall et al., 2012). In  
133 September 2013, the Society for Environmental Toxicology and Chemistry launched a global  
134 horizon scanning project (GHSP) to identify geographically specific research needs to address  
135 stressor impacts on sustainable environmental quality by drawing on the diverse experience  
136 and insights of its members. This project employed a key questions model in which research  
137 questions were widely solicited from SETAC Europe members and subsequently ranked by  
138 experts. Key questions exercises were performed in all of SETAC's geographic units: Africa,  
139 Asia-Pacific, Europe, Latin America and North America. Conclusions from the Latin America  
140 exercise have recently been published (Furley et al., 2018). In this paper, we report the results  
141 and conclusions of the European key questions exercise. We anticipate that the findings of the  
142 paper will be invaluable in the setting of agendas for regulatory and business communities in  
143 Europe and elsewhere

## 144 **METHODS**

145 Questions were initially solicited from the membership of the European branch of the Society  
146 for Environmental Toxicology and Chemistry (SETAC) in 2014/2015. Members (2029



147 individuals from a range of sectors and disciplines) were invited, via email, to submit questions  
148 to the project. Guidance was provided on what would make an ideal question (Sutherland et  
149 al., 2011): i.e. it should address important knowledge gaps, be answerable within about 5  
150 years given sufficient research funding (~ €10 million), be answerable through a realistic  
151 research design, have a factual answer that does not depend on value judgments, cover a  
152 spatial and temporal scale that could realistically be addressed by a research team, not be  
153 answerable by “it all depends,” or “yes” or “no” and should contain a subject, an intervention,  
154 and a measurable outcome. The submitted questions were reviewed by the project team to  
155 remove duplicate questions and questions outside the scope of the exercise. The final list of  
156 questions was then taken forward for discussion at a horizon scanning workshop.

157 The workshop was held in conjunction with the 2015 SETAC Europe Annual Meeting in  
158 Barcelona, Spain and combined plenary and working group discussions. The submitted  
159 questions were allocated to nine themes that were discussed in three breakout sessions by 37  
160 participants with multidisciplinary expertise from the government, academia and industry  
161 sectors. Two themes addressed questions related to aquatic and terrestrial ecotoxicology; two  
162 addressed ecosystem responses to multiple stressors or chemical mixtures; two addressed  
163 risk assessment, regulation and public perception and the final three themes addressed  
164 nanomaterials; contaminant analysis, fate and behaviour; and modelling and predictive  
165 toxicology. The workshop participants were tasked with identifying 2-5 priority research  
166 questions in each theme: breakout group members were free to rephrase or combine  
167 candidate questions, or to propose new questions to address issues not directly covered by  
168 candidate question submissions. The combined list of priority questions was then discussed  
169 and agreed at a final plenary session to generate the priority questions.

170 Finally, an internet-based survey of the broader SETAC Europe membership was used to rank  
171 the priority questions using the best-worst scaling (BWS) approach described in Rudd et al.  
172 (2014). Emails were sent out to all SETAC Europe members asking them to participate in the  
173 survey. We asked respondents to repeatedly examine subsets of four questions drawn from  
174 the full priority list. For each set of four questions they were asked to select which of the  
175 questions were of greatest and least importance. Ranking questions in this way is cognitively  
176 less challenging than full ranking exercises and offers one of the few approaches to effectively  
177 and fully rank large lists of items. It also allowed us to rank order every question for each  
178 respondent and to subsequently calculate calculate the overall rank of all research questions  
179 for the entire sample.

## 180 **RESULTS**

181 A total of 183 questions was submitted by the SETAC Europe membership (see supplementary  
182 information). The removal of duplicate and invalid questions reduced the number to 90, which  
183 were discussed at the workshop. The workshop participants identified 22 of these that they  
184 considered as top priority.

185 The results of the BWS ranking analysis, based on 299 responses are shown in Table 1. The top  
186 ranked questions relate to developing the understanding to deal with complexity in the  
187 environmental risk assessment (ERA) process such as understanding the impacts of multiple  
188 stressors over time and space. Mid-ranked questions deal with issues around mitigation,  
189 extrapolation between endpoints, chemical prioritisation and predictive ecotoxicology.  
190 Lowest ranked questions covered areas such as risk communication, risks from emerging and  
191 future stressors and identification of hotspots of risk around the globe.

192 Below we provide a brief description of each question and the drivers behind the question.  
193 We do not provide a detailed review of an area but attempt to highlight the potential  
194 approaches for answering a question, the likely challenges and the interdependency of each  
195 question with other questions coming out of the exercise. An analysis of the questions  
196 indicated that the priority questions were grouped into three broad categories (Figure 1) so  
197 we have ordered the questions by category.

### 198 **Overarching questions**

199 Five 'overarching questions' covered aspects of which chemicals are negatively impacting the  
200 environment and the identification of regions most heavily impacted; the impacts of global  
201 megatrends on chemical impacts; the identification of the most sustainable pathways for  
202 chemical use; and the definition of protection goals.

#### 203 *1. What are the key ecological challenges arising from global megatrends? (Rank #7)*

204 The accelerating change in urbanization, climate and demographics were highlighted in a  
205 recent assessment of the impact of global megatrends on European environments (EEA,  
206 2015). Urbanization generates multiple environmental stressors, the sources and effects of  
207 which are complex and difficult to untangle (Questions 3, 8 and 10; Johnson and Sumpter,  
208 2014). Understanding climate-induced changes in the abundance and distribution of species  
209 (including pests and disease organisms) coupled with an understanding of how climate change  
210 affects the exposure characteristics and impacts of multiple stressors, is essential for effective  
211 risk assessment and risk management (Stahl et al., 2013). Renewable energy sources (solar,  
212 wind, tidal, biofuels) are key to mitigating the effects of climate change, but are not without  
213 environmental consequences (Spellman, 2014), which also need to be assessed and managed.  
214 Europe's population is ageing rapidly and resulting shifts in housing, transport, technology and

215 infrastructure, as well as changes in pharmaceutical and energy use (Government Office for  
216 Science. 2016), may have significant environmental impacts. These large-scale challenges can  
217 only be addressed via interdisciplinary approaches that account for the complexity and  
218 connectivity of environmental systems and incorporate appropriate spatial and temporal  
219 scales (Questions 11 and 16). In addition to developing a systems-based approach to ERA that  
220 incorporates multiple stressors, it is necessary to consider environmental risk in a global  
221 context, to ensure that national policies do not have unintended adverse global consequences  
222 (Questions 4 and 12, Lenzen et al, 2012).

223 *2. Biodiversity and ecosystem services: what are we trying to protect where, when, why, and*  
224 *how? (Rank #10)*

225 Central to effective land management and environmental protection is a clear articulation of  
226 what is being protected in a specific location/habitat type (where), over what time scales the  
227 protection applies (when) and what the justification for the protection is (why). Only once the  
228 protection goal has been articulated can the correct management (how) be instigated.  
229 Biodiversity is essential to human well-being and provides many benefits (ecosystem services)  
230 (Mace et al., 2012). However, it is not possible to protect everything, everywhere, all of the  
231 time (Holt et al., 2016). Since ecosystems are managed to meet human demands (e.g., water  
232 provision, food production, raw materials, etc.) trade-offs between protecting ecosystem  
233 integrity and guaranteeing human welfare need to be considered. The societal and policy  
234 challenge is deciding which ecosystem services are desired in specific habitats over specified  
235 time periods (Question 22). The scientific challenge is understanding which species and  
236 processes (i.e., service providing units, SPU) deliver the desired ecosystem services and how  
237 stress-induced changes in these ecological components translate into changes in ecosystem

238 service delivery (Questions 6 and 7, Maltby, 2013). Robust ecological production functions  
239 that translate changes in SPU attributes to changes in ecosystem service delivery and  
240 outcomes that people value, are essential to an ecosystem services-based approach to ERA  
241 (Questions 10 and 20, Bruins et al., 2017). The adoption of an ecosystem services-based  
242 approach to ERA would provide a framework for landscape-scale risk management, enabling  
243 the development of spatially explicit protection goals and more targeted risk management  
244 measures (Question 5). Systematic conservation planning approaches (Margules & Pressey,  
245 2000) may play a role here they allow ecological knowledge to be incorporated into practice  
246 and ecosystem functions and services to be considered into the design of protected areas  
247 (Adame et al., 2015)

248 *3. Which chemicals are the main drivers of mixture toxicity in the environment? (Rank #6)*

249 Ecosystems, including humans, are exposed to mixtures of chemicals and not single  
250 compounds (e.g., Moschet et al., 2014). However, the ecotoxicity and toxicity of these  
251 mixtures of chemicals in the environment is often driven primarily by a few compounds (e.g.,  
252 Vallotton and Price, 2016). Consequently, the development of methodologies for the  
253 identification of such “mixture toxicity drivers” is a European research priority (EC, 2012). The  
254 use of Effects Directed Analysis (EDA) methods (Brack, 2003) where a combination of toxicity  
255 testing and sample manipulation is used to home in on the chemical drivers of toxicity, which  
256 are then identified through chemical analysis methods, could help identify mixture toxicity  
257 drivers. The use of cutting-edge chemical analysis techniques such as Time of Flight Mass  
258 Spectrometry for non-targeted analysis of a sample coupled with in silico models for  
259 estimating the toxicity (Question 18) of the identified chemicals (Hollender et al., 2017) and  
260 the use of chemical prioritisation approaches (Question 13) may also be part of the solution.  
261 Chemical composition of environmental mixtures will vary in time and space and different

262 compounds will affect different organisms in different ways. To fully address the question of  
263 drivers of mixture toxicity will therefore likely require intense sampling campaigns at high  
264 temporal and spatial resolutions and the development of high throughput approaches  
265 (Question 19) for characterising the toxicity of mixtures to key taxonomic groups and for  
266 identifying key toxicants.

