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4 **Title:** Prioritisation approaches for substances of emerging concern in groundwater: a critical review

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Abstract

20 Risks from emerging contaminants (ECs) in groundwater to human health and aquatic ecology remain
21 difficult to quantify. The number of ECs potentially found in groundwater presents challenges for
22 regulators and water managers regarding selection for monitoring. This study is the first systematic
23 review of prioritisation approaches for selecting ECs that may pose a risk in groundwater. Online
24 databases were searched for prioritisation approaches relating to ECs in the aquatic environment using
25 standardised key word search combinations. From a total of 672, studies 33 met the eligibility criteria,
26 based primarily on the relevance to prioritising ECs in groundwater. The review revealed the lack of a
27 groundwater specific contaminant prioritisation methodology in spite of widely recognised differences
28 between groundwater and surface water environments in regards to pathways to receptors. The findings
29 highlight a lack of adequate evaluation of methodologies for predicting the likelihood of an EC entering
30 groundwater and highlights knowledge gaps regarding the occurrence and fate of ECs in this
31 environment. The review concludes with a proposal for a prioritisation framework for ECs in
32 groundwater monitoring which enables priority lists to be updated as new information becomes
33 available for substances regarding usage, physico-chemical properties and hazards.

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TOC/Abstract Art.



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Keywords

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Emerging contaminants; Groundwater; Prioritisation; Monitoring

40

41 **1 Introduction**

42 Research on substances of emerging concern in the aquatic environment has expanded in recent years.
43 They are often referred to as ‘emerging contaminants’ (ECs) and as substances “*that are currently not*
44 *included in routine monitoring programmes*” and “*may be candidates for future regulation, depending*
45 *on research on their ecotoxicity*” and “*monitoring data regarding their occurrence*” in the
46 environment.¹ In some cases they are also substances which still require the development of conceptual
47 models to describe their behaviour and occurrence in the environment.² ECs include pharmaceuticals
48 and personal care products (PPCP), illicit drugs, hormones and steroids, industrial substances,
49 disinfection by-products and pesticide degradation products.²⁻⁴ Approximately 860 ECs in the
50 environment that are currently being researched or discussed.¹ There has been an increase in the
51 monitoring of ECs in the environment, largely due to advances in analytical chemistry techniques.
52 Contaminants can be detected in concentration ranges below 1 ng/l that were previously below the Limit
53 of Detection (LOD).^{3,5} New techniques include multi-residue gas and liquid chromatography techniques
54 coupled with mass spectrometry.^{3,5}

55 The potential risks from ECs to human health and aquatic ecology in the environment have been
56 recognised,⁶⁻⁸ and new standards and regulations may be required.^{2,9-11} ECs are now understood to be
57 “*ubiquitous contaminants in the environment*” and there is evidence that these contaminants can have
58 disruptive effects to organisms at different trophic levels, including humans.¹² There is also growing
59 concerns regarding the occurrence of pharmaceuticals in the environment and the build-up of antifungal
60 and antibiotic resistance.¹³

61 There remain many challenges for regulators and water managers regarding the monitoring of ECs in
62 the aquatic environment.¹⁴ These challenges specifically relate to the lack of knowledge on their
63 occurrence and fate, the number of ECs potentially present in the environment and the fact that many of
64 them are unregulated.^{14,15} This is a particular concern for groundwater because the environmental fate
65 of ECs is still not well understood.^{16,17} Groundwater is a valuable resource and amounts to 98% of the
66 Earths’ freshwater¹⁸ and supplies approximately 50% of all drinking water globally.¹⁹ Drinking water
67 treatment might only involve disinfection, meaning there is a risk of ECs contaminating supplies from
68 groundwater.²⁰ ECs have been detected in treated drinking water.^{16,20} Groundwater is also vital to the
69 health of groundwater-dependent ecosystems such as rivers, lakes and wetlands.²¹

70 **1.1 Regulatory background**

71 In Europe, the Water Framework Directive (WFD) (2000/60/EC)²² requires Member States (MS) to
72 manage water in an integrated ecosystem-based approach, and considers that all waters and their
73 dependent ecosystems are inter-linked and inter-dependent. The key objective of the WFD is to establish
74 good ecological status in all surface waters and good chemical and quantitative status in all groundwaters
75 through a formal process until 2027. The WFD does not allow for deterioration in water body status.

