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1 Towards Sustainable Environmental Quality: Priority Research

2 Questions for Europe

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75 # Disclaimer—The author is a staff member of the European Chemicals Agency. The views and
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 CO₂ 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 (Pacifi 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

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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.

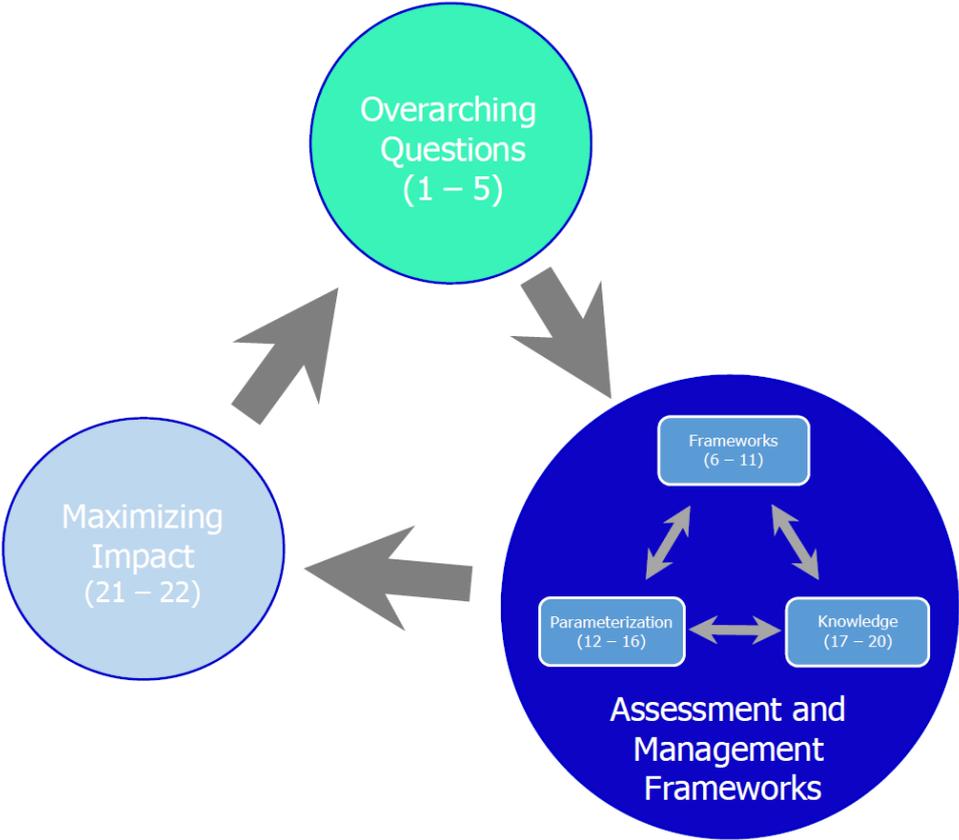


Figure 2. Network map indicating the interrelationships between the different priority questions