267 *4. Where are the hotspots of key contaminants around the globe? (Rank #22)*

268 Much of our understanding of the concentrations of contaminants relates to the North  
269 American, European and Chinese situations with limited or no data available for many other  
270 countries around the globe (e.g. Aus der Beek, 2016). More global scale initiatives are needed  
271 in order to identify pollution hotspots so that mitigation efforts can be focused on these areas  
272 (Kroeze et al., 2016). This could be achieved through global-scale environmental monitoring  
273 studies of key classes of contaminants. For select contaminants this may need new analytical  
274 methodologies (Question 17). These studies would require global collaborations, possibly co-  
275 ordinated by organisations such as SETAC. The use of citizen science-based approaches, similar  
276 to the Freshwater Watch programme on water quality across the globe (Scott et al., 2017) or  
277 on microplastic contamination of European beaches (Lots et al., 2017) could be part of the  
278 solution. Even using these mass sampling methods, it will be impractical to monitor  
279 everywhere so any monitoring activities will likely need to be complemented by modelling  
280 activities to provide high resolution information on levels of contamination in different  
281 regions. The use, use patterns, fate and behaviour and exposure pathways of chemicals are  
282 likely to differ across regions within a country and across countries (Question 16).  
283 Consequently, the identification of contaminant hotspots using modelling approaches will  
284 require a concerted effort to collate information on chemical emissions and local practices  
285 (e.g., for disposal of waste and wastewater), as well as the characteristics of the receiving

286 natural environment (altitude, weather conditions, soil maps, distribution of water bodies and  
287 hydrological regimes) (Keller et al., 2014).

288 *5. How can we develop, assess and select the most effective mitigation measures for chemicals*  
289 *in the environment? (Rank #8)*

290 Mitigation measures are becoming increasingly important to protect the environment from  
291 future pollution and to abate current pollution. A range of approaches are available to limit  
292 the risks of chemicals in the environment, including policy interventions (e.g. banning of a  
293 substance), environmental stewardship, existing and novel treatment technologies and the  
294 application of green chemistry (Schwarzenbach et al., 2006). The development of effective  
295 mitigation methods will require the identification of contaminant classes causing  
296 environmental effects (Question 3) and the locations across the globe at greatest risk  
297 (Question 4). It is likely that a combination of approaches will be needed and that these  
298 combinations will need to be tailored to a particular pollution problem and the location of  
299 interest. Selection of a method will not only need to consider the efficacy of a method for  
300 reducing environmental exposure, but also affordability for the area of interest, social  
301 acceptability, ease of use and the broader environmental costs of an approach such as  
302 increased CO<sub>2</sub> emissions. Selection of an approach will likely require the use of cost-benefit  
303 analyses to weigh up the environmental benefits of reducing the levels of contamination  
304 against the economic, social and other environmental costs of adopting the method. The  
305 ecosystem services concept could be used to frame and assess trade-offs inherent in such  
306 evaluations (Nienstedt et al., 2012; Question 2). To assess how well an approach works could  
307 be achieved through the use of environmental monitoring and the use of social science  
308 methodologies such as public surveys, pre and post adoption of a mitigation approach. These

309 studies may need to run for some time to determine the long-term sustainability of a  
310 particular solution.

### 311 **Assessment and management frameworks**

312 Seventeen questions related to the design, parameterisation and validation of 'Assessment  
313 and management frameworks'. These questions fit within three sub-divisions, questions  
314 around: generation of fundamental knowledge; development of frameworks; and  
315 parameterisation of frameworks.

#### 316 Fundamental knowledge

317 *6. How can we integrate evolutionary and ecological knowledge in order to better determine*  
318 *vulnerability of populations and communities to stressors? (Rank #14)*

319 The vulnerability of populations and communities to stressors is a function of exposure,  
320 inherent sensitivity and recovery (De Lange et al., 2010). Exposure is dependent on the spatio-  
321 temporal co-occurrence of stressor and species, which in turn is a function of habitat  
322 suitability and the ecological processes driving community assembly and species coexistence  
323 (i.e. dispersal, colonization, competition, predation) (Question 11, HilleRisLambers et al 2012).  
324 Differences in the inherent sensitivity of species derive from phylogenetic differences in  
325 morphological, physiological and ecological traits (Rubach et al., 2012), which are shaped by  
326 evolutionary processes (Dallinger and Höckner, 2013). The internal recovery of populations is  
327 dependent on the reproductive output of surviving individuals whereas external recovery is  
328 dependent on immigration processes and the presence of local source populations (Gergs et  
329 al 2016a). The recovery of communities is dependent on recolonization order (e.g. prey  
330 available for predators), the degree of niche specialization of the recolonizing species and the  
331 ecological and evolutionary processes that generate the local species pool (Question 10,



332 Mittelbach & Schemske, 2015). Traits commonly associated with vulnerable species include  
333 restricted distribution and limited dispersal ability, long generation times and low  
334 reproductive rates, specialized habitats and dietary requirements, and narrow physiological  
335 tolerances (Pacifiçi et al. 2015). However, the relative importance of specific traits in  
336 determining vulnerability and how evolutionary and ecological processes shape them,  
337 requires further investigation (Question 11).

338 *7. How do sublethal effects alter individual fitness and propagate to the population and*  
339 *community level? (Rank #9)*

340 ERA is primarily concerned with protecting populations of species and the communities and  
341 ecosystems to which they belong. However, most information is available on the lethal and  
342 sublethal effects of chemicals on individual organisms and therefore the scientific challenge is  
343 understanding and predicting the population- and community-level implications of  
344 (sub)individual-level effects. The use of molecular and cellular responses to chemical exposure  
345 in ERA (i.e. biomarkers) has been criticised as being unlikely to be predictive of adverse effects  
346 at the level of the whole organism, let alone at the population or community level (e.g. Forbes  
347 et al 2006). The development of the Adverse Outcome Pathway (AOP) concept is addressing  
348 this criticism by identifying the chain of causality between chemically-induced molecular  
349 initiating events and adverse outcomes at levels of biological organisation relevant to ERA  
350 (Ankley et al 2010). Quantitative AOPs have a potentially important role to play in screening  
351 and monitoring programmes (Questions 15 and 19), but considerable resources are needed  
352 to generate the mechanistic understanding required (Conolly et al 2017).

353 Individual-level effects, either predicted from AOPs or measured experimentally, can be  
354 extrapolated to population-level effects and beyond, using mechanistic effect models (Forbes

355 & Galic 2016; Question 20). Whether chemical-induced reductions in vital rates (e.g. survival,  
356 growth and reproduction) result in population declines, depends on the physiological  
357 processes affected by the chemical (Martin et al 2014) and density-mediated compensatory  
358 mechanisms operating in natural populations (Rohr et al 2016). At the community level,  
359 adverse effects on species may be counteracted by changes in biotic interactions (i.e. reduced  
360 competition or predation) and adverse effects on ecological processes may occur despite little  
361 effect on the abundance of individual populations (Galic et al 2017) or species richness (Spaak  
362 et al 2017). Greater mechanistic and ecological understanding is needed to reduce the  
363 uncertainties associated with extrapolating from what we measure ((sub)individual-level  
364 responses) to what we want to protect (populations, communities and the ecosystem services  
365 they provide).

366 *8. How can we define, distinguish, and quantify the effects of multiple stressors on ecosystems?*  
367 *(Rank #3)*

368 Ecosystems face an increasing complexity of anthropogenic and natural stressors (see  
369 Question 1) and understanding, quantifying and predicting their interactive effects remains a  
370 challenge (Segner et al., 2014, Jackson et al., 2016). Distinguishing the effects of multiple  
371 stressors on ecosystems requires multiple lines of evidence that can be generated from a  
372 range of approaches, including in situ toxicity identification and evaluation (Steigmeyer et al  
373 2017), molecular-based diagnostic tools (Dafforn et al 2016), eco-epidemiology (Postuma et  
374 al 2016) and Bayesian network-relative risk models (Landis et al 2017). Our limited  
375 understanding of the combined effects of multiple stressors on ecosystems is hampering the  
376 development of sound risk assessment and management strategies (Van den Brink et al.,  
377 2016; Question 10). One reason for our poor understanding is the limited availability of

378 detailed ecological information over sufficient spatial and temporal scales (Questions 11) to  
379 distinguish chemical effects from natural variability and to identify robust associations  
380 between exposure and effect (Question 10). The use of emerging technologies such as remote  
381 sensing and high-throughput genomic sequencing techniques (Question 19) will enable a  
382 more rapid and economical collection of ecological datasets on a similar or greater scale, when  
383 compared to physical and chemical monitoring (Chariton et al., 2016). However, as these  
384 methods evolve, care must be taken to ensure that the granularity and scale, as well as  
385 relevance and narrative intent, of different measures are properly taken into account. Field  
386 surveys and weight of evidence approaches alone cannot definitively establish causality  
387 (Stevenson & Chapman, 2017), what is required is a combination of comprehensive field  
388 surveys (covering a wide range of stressor interactions) and experimental studies.

389 *9. Which interactions are not captured by currently accepted mixture toxicity models? (Rank*  
390 *#17)*

391 The standard mixture toxicity models, i.e. concentration addition (CA) and independent action  
392 (IA), also known as response addition), are based on the assumption that the components in  
393 a mixture do not interact (Backhaus and Faust, 2012). However, in the real world, chemicals  
394 can interact in a mixture, at the chemical, organismal and/or ecological level. Such interactions  
395 are sometimes pronounced enough to lead to deviations from predictions based on the CA or  
396 IA models, patterns that are often termed “synergism” or “antagonism” (respectively higher  
397 or lower toxicity than the sum of single toxic effects). Given that CA as well as IA are  
398 exceptionally coarse simplifications of complex biological and ecological systems, deviations  
399 from CA- or IA-based mixture toxicity predictions are to be expected. The crucial question is  
400 therefore whether the observed deviations are unacceptably high, which depends on the

401 specific protection goal, the endpoint studied and how often such deviations occur. A  
402 systematic exploration of interactions to identify which combinations of chemicals deviate  
403 from the IA or CA models is a major challenge, as an enormous number of different biological  
404 receptors and biochemical pathways from myriad organisms with different life cycles and  
405 traits, interacting with each other in complex ecological communities, are involved. Meeting  
406 this challenge will likely need to involve the use of high-throughput screening approaches  
407 discussed in Question 19. The assessment of the mechanisms and consequences of  
408 interactions between chemicals on an ecological level closely resembles the analysis of  
409 multiple stressor effects discussed in Question 10.