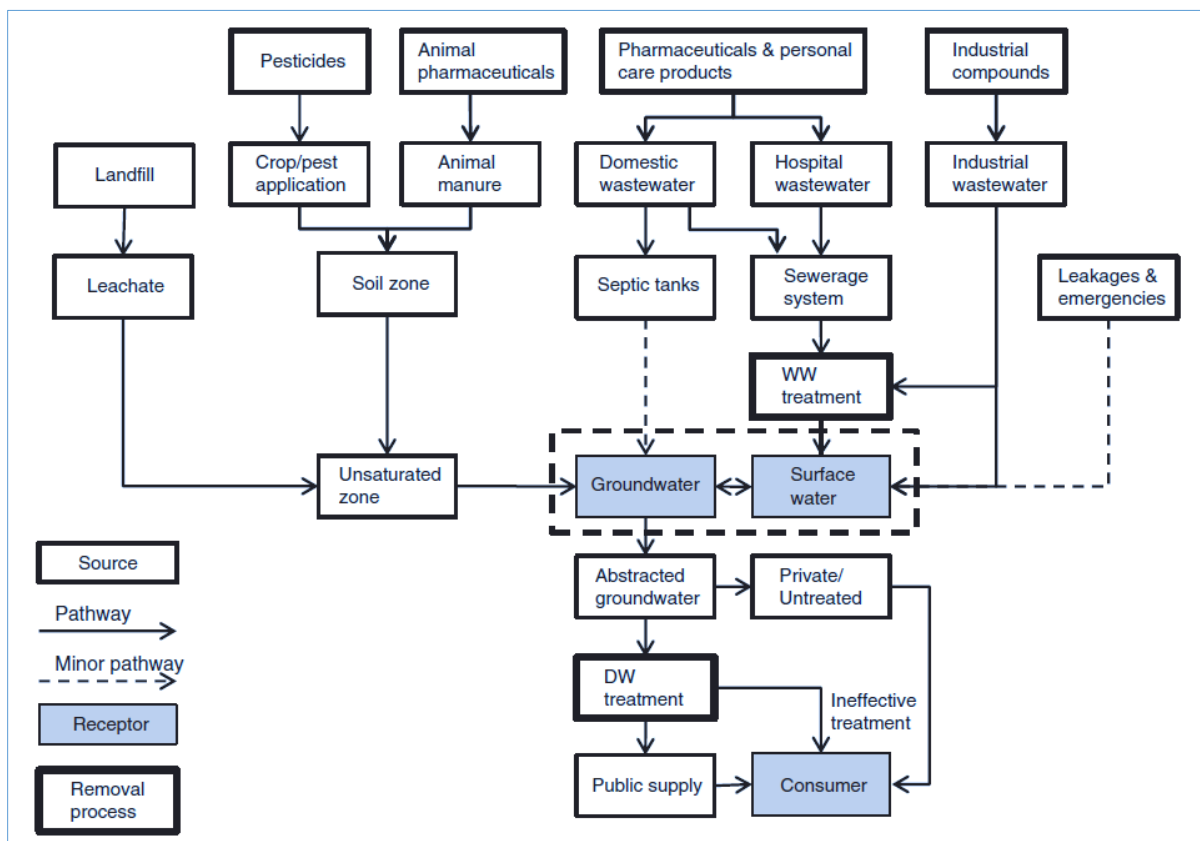
76 The Groundwater Daughter Directive (GWDD) (2006/118/EC)²¹ further describes how the chemical
77 status of groundwater bodies is defined using Threshold Values (TVs). They indicate environmental risk
78 and trigger the requirement for further investigation.²³ Many of the TVs relate to the protection of
79 groundwater receptors such as rivers, groundwater-dependent terrestrial ecosystems or drinking water
80 supplies.^{16,17} For many ‘classical’ contaminants there is sufficient information about the pathways and
81 toxicity to receptors; however, not enough is known about ECs to define TVs.¹⁶