#### 410 Development of assessment and management frameworks

411 *10. How can interactions among different stress factors operating at different levels of*  
412 *biological organization be accounted for in environmental risk assessment? (Rank #1)*

413 One of the most difficult and evasive goals of ERA is the understanding of the effects of  
414 multiple stressors on individuals, populations, and ultimately groups of interacting species at  
415 different spatial scales (e.g., Kapo et al., 2014). Prospective ERAs primarily focus on single or  
416 a limited number of stressors in a few model species, under (semi)controlled conditions over  
417 limited time scales (Hommen et al., 2010). Retrospective ERAs are inevitably concerned with  
418 multiple stressor impacts on dynamic and complex ecosystems, which may have been exposed  
419 over many years and for which assignment of causality is difficult (Question 8, Fischer et al.,  
420 2013). Ecosystems are subject to a multitude of chemical (e.g. pH), physical (e.g. temperature,  
421 sedimentation) and biological (e.g. parasitism, invasive species) stressors that may enhance  
422 or reduce the impact of anthropogenic chemical exposures. Stressor interactions can  
423 influence chemical bioavailability and uptake (Karlsson et al 2017) as well as detoxification

424 and other defence mechanisms (Janssens & Stoks 2017), which may result in antagonistic or  
425 synergistic effects on individual organisms. Stressor-induced changes in phenology, species  
426 tolerance, community composition and biotic interactions can result in ecosystems being  
427 more or less resilient to anthropogenic chemicals (Question 6, Rohr et al 2016).

428 Accounting for multistressor effects in ERA requires the development of mechanistic exposure  
429 and effects models that capture stressor interactions at relevant spatiotemporal scales and  
430 enable extrapolation across levels of biological organization (Question 20). This will require  
431 greater understanding of stressor interactions in natural systems as well as information from  
432 manipulative experiments at appropriate temporal and spatial scales, and field surveys  
433 spanning wide gradients of focal stressors at multiple locations (Beketov and Liess, 2012).  
434 Model development and implementation will be facilitated by the development of  
435 environmental scenarios for combined exposure and effect assessment (Question 11).

436 *11. How do we improve risk assessment of environmental stressors to be more predictive*  
437 *across increasing environmental complexity and spatiotemporal scales? (Rank #2)*

438 Stressors may be distributed across multiple habitats and transported considerable distances  
439 from the point of release. Spatiotemporal variation in stressor exposure is superimposed on  
440 variation in the distribution of biological species, ecological processes and the ecosystem  
441 services they provide. Risk is therefore variable and context dependent; it varies according to  
442 the location, type and quality of habitats and the exposure to stressors within the landscape  
443 (Landis et al 2017). Current ERA frameworks do not account explicitly for the environmental  
444 complexity that drives spatiotemporal variation in risk at different scales (SCHER et al 2013a,  
445 Question 10), but how important is this for environmental decision making? Current  
446 approaches adopt 'realistic worst case' assumptions and are designed to be conservative

447 rather than realistic. How appropriate are these assumptions and what is the degree of over-  
448 or under-protection? A more spatially defined ERA would allow for targeting of interventions  
449 (e.g. restrictions, mitigation measures) where protection is most needed, whilst limiting  
450 opportunity costs of overprotection elsewhere.

451 How much of this complexity needs to be incorporated into assessments of risk? Overly  
452 simple models do not represent important aspects of the system's dynamics and have large  
453 model bias. Overly complex models require detailed knowledge of species and environmental  
454 interactions and need a large number of parameters to specify detailed dynamics; they have  
455 large parameter uncertainty (Collie et al 2016). An alternative approach to building complex  
456 models is to develop scenarios that are defined in terms of landscape structure and  
457 environmental conditions, incorporate spatial and temporal variability and link to protection  
458 goals (Rico et al., 2016b; Question 2). Landscape ecotoxicology provides a conceptual  
459 framework for bringing together mechanistic exposure and effect modelling and the  
460 increasing availability of spatially- and temporally-explicit datasets provide an exciting  
461 opportunity to develop mapping and modelling tools that are both spatially defined and make  
462 predictions in real-time (Focks, 2014).

463 *12. How can we assess the environmental risk of emerging and future stressors? (Rank #18)*

464 Over the past decade, there has been increasing interest in the environmental risks of the so  
465 called emerging contaminants. Emerging contaminants encompass a broad range of  
466 substances including those that have been used for some time (e.g. pharmaceuticals and  
467 personal care products, veterinary medicines and plastics) and their transformation products  
468 and new technologies such as nanomaterials and biologicals (Boxall et al., 2012). The main  
469 concern is that existing paradigms and models used for ERA may not be appropriate as the

470 drivers of their environmental fate, behaviour and effects differ from traditional chemicals  
471 (Question 15). For example, for nanomaterials and microplastics, the partitioning concept  
472 used in risk assessment for assessing the distribution of 'traditional' chemicals between  
473 environmental compartments, is inappropriate for use on particulate material (Praetorius et  
474 al, 2014). Exposure models are therefore needed that take into account processes relevant  
475 for particles (e.g., Praetorius et al., 2012). Approaches for combining exposure predictions  
476 with data from effects studies for particles are also poorly developed. For pharmaceuticals  
477 and veterinary medicines, many compounds are ionised at environmental pH values so models  
478 for estimating sorption, uptake and toxicity that are embedded into risk assessment schemes  
479 are inappropriate. New approaches are also needed for assessing the risks of micro and nano-  
480 encapsulated bioactive materials such as nanopesticides (Kookana et al., 2014). A wealth of  
481 data and knowledge have been generated over the past few years on the fate and effects of  
482 many classes of emerging contaminants and numerous models and tools are being proposed  
483 for assessing the properties, exposure and effects of these substances. These approaches now  
484 need to be evaluated and, where appropriate, then embedded into ERA processes. In  
485 instances where models are not available for key substance classes and endpoints, these need  
486 to be developed. Much of the existing data are held by industry so the development of new  
487 models could be facilitated through improvements in approaches to share data (Question 21).

488 *13. What approaches should be used to prioritize compounds for environmental risk*  
489 *assessment and management? (Rank #11)*

490 It is estimated that around 120,000 chemicals are manufactured and imported in Europe  
491 (<https://echa.europa.eu/information-on-chemicals>). During use and following emission to the  
492 natural environment, these chemicals can be metabolised or degraded to transformation

493 products (Boxall et al., 2004) so the environment will be exposed to an even greater number  
494 of chemicals. However, we only have data on the environmental occurrence, fate, effects and  
495 risks of a small proportion of these substances and even fewer are regulated. Methods have  
496 been proposed to prioritise chemicals for testing and risk assessment (i.e. substances with  
497 limited data), the methods are typically reliant on predictive models and algorithms or read-  
498 across approaches (Burns et al., 2018; Question 18). The objective of prioritizing chemicals  
499 requires inputs from most of the priority questions identified in this paper. A better  
500 understanding of the distribution, exposure, effects and relevance of multiple chemicals, to a  
501 range of endpoints, in the context of a changing environment, multiple stressors, and evolving  
502 expectations of landscapes and services must be integrated in order to develop regionally  
503 relevant priority lists (Question 16). The current approaches have shortcomings when it comes  
504 to focus on 'what matters'. They, however, constitute a good starting point that can be  
505 complemented with experience and existing exchanges on prioritisation approaches between  
506 different regulatory systems. Further efforts could, for example, be directed towards better  
507 understanding and application of commonalities between approaches. The use of the EDA  
508 approaches, discussed in Question 3, could also be used to identify those contaminants in an  
509 area of concern that require management.

510 *14. How can we integrate comparative risk assessment, LCA, and risk benefit analysis to*  
511 *identify and design more sustainable alternatives? (Rank #19)*

512 Synthetic chemicals are essential to modern life, but they may have unacceptable  
513 environmental or human health impacts. There is therefore a strong desire to substitute the  
514 most hazardous chemicals with non-hazardous alternatives that have the same function  
515 (ECHA, 2018). Chemical risk assessment and management in Europe is fragmented and single-



516 chemical focussed. Different research communities drive forward advances in risk assessment,  
517 life cycle analysis (LCA) and risk benefit analysis, with little interaction or awareness of each  
518 other's activities. However, the integration of comparative risk assessment, LCA and risk  
519 benefit analysis is essential for effective decision making. An holistic approach is needed to  
520 consider all stages of a chemical's life cycle and to minimise the risk of unintended  
521 consequences; including the loss of socio-economic benefits of chemical use and regional  
522 displacement of environmental impacts due to shifts in global production. A more integrated  
523 approach will facilitate the identification and design of less hazardous chemicals or chemical  
524 alternatives, while maintaining intended functions and represents an opportunity to fuel  
525 innovation and economic growth while protecting public health and the environment  
526 (Zimmerman and Anastas, 2015, DeVito, 2016). In particular, incorporating toxicology into  
527 the molecular design process, possibly using the tools developed in response to Question 18,  
528 provides the potential to producing safer chemicals, but further multidisciplinary research is  
529 needed to ensure that this potential is realised (Coish et al., 2016).

530 *15. How can monitoring data be used to determine whether current regulatory risk assessment*  
531 *schemes are effective for emerging contaminants? (Rank #12)*

532 As discussed under Question 12, there is concern that existing experimental and modelling  
533 methods, used to support environmental risk assessment, may not be appropriate for many  
534 classes of emerging contaminants, in particular particulate contaminants such as  
535 nanomaterials and microplastics. Chemical and biological monitoring of exposed  
536 environments could help identify whether current risk assessment schemes are effective and,  
537 if not, where the frameworks fall down. This could be achieved through monitoring studies of  
538 an emerging contaminant of interest at the different stages in the source-pathway-receptor

539 relationship. The results could then be used to evaluate exposure models and laboratory fate  
540 and effects studies used in the risk assessment process. As many emerging contaminants are  
541 difficult to measure, to answer this question will require robust and sensitive analytical  
542 methods to be developed for many of these compounds (Question 17). While this question  
543 focuses on emerging contaminants, the question is also relevant to environmental  
544 contaminants more generally.

#### 545 Parameterisation

546 *16. How can we properly characterize the chemical use, emissions, fate and exposure at*  
547 *different spatial and temporal scales? (Rank #5)*

548 Environmental assessment of chemicals is typically done without a specific spatial and  
549 temporal scale in mind. Obtaining data on the emissions, fate and exposure of chemicals at  
550 high spatial and temporal resolutions would provide better information on which organisms  
551 are really exposed throughout their lifetime and what they are exposed to and help to answer  
552 many of the other priority questions (e.g. Questions 4, 11, 13, 15). A wide range of  
553 technologies (including mobile phones, passive sampling devices, miniaturised sensing  
554 devices, high-resolution spatial models, remote sensing, robotics and state-of-the-art  
555 analytical techniques such as time of flight mass spectrometry) are now available (e.g.,  
556 <http://www.intcatch.eu/>) that could provide new insights into chemical exposure. These  
557 technologies could allow assessors to: 1) quantify levels of pollution at greater frequencies  
558 and spatial resolutions than is currently possible; 2) monitoring locations that in the past have  
559 been difficult to sample (e.g., hostile environments or systems with accessibility issues); and  
560 3) characterising human and ecological exposure to the plethora of chemicals that have never  
561 been monitored before. Effective application of various technologies will provide a much

562 better understanding of the degree of exposure of humans and wildlife to pollutants and  
563 hence the risks these pollutants pose to the health of ecosystems and humans. These  
564 technologies have the potential to be used to inform mitigation measures, both in the short  
565 term and over longer timescales. The use of new technologies will, however, also raise  
566 challenges, like quality control, regulatory acceptance, social and ethical issues and the  
567 analysis and interpretation of the resulting “big data” (Dafforn et al., 2016).

568 *17. How do we detect and characterize difficult-to-measure substances in the environment?*

569 *(Rank #21)*

570 Robust and sensitive analytical methods have been available for metals, pesticides and many  
571 persistent organic compounds for some time. However, for many contaminant classes,  
572 analysis is still challenging. Good examples are the products of Unknown or Variable  
573 Composition, Complex Reaction Products and Biological Materials (UVCB), nanomaterials,  
574 plastics and other polymers. For example, UVCB substances are comprised of individual  
575 constituents, each of which may possess different physico-chemical and fate properties. UVCB  
576 substances cannot be sufficiently identified by their chemical composition, which creates  
577 complications for testing using standard guideline methodologies. (ECHA 2017). The potential  
578 toxicity, behaviour and fate of nanomaterials and microplastics are affected by a wide range  
579 of factors including particle number and mass concentration, surface area, charge, chemistry  
580 and reactivity, size and size distribution, state of hetero/homo-agglomeration/aggregation,  
581 elemental composition, as well as structure and shape (Borm et al., 2006; Handy et al., 2008;  
582 Benoit et al., 2013; Coutris et al., 2012). Therefore, when analysing nano- and microparticles  
583 in different matrices, it is not only the composition and concentration that will need to be  
584 determined, but also the physical and chemical properties of the particles within the sample

585 and the chemical characteristics of any capping/functional layer on the particle surface. A  
586 range of new analytical techniques, including microscopy-based approaches,  
587 chromatography, centrifugation, filtration, fractionation, spectroscopic and related  
588 techniques and single-particle ICP-MS (spICP-MS) have been reported in the literature that  
589 could be used (Hässellöv et al., 2008; Hildago-Ruz et al., 2012). However, while many of these  
590 approaches work when used in controlled laboratory-based studies, they can lack the  
591 sensitivity and specificity for application to environmental monitoring. Work therefore needs  
592 to continue on the development of methods that are able to measure these substances at  
593 concentrations that are expected to occur in the environment.

594 *18. How can we improve in silico methods for environmental fate and effects estimation? (Rank*  
595 *#13)*

596 In-silico approaches, such as (quantitative) structure-activity relationships, (quantitative)  
597 structure-property relationships, read across and expert systems have been available for some  
598 time for estimating the properties, persistence and environmental effects of a chemical based  
599 on its chemical structure (ECETOC, 1998). While these predictive approaches work well for  
600 select classes of chemicals (e.g. neutral organics) and endpoints (e.g. log Kow and acute  
601 toxicity), we are not yet at a stage where we have robust models for all classes of chemicals  
602 and all the environmental endpoints that we consider in the risk assessment process. In  
603 particular, we need improved models for chronic toxicity, biodegradation in environmental  
604 matrices, sorption and uptake of ionisable compounds, effects models for specifically acting  
605 compounds and property and effect models for nanomaterials and microplastics (e.g. Cronin,  
606 2017; Winkler et al., 2015). The development of new models might be achieved through the  
607 adoption of new data mining technologies such as machine learning techniques (Devinyak and

608 Lesyk, 2016) and, for molecules like pharmaceuticals, mammalian to environmental read  
609 across approaches (Rand Weaver et al., 2013). To develop these new approaches in a timely  
610 manner will require generation of data for training and evaluation of models, perhaps using  
611 some of the high-throughput methodologies discussed in Question 19 as well as increased  
612 sharing of existing data (and metadata) that has been generated by the research community  
613 and industry over the years (Question 21).

614 *19. How do we create high-throughput strategies for understanding environmentally effects*  
615 *and processes? (Rank #15)*

616 To experimentally establish the environmental properties and effects of a chemical will  
617 typically involve the use of OECD-type test methodologies. These methods can be time  
618 consuming, costly and, in the case of ecotoxicity testing, involves the use of whole animals.  
619 The use of alternative high-throughput strategies could allow us to generate information on  
620 the fate, behaviour and effects of large numbers of chemicals in a significantly shorter time  
621 than the traditional approaches. The availability of such approaches would enable us to  
622 generate the data to support work to answer other questions such as Questions 3, 9 and 18.  
623 Potential solutions include the adaptation of existing standard methods to either shorten the  
624 study and/or reduce the number of animals used. A good example is the use of the so-called  
625 minimised bioconcentration study which uses up to 70% fewer animals than the standard  
626 OECD approach and which could be run over shorted time periods (Springer et al., 2008; Carter  
627 et al., 2014). Technologically-led solutions include the use of in vitro and micro-scale assays.  
628 High-throughput testing routinely employs in vitro models used for pharmaceutical  
629 development and alternative animal systems (e.g., embryonic zebrafish) to rapidly collect  
630 information on bioactivity and toxic potential for diverse industrial and speciality chemicals.  
631 High-throughput testing uses modern robotics, computing and miniaturization, and relies

632 largely on batteries of in-vitro bioassays that may effectively screen chemicals for their ability  
633 to exert specific biological activities or perturbations. High-throughput testing has the  
634 attraction of being able to perform hundreds or thousands of biological determinations in  
635 relatively short times and with a potential high degree of experimental standardization  
636 (Schroeder et al., 2016). We are still far from being able to predictively extrapolate high-  
637 throughput testing results to ecologically important endpoints. However, adverse outcome  
638 pathways may translate biological activities mapped at the molecular level to traditional and  
639 regulatory meaningful apical end-points (such as growth or reproduction impairments).  
640 Efforts such as recently described by Ankley et al. (2016) are needed to address the biological  
641 domain of applicability of high-throughput testing data in the context of application to ERA.  
642 Both the USA National Research Council (NRC, 2007) and the European Commission (Worth  
643 et al., 2014) advocate for moving away from the traditional reliance on whole-animal toxicity  
644 testing towards in vitro and micro-scale bioassays (Krewski et al., 2010).

645 *20. How can we develop mechanistic modelling to extrapolate adverse effects across levels of*  
646 *biological organization? (Rank #4)*

647 Most regulatory toxicity studies measure the effect of chemicals on individual organisms and  
648 do not consider impacts on higher levels of biological organisation and ecosystem services,  
649 which is what we want to protect (Question 2). There is therefore a need to extrapolate  
650 effects across levels of biological organization and mechanistic modelling is one way to do this  
651 (Question 7). Mechanistic effect models include: toxicokinetic-toxicodynamic (TK-TD) models  
652 and adverse outcome pathways that extrapolate chemical concentrations or molecular  
653 initiating events to individual-level effects (Ankley et al 2010, Ashauer et al 2011; Ashauer and  
654 Jager, 2018); dynamic energy budget (DEB) models that extrapolate changes in physiological

655 responses to vital rates (Kooijman 2010); individual-based (IBM) and population models that  
656 extrapolate individual-level effects to population-level consequences (Forbes et al 2011,  
657 Martin et al 2013); food web models that extrapolate effects on populations to community-  
658 level consequences (Pastorok et al 2002); ecological production functions that extrapolate  
659 from changes in biophysical structure or process to ecosystem functions driving ecosystem  
660 services (Bruins et al 2017). Recent advances include the development of good modelling  
661 practice (Grimm et al 2014); the integration of TK-TD, DEB and IBM approaches (e.g. Gergs et  
662 al 2016b) and the use of scenarios and trait-based approaches to improve the general  
663 applicability of models (Van den Brink et al 2013, Rico et al 2016b). In addition to approaches  
664 for extrapolating across levels of biological organisation, there are also emerging  
665 computational approaches for extrapolating across species based on the conservation of key  
666 biological traits and molecular processes (e.g., LaLone et al., 2016; Ankley et al., 2016,  
667 Question 6). However, the use of these approaches in ERA is limited and considerable research  
668 is still required to make the models suitable for regulatory risk assessment (Forbes and Galic,  
669 2016, Hommen et al 2016). In particular, there is a need for more in-depth knowledge of  
670 mechanistic linkages between different levels of biological organisation (Question 7) and  
671 increased availability of trait data for species that are relevant to key protection goals  
672 (Question 2).

### 673 **Maximising impact**

674 Two questions were around 'maximising the impact' of the work of the community through  
675 better communication of risks and the more effective collation and sharing of data.

676 *21. How can we better manage, use and share data to develop more sustainable and safer*  
677 *products? (Rank #16)*

678 A wealth of data on the environmental fate behaviour and effects of chemicals has been  
679 produced over the years by the research community and the business sector. Exploitation of  
680 all this information could help us to much better assess the environmental risk of the  
681 chemicals in use today and to help identify safer alternatives. Significant resource investment  
682 has resulted in diverse toxicity datasets, available in both the public and private domains, for  
683 many environmental contaminants e.g. the ECHA unique database on chemicals in Europe  
684 (ECHA), European Union Observatory for nanomaterials (EUON), and the USEPA ECOTOX  
685 database (EPA, 2018). These can be used to develop quantitative structure activity  
686 relationships (QSAR; Cherkasov et al., 2014), group chemicals by common modes of action  
687 (Barron et al., 2015), and develop (Kostal et al., 2015) and evaluate (Connors et al., 2014)  
688 sustainable design guidelines for less hazardous chemicals. The databases probably only cover  
689 a small proportion of the data that have been generated, they differ in their contents, there  
690 are large differences in data quality and they often do not contain the metadata needed for  
691 use in chemical assessment and the model development work (e.g. needed to address  
692 Question 14). To fully exploit the wealth of data that are available will require new ways of  
693 working: researchers and the business sector need to be more transparent and open in sharing  
694 their data; improved mechanisms are needed to support data sharing; standardisation is  
695 needed in the presentation of data and metadata; and assessment approaches are needed to  
696 determine the quality of the data. Societies such as SETAC could play an important role here.