82 A ‘chicken or egg dilemma’ prevails, as the gaps in knowledge relating to the occurrence and risk of
83 ECs delay regulation and the lack of regulation delays the generation of monitoring data.²⁴ The number
84 of ECs makes it difficult to identify which ones should be monitored.²⁵ In Europe, this has been
85 addressed by developing a watch list for pollutants which aims “*to increase the availability of*
86 *monitoring data on substances posing a risk or potential risk to bodies of groundwater, and thereby*
87 *facilitate the identification of substances, including emerging pollutants, for which groundwater quality*
88 *standards or TVs should be set*” (2014/80/EU).²⁶ The first watch list under the Priority Substances
89 Directive (2008/105/EC²⁷ as amended by 2013/39/EU), has already been adopted for surface water in
90 2015. Ten new substances including 17 α -ethinyloestradiol, 17 β -estradiol and diclofenac are listed.²⁸

91 A similar situation occurs elsewhere in the world for the regulation of ECs. The US Environment
92 Protection Agency (USEPA) published a Contaminant Candidate List (CCL) for drinking water.²⁹ This
93 is required under the Safe Drinking Water Act (SDWA) for contaminants known or anticipated to occur
94 in drinking waters and may require regulation in the future.²⁹ The latest CCL (no. 4) from 2016 includes
95 97 chemicals from industrial use, pesticides, disinfection by-products and pharmaceuticals.

96 **1.2 Emerging contaminants in groundwater**

97 Most research on ECs in the environment focuses on wastewater and surface water, while there has been
98 less emphasis on groundwater.³⁰ ECs have the potential to leach through subsoils to groundwater and
99 have been detected in aquifers since the 1990s.³¹ ECs may get into groundwater from numerous origins
100 as shown in Figure 1, but wastewater has been identified as the primary source.¹⁶ Point sources include
101 private wastewater treatment systems, animal waste lagoons and landfill leachate.¹⁶ Managed artificial
102 recharge of partially treated wastewater or surface water (i.e. bank infiltration) can also be important
103 sources of ECs in groundwater.¹⁷ Diffuse sources include application of manure, pesticides, biosolids
104 from sewage sludge, and atmospheric deposition.^{16,17,32,33}



105

106 **Figure 1 Sources of emerging contaminants and pathways towards receptors¹⁷**

107

108 Numerous studies in the USA^{34,35} and Europe^{17,30,36} provide an overview of the occurrence of ECs in
 109 groundwater. A global review of studies¹⁶ published since 1993 documented significant concentrations
 110 (10^2 to 10^4 ng/l) of ECs, which included a range of PPCPs (e.g. carbamazepine and ibuprofen), industrial
 111 compounds, and caffeine. Transformation products can be found more frequently, and in higher
 112 concentrations, than their parent compounds.^{4,16}

113 Previous studies have demonstrated that concentrations of ECs in surface waters are higher than those
 114 in groundwaters.^{7,34,35,37} In addition, the lists of ECs most frequently detected in groundwater differ from
 115 those in surface waters.^{7,34,35,37} For example, a comparative survey³⁷ of 70 groundwater and 71 surface
 116 water samples in France, found that several pharmaceuticals detected in surface water were not present
 117 in groundwater. This is because the main source of ECs in the aquatic environment is wastewater
 118 effluent, which discharges directly into surface waters, while groundwater is generally less vulnerable
 119 to contaminants due to the protective properties of soils and the unsaturated zone. However, groundwater
 120 bodies in areas with an absence or only a thin layer of subsoils have increased vulnerability to
 121 contamination, including by ECs.^{38,39} The occurrence of ECs in United Kingdom, French and Italian
 122 groundwater, also showed higher concentrations in karstic aquifers relating to high transmissivity, and
 123 conduits.^{39,40} In addition to infiltration through the subsurface environment, another pathway of ECs to

124 groundwater is via surface water-groundwater exchange.¹⁶ There remain gaps in the understanding of
125 EC sources, the pathways to receptors and toxicity mechanisms and levels.²