697 *22. How can we improve the communication of risk to different stakeholders? (Rank #20)*

698 The environmental risk assessment of chemicals and other stressors is performed to inform  
699 risk management and therefore needs to be communicated in a way that enables effective  
700 science-based decision making. This means that the risk assessment should address the



701 protection goals that society values (Question 2) and be relevant to the challenges it faces  
702 (Question 1). The outcome of the assessment should be directly relevant to public and  
703 regulatory decision making (SCHER, 2013b) and be communicated in terms that are accessible  
704 to a range of stakeholders, including other risk assessors, risk managers, policy makers and  
705 the general public. In order to establish trust in the risk assessment process, information  
706 needs to be robust, transparent and reported objectively, without advocacy or hype (Calow  
707 2014). Communication about risks based on ERA methods is often challenged with the “so  
708 what?” question (Faber and Van Wensem 2012), for instance, what does it mean when  
709 threshold values for contaminants have been exceeded? How should a risk manager or a  
710 member of the general public interpret this type of information? If risk assessment specialists  
711 have difficulty in translating a laboratory toxicity value for a chemical or the exceedance of an  
712 environmental quality standard to actual changes in biodiversity or ecological processes in the  
713 field (e.g. Questions 6, 7, 11), how is a non-specialist expected to use this information? What  
714 also puzzles stakeholders is that, despite robust prospective risk assessment and risk  
715 management processes, critical levels of chemicals may still occur in the environment. This  
716 may be due either to improper use or misuse of the chemical or be a consequence of the  
717 protection level used in the risk assessment (e.g. protection set at the population level, but  
718 effects observed at the (sub)individual level). Reporting of these, sometimes high profile,  
719 events erodes trust in the risk assessment process and drives calls for precautionary, hazard  
720 based assessments or even the rejection of scientific evidence (Apitz et al 2017). Several  
721 authors have suggested that a risk management process that is focused on the effects of  
722 stressors on natural capital and the ecosystem services it provides, and which clearly  
723 articulates uncertainties, trade-offs and the consequences of chemical use/non-use, may

724 provide an effective framework for risk communication and risk assessment (e.g. Nienstedt et  
725 al., 2012; Maltby et al 2013, Question 2).

## 726 **OUTLOOK**

727 Europe faces significant challenges around the risk assessment and management of chemicals  
728 and other stressors. This constrains the region's ability to contribute to the achievement of  
729 the global goals for sustainable development. Both the environmental science and the  
730 regulatory communities are often working in apparent isolation. The present paper is the first  
731 attempt to set a research agenda for the European research community for the assessment  
732 and management of stressor impacts on environmental quality. The questions arising from  
733 this exercise are complex. To answer them, it will be necessary to adopt a systems approach  
734 for environmental risk assessment and management. In particular, it is important that we  
735 establish novel partnerships across sectors, disciplines and policy areas, which requires new  
736 and effective collaboration, communication and co-ordination.

737 This exercise is an important first step in a longer-term process. The results of this project now  
738 need to be disseminated to the policy, business and scientific communities. The output should  
739 be used for setting of research agendas and to inform the organisation of scientific networking  
740 activities to discuss these questions in more detail and identify pathways for future work.  
741 Because there are strong interdependencies between the questions (Figure 2), one way  
742 forward would be to establish a large 'chemicals in the environment' research programme  
743 that extends from the 'goals' through to the 'solutions'. For example, An EU Framework  
744 programme, involving a number of projects tackling different questions coming out of this  
745 exercise, would provide such an opportunity.

746 The outputs from this European effort should increase the relevance of environmental  
747 research by decreasing scientific uncertainty in assessing and managing environmental risks,  
748 and increasing the credibility of technical and policy responses to global environmental  
749 stressors. The research questions described here are not specific to Europe so should  
750 therefore be considered in the light of parallel horizon scanning activities that have taken  
751 place in Africa, Asia-Pacific, Latin America and North America. By answering the research  
752 questions identified, the European research community will play a pivotal role in achieving the  
753 SDGs.

754

755 References

- 756 Adame MF, Hermoso V, Perhans K, Lovelock CE, Herrera-Silveira JA. 2015 Selecting cost-  
757 effective areas for restoration of ecosystem services. *Conserv. Biol.* 29, 493–502.
- 758 Ankley G.T., Bennett R.S., Erickson R.J., Hoff D.J., Hornung M.W., Johnson R.D., Mount D.R.,  
759 Nichols J.W., Russom C.L., Schmieder P.K., Serrano P.K., Tietge J.E., Villeneuve D.L. (2010)  
760 Adverse outcome pathways: a conceptual framework to support ecotoxicology research and  
761 risk assessment. *Environ Toxicol Chem* 29:730–741.
- 762 Ankley G.T., LaLone C.A., Gray L.E., Villeneuve D.L., Hornung M. (2016) Evaluation of the  
763 scientific underpinnings for identifying estrogenic chemicals in non-mammalian taxa using  
764 mammalian test systems. *Environ Toxicol Chem* 35:2806-2816.
- 765 Apitz S.E., Backhaus T., Chapman P.M., Landis W., Suter G. (2017) Science, antiscience, and  
766 environmental decision making: A call to action. *Integr Environ Assess Manag* 13:557-559
- 767 Ashauer R., Agatz A., Albert C., Ducrot V., Galic N., Hendriks A.J., Jager T., Kretschmann A.,  
768 O'Connor I., Rubach M.N., Ruotsalainen A-M., Schmitt W., Stadnicka J., Van den Brink P.J.,  
769 Preuss T.G. (2011) Toxicokinetic-toxicodynamic modelling of quantal and graded sub-lethal  
770 endpoints: a brief discussion of concepts. *Environ Toxicol Chem* 30:2519-2524.
- 771 Ashauer, R., Jager, T., (2018) Physiological modes of action across species and toxicants: the  
772 key to predictive ecotoxicology. *Environ. Sci. Process. Impacts* 20: 48-57
- 773 Aus Der Beek T., Weber F.A., Bergmann A., Hickmann S., Ebert I., Hein A., Küster A. (2016)  
774 Pharmaceuticals in the environment: global occurrence and perspectives. *Environ Toxicol*  
775 *Chem* 35(4): 823-835.

776 Backhaus T., Faust M. (2012) Predictive environmental risk assessment of chemical mixtures:  
777 a conceptual framework. *Environ Sci Technol* 46:2564–2573

778 Barron M.G., Lilavois C.R., Martin T.M. (2015) MOAtox: A comprehensive mode of action and  
779 acute aquatic toxicity database for predictive model development. *Aquat Toxicol* 161:102–  
780 107

781 Beketov M.A., Liess M. (2012) Ecotoxicology and macroecology – Time for integration. *Environ*  
782 *Pollut* 162:247–254.

783 Benoit R., Wilkinson K.J., Sauve S. (2013) Partitioning of silver and chemical speciation of free  
784 Ag in soils amended with nanoparticles. *Chem Cent J* 7:75

785 Borm P.J.A., Robbins D., Haubold S., Kuhlbusch T., Fissan H., Donaldson K., Schins R., Stone V.,  
786 Kreyling W., Lademann J., Krutmann J., Warheit D., Oberdorster E. (2006) The potential risks  
787 of nanomaterials: a review carried out for ECETOC. *Particle Fibre Toxicol* 3:11.

788 Boxall A.B.A., Sinclair C.J., Fenner K., Kolpin D.W., Maund S. (2004) When synthetic chemicals  
789 degrade in the environment. *Environ Sci Technol* 38:369A-375A.

790 Boxall A.B.A., Rudd M.A., Brooks B.W., Caldwell D., Choi K., Hickmann S., Innes E., Ostapyk K.,  
791 Staveley J., Verslycke T., Ankley G.T., Beazley K., Belanger S., Berninger J.P., Carriquiriborde P.,  
792 Coors A., DeLeo P., Dyer S., Ericson J., Gagne F., Giesy J.P., Gouin T., Hallstrom L., Karlsson M.,  
793 Larsson D.G.J., Lazorchak J., Mastrocco F., McLaughlin A., McMaster M., Meyerhoff R., Moore  
794 R., Parrott J., Snape J., Murray-Smith R., Servos M., Sibley P.K., Straub J.O., Szabo N., Tetrault  
795 G., Topp E., Trudeau V.L., van Der Kraak G. (2012) Pharmaceuticals and personal care products  
796 in the environment: What are the big questions? *Environ Health Perspect* 120:1221-1229.

797 Boxall, A.B.A. (2012) New and Emerging Water Pollutants arising from Agriculture. OECD,  
798 Paris.

799 Brack, W. (2003) Effect-directed analysis: a promising tool for the identification of organic  
800 toxicants in complex mixtures? *Anal Bioanal Chem.* 377(3):397-407

801 Bruins R., Canfield T., Duke C., Kapustka L., Nahlik A., Schäfer R.. (2017) Using ecological  
802 production functions to link ecological processes to ecosystem services. *Integr Environ Assess*  
803 *Manag* 13: 52–61

804 Burns, E.E., Carter, L.J., Snape, J., Thomas-Oates, J., Boxall, A.B.A. (2018): Application of  
805 prioritization approaches to optimize environmental monitoring and testing of  
806 pharmaceuticals. *J Toxicol Environ Hlth B*

807 Calow P. (2014) Environmental risk assessors as honest brokers or stealth advocates. *Risk*  
808 *Analysis* 34:1972-1977

809 Carter L. J., Ashauer A., Ryan J. J., Boxall A. B. A. (2014) Minimised Bioconcentration Tests: A  
810 Useful Tool for Assessing Chemical Uptake into Terrestrial and Aquatic Invertebrates? *Environ*  
811 *Sci Technol* 48(22): 13497-13503.

812 Chariton A., Sun M., Gibson J., Webb A., Leung K., Hickey C., Hose G. (2016) Emergent  
813 technologies and analytical approaches for understanding the effects of multiple stressors in  
814 aquatic environments. *Mar Freshw Res* 67:414–428.

815 Cherkasov A., Muratov E.N., Fourches D., Varnek A., Baskin I.I., Cronin M., Dearden J.,  
816 Gramatica P., Martin Y.C., Todeschini R., Consonni V., Kuzmin V.E., Cramer R., Benigni R., Yang  
817 C., Rathman J., Terfloth L., Gasteiger J., Richard A., Tropsha A. (2014) QSAR modeling: Where  
818 have you been? Where are you going to? *J Med Chem* 57:4977–5010.

819 Civantos E., Thuiller W., Maiorano L., Guisan A., Araújo M.B. (2012) Potential impacts of  
820 climate change on ecosystem services in Europe: the case of pest control by vertebrates.  
821 *BioScience* 62:658-666.

822 Coish P., Brooks B.W., Gallagher E.P., Kavanagh T.J., Voutchkova-Kostal A., Zimmerman J.B.,  
823 Anastas P.T. (2016) Current status and future challenges in molecular design for reduced  
824 hazard. *ACS Sustain Chem Eng* 4:5900–5906

825 Collie J.S., Botsford L.W., Hastings A., Kaplan I.C., Largier J.L., Livingston P.A., Plagányi E., Rose  
826 K.A., Wells B.K., Werner F.E. (2016) Ecosystem models for fisheries management: finding the  
827 sweet spot. *Fish and Fisheries* 17: 101-125

828 Connors K.A., Voutchkova-Kostal A.M., Kostal J., Anastas P., Zimmerman J.B., Brooks B.W.  
829 (2014) Reducing aquatic toxicity: Probabilistic hazard evaluation of sustainable molecular  
830 design guidelines. *Environ Toxicol Chem* 33:1894–1902.

831 Conolly R.B., Ankley G.T., Cheng W.Y., Mayo M.L., Miller D.H., Perkins E.J., Villeneuve D.L.,  
832 Watanabe K.H. (2017) Quantitative adverse outcome pathways and their application to  
833 predictive toxicology. *Environ Sci Technol* 51: 4661-4672.

834 Coutris C., Joner E.J., Oughton D.H. (2012) Aging and soil organic matter content affect the  
835 fate of silver nanoparticles in soil. *Sci Total Environ* 420: 327-333.

836 Cronin, M.T.D. (2017) (Q)SARs to predict environmental toxicities: current status and future  
837 needs. *Environ. Sci.: Processes Impacts*, 19 213-220

838 Dafforn K.A., Johnston E.A., Ferguson A., Humphrey C., Monk W., Nichols S., Simpson S.,  
839 Tulbure M., Baird D.J. (2016) Big data opportunities for assessing multiple stressors across  
840 scales in aquatic ecosystems. *Mar Freshw Res* 67:393–413.

841 Dallinger R., Höckner M. (2013) Evolutionary concepts in ecotoxicology: tracing the genetic  
842 background of differential cadmium sensitivities in invertebrate lineages. *Ecotoxicology*  
843 *22:767–778*.

844 De Lange H.J., Sala S., Vighi M., Faber J.H. (2010) Ecological vulnerability in risk assessment —  
845 A review and perspectives. *Sci Total Environ* 408:3871–3879

846 Devinyak, O.T., Lesyk, R.B. (2016) 5-Year Trends in QSAR and its Machine Learning Methods.  
847 *Curr Comput Aided Drug Des.* 12(4):265-271.

848 DeVito S.C. (2016) On the design of safer chemicals: a path forward. *Green Chem*  
849 *18:4332–4347*.

850 EC. (2012) The combination effects of chemicals – Chemical mixtures. communication from  
851 the commission to the council. COM(2012) 252 final. European Commission. Brussels,  
852 Belgium.

853 ECETOC (1998) QSARs in the assessment of the environmental fate and effects of chemicals.  
854 ECETOC Technical Report 74, ECETOC, Brussels.

855 ECHA, 2017, Read-Across Assessment Framework (RAAF) - considerations on multi-  
856 constituent substances and UVCBs, ECHA-17-R-04-EN  
857 ([https://echa.europa.eu/documents/10162/13630/raaf\\_uvcb\\_report\\_en.pdf/3f79684d-](https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316)  
858 [07a5-e439-16c3-d2c8da96a316](https://echa.europa.eu/documents/10162/13630/raaf_uvcb_report_en.pdf/3f79684d-07a5-e439-16c3-d2c8da96a316) )

859 ECHA (2018a) Strategy to promote substitution to safer chemicals through innovation,  
860 Helsinki,  
861 ([https://echa.europa.eu/documents/10162/13630/250118\\_substitution\\_strategy\\_en.pdf/bc](https://echa.europa.eu/documents/10162/13630/250118_substitution_strategy_en.pdf/bce91d57-9dfc-2a46-4afd-5998dbb88500)  
862 [e91d57-9dfc-2a46-4afd-5998dbb88500](https://echa.europa.eu/documents/10162/13630/250118_substitution_strategy_en.pdf/bce91d57-9dfc-2a46-4afd-5998dbb88500)).



863 ECHA (2018b) European Union unique chemical database.  
864 <https://echa.europa.eu/information-on-chemicals>

865 EEA. 2015. The European environment — state and outlook 2015: synthesis report. European  
866 Environment Agency. Copenhagen, Denmark.

867 EPA (2018) ECOTOX Knowledgebase. <https://cfpub.epa.gov/ecotox/>

868 EUON (2018) European Observatory for nanomaterials. <https://euon.echa.europa.eu/>

869

870 Faber J.H., Van Wensem J. (2012) Elaborations on the use of the ecosystem services concept  
871 for application in ecological risk assessment for soils. *Sci Total Environ* 415:3–8.

872 Fischer B.B., Pomati F., Eggen R.I.L. (2013) The toxicity of chemical pollutants in dynamic  
873 natural systems: The challenge of integrating environmental factors and biological complexity.  
874 *Sci Total Environ* 449:253–259.

875 Fleishman E., Blockstein D.E., Hall J.A., Mascia M.B., Rudd M.A., Scott J.M., et al. (2011) Top  
876 40 priorities for science to inform conservation and management policy in the United States.  
877 *Bioscience* 61:290–300.

878 Focks A. (2014) The Challenge: Landscape ecotoxicology and spatially explicit risk assessment.  
879 *Environ Toxicol Chem* 33:1193.

880 Forbes V.E., Calow P., Grimm V., Hayashi T.I., Jager T., Katholm A., Palmqvist P., Pastorok R.,  
881 Salvito D., Sibly, R., Spromberg J., Stark J., Stillman J.A. (2011) Adding value to ecological risk  
882 assessment with population modelling. *Hum Ecol Risk Assess* 17: 287–299.

883 Forbes V.E., Galic N. (2016) Next-generation ecological risk assessment: Predicting risk from  
884 molecular initiation to ecosystem service delivery. *Environ Int* 91:215-219.

885 Forbes V.E., Palmqvist A., Bach L. (2006) The use and misuse of biomarkers in ecotoxicology.  
886 *Environ Toxicol Chem* 25:272–280.

887 Furley T.H., Brodeur J., Silva de Assis H.C., Carriquiriborde P., Chagas Jone Corrales K.R.,  
888 Denadai M., Fuchs J., Mascarenhas R., Miglioranza K.S.B., Margarita Miguez Caramés D., Maria  
889 Navas J., Nugegoda D., Planes E., Alejandro Rodriguez-Jorquera I., Orozco-Medina M., Boxall  
890 A.B.A., Rudd M.A., Brooks B.W. (2018) Toward sustainable environmental quality: Identifying  
891 priority research questions for Latin America. *Integr. Environ. Assess. Manag.* 14(3): 344-357.

892 Galic N., Grimm V., Forbes V. (2017) Impaired ecosystem process despite little effects on  
893 populations: modeling combined effects of warming and toxicants. *Global Change Biology* 23:  
894 2973-2989

895 Gergs A., Classen S., Strauss, T., Ottermanns R., Brock T.C.M., Ratte H.T., Hommen U., Preuss  
896 T.G. (2016a) Ecological recovery potential of freshwater organisms: consequences for  
897 environmental risk assessment of chemicals. *Reviews of Environmental Contamination and*  
898 *Toxicology* 236: 259-294.

899 Gergs A., Gabsi F., Zenker A., Preuss T.G. (2016b) Demographic toxicokinetic–toxicodynamic  
900 modeling of lethal effects. *Environ Sci Technol* 50:6017–6024

901 Government Office for Science (2016) Future of an Ageing Population. Foresight Report,  
902 Government Office for Science, London.

903 Grimm V., Augusiak J., Focks A., Frank B., Gabsi F., Johnston A.S.A., Liu C., Martin B.T., Meli M.,  
904 Radchuk V. et al. (2014) Towards better modelling and decision support: Documenting model  
905 development, testing, and analysis using TRACE. *Ecol Model* 280:129–139.

906 Handy R., Owen R., Valsami-Jones E. (2008) The ecotoxicology of nanoparticles and  
907 nanomaterials: current status, knowledge gaps, challenges and future needs. *Ecotoxicology*  
908 17:315-325.

909 Hässellöv M., Readman J.W., Ranville J.F., Tiede K. (2008) Nanoparticle analysis and  
910 characterization methodologies in environmental risk assessment of engineered  
911 nanoparticles. *Ecotoxicology* 17:344-361.

912 Hildago-Ruz V., Gutow L., Thompson R.C., Thiel M. (2012) Microplastics in the Marine  
913 Environment: A Review of the Methods Used for Identification and Quantification. *Environ Sci*  
914 *Technol* 46:3060-3075.

915 HilleRisLambers J., Adler P.B., Harpole W.S., Levine J.M., Mayfield M.M. (2012) Rethinking  
916 community assembly through the lens of coexistence theory. *Annual Review of Ecology*  
917 *Evolution and Systematics* 43: 227-248

918 Hollender J., Schymanski E.L., Singer H.P., Ferguson, P.L. (2017) Nontarget Screening with High  
919 Resolution Mass Spectrometry in the Environment: Ready to Go? *Environ. Sci. Technol.* 51(20):  
920 11505-11512

921 Holt A., Alix A., Thompson A., Maltby L. (2016) Food production, ecosystem services and  
922 biodiversity: We can't have it all everywhere. *Sci Total Environ.* 15(573):1422-1429.

923 Hommen U., Baveco J.M., Galic N., Van den Brink P.J. (2010) Potential application of ecological  
924 models in the European environmental risk assessment of chemicals I: Review of protection  
925 goals in EU directives and regulations. *Integr Environ Assess Manag* 6:325-337.

926 Hommen U., Forbes V., Grimm V., Preuss T.G., Thorbek P., Ducrot V. (2016) How to use  
927 mechanistic effect models in environmental risk assessment of pesticides: Case studies and

928 recommendations from the SETAC Workshop MODELINK. *Integr Environ Assess Manag* 12:21–  
929 31

930 Jackson M.C., Loewen C.J., Vinebrooke R.D., Chimimba C.T. (2016) Net effects of multiple  
931 stressors in freshwater ecosystems: a meta-analysis. *Glob Chang Biol* 22:180-189.

932 Janssens L., Stoks R. (2017) Chlorpyrifos-induced oxidative damage is reduced under warming  
933 and predation risk: Explaining antagonistic interactions with a pesticide. *Environ Pollut* 226:79-  
934 88

935 Johnson A.C., Sumpter J.P. (2014) Putting pharmaceuticals into the wider context of  
936 challenges to fish populations in rivers. *Phil Trans R Soc B* 369:20130581.

937 Kapo K.E., Holmes C.M., Dyer S.D., de Zwart D., Posthuma L. (2014) Developing a foundation  
938 for eco-epidemiological assessment of aquatic ecological status over large geographic regions  
939 utilizing existing data resources and models. *Environ Toxicol Chem* 33:1665-1677.

940 Karlsson M.V., Carter L.J., Agatz A., Boxall A.B.A. (2017) Novel Approach for characterizing pH-  
941 dependent uptake of ionizable chemicals in aquatic organisms. *Environ Sci Technol* 51: 6965-  
942 6971.

943 Keller V.D.J., Williams R.J., Lofthouse C., Johnson A.C. (2014) Worldwide estimation of river  
944 concentrations of any chemical originating from sewage-treatment plants using dilution  
945 factors. *Environ Toxicol Chem* 33:447–452.

946 Kooijman, S.A.L.M. (2010) *Dynamic Energy Budget Theory for Metabolic Organisation*, 3rd ed.  
947 Cambridge University Press, Cambridge, UK.

948 Kookana R.S., Boxall A.B.A., Reeves P.T., Ashauer R., Beulke S., Chaudhry Q., Cornelis G.,  
949 Fernandes T.F., Gan J., Kah M., Lynch I., Ranville J., Sinclair C., Spurgeon D., Tiede K., Van den

950 Brink P.J. (2014) Nanopesticides: Guiding Principles for Regulatory Evaluation of  
951 Environmental Risks. *J Agric Food Chem* 62:4227-4240.

952 Kostal J., Voutchkova-Kostal A., Anastas P.T., Zimmerman J. (2015) Identifying and designing  
953 chemicals with minimal acute aquatic toxicity. *Proc Natl Acad Sci U S A* 112:6289–6294.

954 Krewski D., Acosta D., Andersen M., Anderson H., Bailar III J.C., Boekelheide K., Brent R.,  
955 Charnley G., Cheung V.G., Green S., Kelsey K.T., Verkvliet N.I., Li A.A., McCray L., Meyer O.,  
956 Patterson R.D., Pennie W., Scala R.A., Solomon G.M., Stephens M., Yager J., Zeise L. (2010)  
957 Toxicity testing in the 21st century: A vision and a strategy. *J Toxicol Environ Health B Crit Rev*  
958 13:51–138.

959 Kroeze C., Gabbert S., Hofstra N., Koelmans A.A., Li A., Löhr A., Ludwig F., Strokal M., Verburg  
960 C., Vermeulen L., van Vliet M.T.H., de Vries W., Wang M., van Wijnen J. (2016) Global  
961 modelling of surface water quality: a multi-pollutant approach. *Curr Opin Environ Sustain* 23:  
962 35–45.

963 LaLone C.A., Villeneuve D.L., Lyons D., Helgen H.W., Robinson S.L., Swintek J.A., Saari T.W.,  
964 Ankley G.T. (2016) Sequence alignment to predict across species susceptibility (SeqAPASS): A  
965 web-based tool for addressing the challenges of cross-species extrapolation of chemical  
966 toxicity. *Toxicol Sci* 153:228-245.

967 Landis W.G., Ayre K.K., Johns A.F., Summers H.M., Stinson J., Harris M.J., Herring C.E.,  
968 Markiewicz A.J. (2017) The multiple stressor ecological risk assessment for the mercury-  
969 contaminated South River and Upper Shenandoah River using the Bayesian Network-Relative  
970 Risk Model *Integr Environ Assess Manag* 13:85–99

971 Leip A., Billen G., Garnier J., Grizzetti B., Lassaletta L., Reis S., Simpson D., Sutton M.A., de Vries  
972 W., Weiss F., Westhoek H. (2015) Impacts of European livestock production: nitrogen, sulphur,

973 phosphorus and greenhouse gas emissions, land-use, water eutrophication and biodiversity.  
974 *Environ Res Lett* 10:115004.

975 Lenzen M., Moran D., Kanemoto K., Foran B., Lobefaro L., Geschke A. (2012) International  
976 trade drives biodiversity threats in developing nations. *Nature* 486:109-112.

977 Lots F.A.E., Behrens P., Vijver M.G., Horton A.A. Bosker T. (2017) A large-scale investigation of  
978 microplastic contamination: abundance and characteristics of microplastics in European  
979 beach sediment. *Marine Pollution Bulletin*, 123, 219-226

980 Mace G.M., Norris K., Fitter A.H. (2012) Biodiversity and ecosystem services: a multi-layered  
981 relationship. *Trends Ecol Evol* 27:19-26.

982 Maltby L. (2013) Ecosystem services and the protection, restoration and management of  
983 ecosystems exposed to chemical stressors. *Environ Toxicol Chem* 32:974-983.

984 Margules CR, Pressey RL. 2000 Systematic conservation planning. *Nature* 405, 243–253.

985 Martin B.T., Jager T., Nisbet R.M., Preuss T.G., Hammers-Wirtz M., Grimm V. (2013)  
986 Extrapolating ecotoxicological effects from individuals to populations: a generic approach  
987 based on Dynamic Energy Budget theory and individual-based modeling. *Ecotoxicology*  
988 22:574–583.

989 Mittlebach G.C., Schemske D.W. (2015). Ecological and evolutionary perspectives on  
990 community assembly. *Trends in Ecology and Evolution* 30: 241-247

991 Moschet C., Wittmer I., Simovic J., Junghans M., Piazzoli A., Singer H., Stamm C., Leu C.,  
992 Hollender, J. (2014) How a complete pesticide screening changes the assessment of surface  
993 water quality. *Environ Sci Technol* 48:5423–5432.

994 Nienstedt K.M., Brock T.C.M., Van Wensem J., Montforts M., Hart A., Aagaard A., Alix A.,  
995 Boesten J., Bopp S.K., Brown C., Capri E., Forbes V., Köpp H., Liess M., Luttik R., Maltby L.,  
996 Sousa J.P., Streissl F., Hardy A.R. (2012) Development of a framework based on an ecosystem  
997 services approach for deriving specific protection goals for environmental risk assessment of  
998 pesticides. *Sci Total Environ* 415:31–38.

999 NRC. (2007) *Toxicity Testing in the 21st Century: A Vision and a Strategy*. National Research  
1000 Council, Committee on Toxicity Testing and Assessment of Environmental Agents. National  
1001 Academies Press, Washington, DC, USA

1002 Pacifici M., Foden W.B., Visconti P., Watson J.E.M., Butchart S.H.M., Kovacs K.M., Scheffers  
1003 B.R., Hole D.G., Martin T.G., Akçakaya H.R., Corlett R.T., Huntley B., Bickford D., Carr J.A.,  
1004 Hoffmann A.A., Midgley G.F., Pearce-Kelly P., Pearson R.G., Williams S.E., Willis S.G., Young  
1005 B., Rondinini C. (2015) Assessing species vulnerability to climate change. *Nature Climate  
1006 Change* 5: 215-225

1007 Pastorok R.A., Bartell S.M., Ferson S. (2002) *Ecological modeling in risk assessment: chemical  
1008 effects on populations, ecosystems, and landscapes*. Boca Raton (FL): Lewis. 328 p.

1009 Posthuma L., Dyer S.D., de Zwart D., Kapo K., Holmes C.M., Burton G.A. (2016) Eco-  
1010 epidemiology of aquatic ecosystems: Separating chemicals from multiple stressors. *Sci Total  
1011 Environ* 573:1303–1319

1012 Praetorius A., Tufenkji N., Goss K-U., Scheringer M., von der Kammer F., Elimelech M. (2014)  
1013 The road to nowhere: equilibrium partition coefficients for nanoparticles. *Environ Sci Nano*  
1014 1:317–323.

1015 Praetorius A., Scheringer M., Hungerbühler K. (2012) Development of Environmental Fate  
1016 Models for Engineered Nanoparticles – A Case Study of TiO<sub>2</sub> Nanoparticles in the Rhine River.  
1017 Environ Sci Technol 46:6075–6713.

1018 Rand-Weaver M., Margiotta-Casaluci L., Patel A., Panter G.H., Owen S.F., Sumpter J.P. (2013)  
1019 The Read-Across Hypothesis and Environmental Risk Assessment of Pharmaceuticals. Environ.  
1020 Sci. Technol. 47(20): 11384–11395.

1021 Rico A., Van den Brink P.J., Gylstra R., Focks A., Brock T.C.M. (2016). Developing ecological  
1022 scenarios for the prospective aquatic risk assessment of pesticides. Integr Environ Assess  
1023 Manag 12:510–521.

1024 Rohr J.R., Salice C.J., Nisbet R.M. (2016) The pros and cons of ecological risk assessment based  
1025 on data from different levels of biological organization. Critical Reviews in Toxicology 46: 756-  
1026 784.

1027 Rudd MA, Beazley KF, Cooke SJ, Fleishman E, Lane DE, Mascia MB, Roth R, Tabor G,  
1028 Bakker JA, Bellefontaine T, Berteaux D, Cantin B, Chaulk KF, Cunningham K, Dobell R, Fast  
1029 E, Ferrara N, Findlay CS, Hallstrom LK, Hammond T, Hermantuz L, Hutchings JA, Lindsay  
1030 KE, Marta TJ, Nguyen VM, Northey G, Prior K, Ramirez-Sanchez S, Rice J, Sleep DJH, Szabo  
1031 ND, Trottier G, Toussaint JP, Veilleux JP. 2011. Generation of priority research questions to  
1032 inform conservation policy and management at a national level. Conservation Biology 25: 476-  
1033 484.

1034 Rudd MA, Boxall ABA, Ankley GT, Brooks BW. 2014. International scientists' priorities for  
1035 research on pharmaceutical and personal care products in the environment. Integrated  
1036 Environmental Assessment and Monitoring 10: 576-587. SCHER (Scientific Committee on  
1037 Health and Environmental Risks), SCENIHR (Scientific Committee on Emerging and Newly



1038 Identified Health Risks), SCCS (Scientific Committee on Consumer Safety). (2013a) Addressing  
1039 the New Challenges for Risk Management. European Union, Brussels Belgium

1040 SCHER (Scientific Committee on Health and Environmental Risks), SCENIHR (Scientific  
1041 Committee on Emerging and Newly Identified Health Risks), SCCS (Scientific Committee on  
1042 Consumer Safety) (2013b) Making Risk Assessment More Relevant for Risk Management,  
1043 2013, European Union, Brussels.

1044 Schroeder A.L., Ankley G.T., Houck K.A., Villeneuve D.L. (2016) Environmental surveillance and  
1045 monitoring – The next frontiers for high-throughput toxicology. *Environ Toxicol Chem* 35:513-  
1046 525.

1047 Schwarzenbach R.P., Escher B.I., Fenner K., Hofstetter T.B., Johnson C.A., von Gunten U.,  
1048 Wehrli B. (2006) The Challenge of Micropollutants in Aquatic Systems. *Science* 313: 1072-  
1049 1077.

1050 Scott, A.B. et al. (2017) Monitoring Water Quality in Toronto’s Urban Stormwater Ponds:  
1051 Assessing Participation Rates and Data Quality of Water Sampling by Citizen Scientists in the  
1052 FreshWater Watch. *Science of the Total Environment*. 592:738-744

1053 Segner H., Schmitt-Jansen M., Sabater S. (2014) Assessing the impact of multiple stressors on  
1054 aquatic biota: the receptor’s side matters. *Environ Sci Technol* 48:7690-7696.

1055 Spaak J.W., Baert J.M., Baird D.J., Eisenhauer N., Maltby L., Pomati F., Radchuk V., Rohr J.R.,  
1056 Van den Brink P.J., De Leander F. (2017) Shifts in community composition and population  
1057 density substantially affect ecosystem function despite invariant richness. *Ecology Letters* 20:  
1058 1315-1324

1059 Spellman F. (2014) Environmental impacts of renewable energy. CRC Press, Boca Raton, FL,  
1060 USA.

1061 Springer T. A., Guiney P. D., Krueger H. O., Jaber, M. J. (2008) Assessment of an approach to  
1062 estimating aquatic bioconcentration factors using reduced sampling. *Environ. Toxicol. Chem.*  
1063 27(11): 2271–2280.

1064 Stahl R.G. Jr., Hooper M.J., Balbus J.M., Clements W., Fritz A., Gouin T., Helm R., Hickey C.,  
1065 Landis W., Moe S.J. (2013) The influence of global climate change on the scientific foundations  
1066 and applications of Environmental Toxicology and Chemistry: Introduction to a SETAC  
1067 international workshop. *Environ Toxicol Chem* 32:13-19.

1068 Stegemeier J.P., Schwab F., Colman B.P., Webb S.M., Newville M., Lanzirotte A., Winkler C.,  
1069 Wiesner M.R., Lowry G.V. (2015) Speciation matters: Bioavailability of silver and silver sulfide  
1070 nanoparticles to alfalfa (*Medicago sativa*). *Environ Sci Technol* 49:8451-8460.

1071 Stevenson R.W., Chapman P.M. (2017) Integrating causation in investigative ecological weight  
1072 of evidence assessments. *Integr Environ Assess Manag* 13:702–713

1073 Sutherland W.J., Fleishman E., Mascia M.B., Pretty J., Rudd M.A. (2011) Methods for  
1074 collaboratively identifying research priorities and emerging issues in science and policy.  
1075 *Methods Ecol Evol* 2:238–247.

1076 UN. (2015) Transforming Our World: The 2030 Agenda for sustainable development.  
1077 A/RES/70/1. United Nations. New York, USA.

1078 Vallotton N., Price P.S. (2016) Use of the Maximum Cumulative Ratio As an Approach for  
1079 Prioritizing Aquatic Coexposure to Plant Protection Products: A Case Study of a Large Surface  
1080 Water Monitoring Database. *Environ Sci Technol* 50:5286–5293.

1081 Van den Brink P.J., Baird D.J., Baveco H., Focks A. (2013) The use of traits-based approaches  
1082 and eco(toxico)logical models to advance the ecological risk assessment framework for  
1083 chemicals. *Integr Environ Assess Manag* 9:e47-e57.

1084 Van den Brink P.J., Bo Choung C., Landis W., Mayer-Pinto M., Pettigrove V., Scanes P., Smith  
1085 R., Stauber J. (2016) New approaches to the ecological risk assessment of multiple stressors.  
1086 *Mar Freshw Res* 67:429–439.

1087 Winkler D.A., Mombelli E., Pietroiusti A., Tran L., Worth A., Fadeel B., McCall M.J. (2013)  
1088 Applying quantitative structure-activity relationship approaches to nanotoxicology: current  
1089 status and future potential. *Toxicology*13(1):15-23.

1090 Worth A., Barroso J., Bremer S., Burton J., Casati S., Coecke S., Corvi R., Desprez B., Dumont  
1091 C., Gouliarmou V., Goumenou M., Grapel R., Griesinger C., Halder M., Janusch Roi A., Kienzler  
1092 A., Madia F., Munn S., Nepelska M., Paini A., Price A., Prieto P., Rolaki A., Schaffer M., Triebe  
1093 J., Whelan M., Wittwehr C., Zuang V. (2014) Alternative methods for regulatory toxicology - a  
1094 state-of-the-art Review. JRC science and policy report, JRC91361/EUR 26797 Brussels,  
1095 Belgium.

1096 Zimmerman J.B., Anastas P.T. (2015) Toward substitution with no regrets. *Science*  
1097 347:1198–1199.

*Table 1. The top 22 research questions arising from the European Horizon Scanning workshop and their ranking and scores.*

Rank	Question	Mean	95% Lower	95% Upper
1	How can interactions among different stress factors operating at different levels of biological organization be accounted for in environmental risk assessment?	7.41	7.07	7.76
2	How do we improve risk assessment of environmental stressors to be more predictive across increasing environmental complexity and spatiotemporal scales?	7.03	6.70	7.36
3	How can we define, distinguish, and quantify the effects of multiple stressors on ecosystems?	6.68	6.27	7.08
4	How can we develop mechanistic modelling to extrapolate adverse effects across levels of biological organization?	6.13	5.67	6.59
5	How can we properly characterize the chemical use, emissions, fate and exposure at different spatial and temporal scales?	5.32	4.95	5.69
6	Which chemicals are the main drivers of mixture toxicity in the environment?	5.24	4.81	5.68
7	What are the key ecological challenges arising from global megatrends?	5.20	4.84	5.57

8	How can we develop, assess and select the most effective mitigation measures for chemicals in the environment?	5.01	4.58	5.44
9	How do sublethal effects alter individual fitness and propagate to the population and community level?	5.00	4.53	5.48
10	Biodiversity and ecosystem services: what are we trying to protect where, when, why, and how?	4.57	4.10	5.05
11	What approaches should be used to prioritize compounds for environmental risk assessment and management?	4.34	3.95	4.72
12	How can monitoring data be used to determine whether current regulatory risk assessment schemes are effective for emerging contaminants?	4.17	3.81	4.53
13	How can we improve in silico methods for environmental fate and effects estimation?	4.07	3.66	4.47
14	How can we integrate evolutionary and ecological knowledge in order to better determine vulnerability of populations and communities to stressors?	3.95	3.57	4.33
15	How do we create high-throughput strategies for predicting environmentally relevant effects and processes?	3.82	3.42	4.21
16	How can we better manage, use and share data to develop more sustainable and safer products?	3.79	3.39	4.20

17	Which interactions are not captured by currently accepted mixture toxicity models?	3.79	3.46	4.11
18	How can we assess the environmental risk of emerging and future stressors?	3.26	2.89	3.64
19	How can we integrate comparative risk assessment, LCA, and risk benefit analysis to identify and design more sustainable alternatives?	3.10	2.66	3.53
20	How can we improve the communication of risk to different stakeholders?	2.98	2.57	3.39
21	How do we detect and characterize difficult-to-measure substances in the environment?	2.80	2.41	3.19
22	Where are the hotspots of key contaminants around the globe?	2.34	1.94	2.73

Figure 1. Broad categorisation of the 22 priority questions showing the interlinkages between the questions.

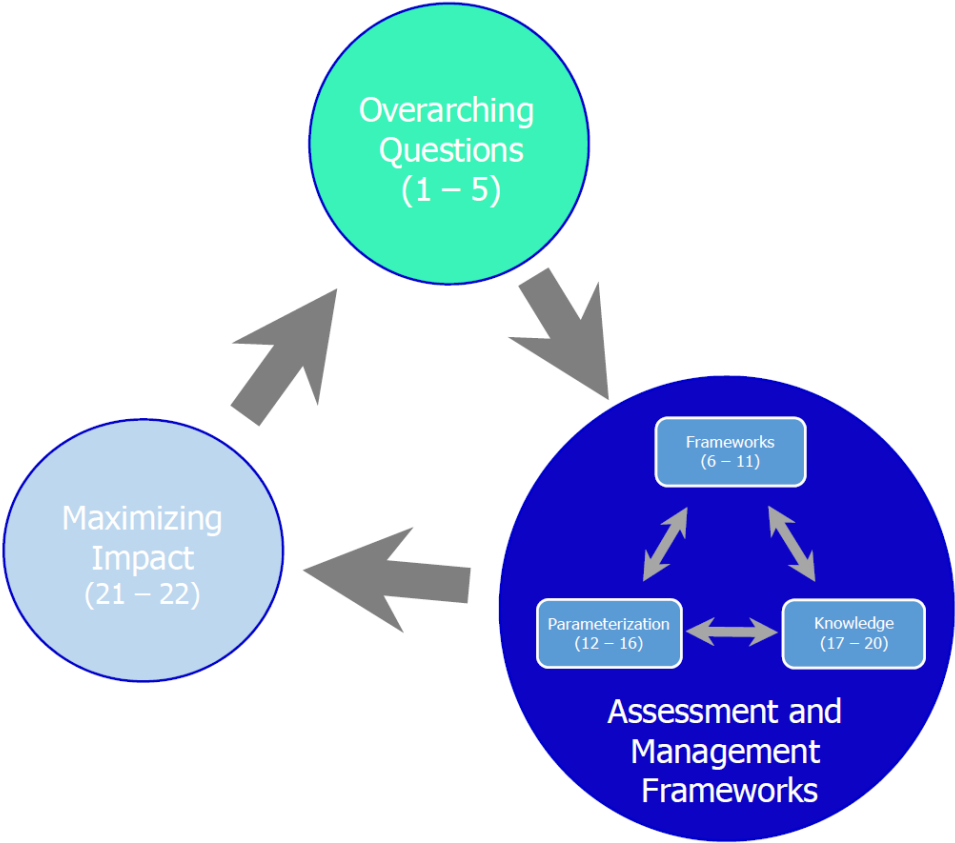


Figure 2. Network map indicating the interrelationships between the different priority questions