126 **1.3 Prioritisation approaches for monitoring contaminants in groundwater**

127 Given the lack of knowledge about the behaviour and impacts of ECs on groundwater receptors, many
128 ECs are not routinely monitored in groundwater.² Both the number of ECs, and the fact that not all of
129 them will be harmful to human health or the aquatic environment, means that prioritisation is required
130 to develop cost effective monitoring programmes that target the highest risk ECs, which may warrant
131 regulation in the future.^{2,11,14} As demonstrated by previous studies^{35,37}, EC occurrence in groundwater
132 can differ from surface water; in regard to the types of contaminants, detection frequencies, and
133 concentrations. Consequently, it appears inappropriate to use priority lists developed for surface waters.
134 Existing techniques for prioritising chemicals are generally based on the principles of risk assessment.²⁵

135 The risk is the probability of the occurrence of exposure of a chemical to a biological receptor multiplied
136 by the associated effect, known as the hazard.²⁵ The way exposure and hazard are combined to calculate
137 the risk, varies between prioritisation approaches and this can affect the results.⁴¹ There is no standard
138 approach for prioritising ECs in groundwater. The Common Implementation Strategy Working Group
139 for Groundwater (CIS WGGW, 2018) has outlined a process for developing a voluntary groundwater
140 watch list (GWWL) at an EU level.^{42,43} The NORMAN Network¹, a group of stakeholders interested in
141 emerging contaminants (which includes academia, industry and regulators), are also developing a
142 prioritisation methodology for groundwater (currently unavailable).

143 Exposure relates to the environmental occurrence of a substance, which can be estimated using simple
144 equations or environmental fate models.^{40,44,45} Occurrence in groundwater is not solely dependent on
145 source factors and the characteristics of the pathway also warrant consideration.^{11,16} Migration through
146 the subsurface is determined by several factors,^{4,46-49} such as physico-chemical properties of the
147 compounds as well as those of soils and subsoils. Indices have been developed for estimating the
148 leaching potential of contaminants (mainly for pesticides).⁵⁰ Existing prioritisation approaches for
149 groundwater have used these for characterising environmental exposure. For example: the Groundwater
150 Ubiquity Score (GUS index)⁵¹ based on the physico-chemical properties of the compounds was used to
151 prioritise pesticides in South African groundwater⁵²; and the Attenuation Factor (AF) also based on the
152 physico-chemical properties, as well as soil properties, the subsurface depth and recharge⁵³ was used for
153 estimating the leaching quantity of sixteen ECs in Ireland⁵⁴.

154 While there are numerous studies on the prioritisation of chemicals in the aquatic environment, there is
155 a lack of consensus on critical components, such as determining exposure in groundwater and
156 quantifying the hazard.^{10,55} Only one published study² so far had specifically set out to review
157 prioritisation for groundwater monitoring, but neither analysed approaches in detail nor proposed any
158 groundwater specific techniques. Consequently, there is a need to review prioritisation techniques to

159 determine the best approach for prioritising ECs in groundwater. This will help to focus groundwater
160 monitoring efforts on those ECs that present the highest risk to human health or ecological receptors.

161 To the authors knowledge this paper provides the first critical review of prioritisation approaches for
162 selecting ECs for monitoring that may pose a risk in groundwater. It reviews existing approaches to
163 provide a synthesis of their elements which may be appropriate for groundwater and to identify
164 knowledge gaps. The specific objectives of the review are to: 1) review existing prioritisation approaches
165 for ECs with an emphasis on methodologies that can be used for groundwater; 2) evaluate the
166 methodologies within these prioritisation approaches for predicting EC occurrence in groundwater; 3)
167 analyse the prioritisation results from a subset of studies to examine similarities and differences, and the
168 impact of an approach on the result; and 4) describe a framework for a prioritisation approach for ECs
169 in groundwater and make recommendations for further research.

170 **2 Systematic review criteria**

171 The systematic review was conducted following the general principles published in “*The Production of*
172 *Quick Scoping Reviews and Rapid Evidence Assessments*”.⁵⁶ A predefined protocol was developed by
173 the authors and extracts are available in Supplementary Information A. The keywords searched are
174 outlined Supplementary Information A, the record of results returned is in Supplementary Information
175 B. The search source of published literature was the online database Scopus. Some of the recent work
176 in this field has not been published within peer-reviewed journals, therefore, websites of relevant
177 specialist organisations such as USEPA and EU Joint Research Council (JRC) were also searched.

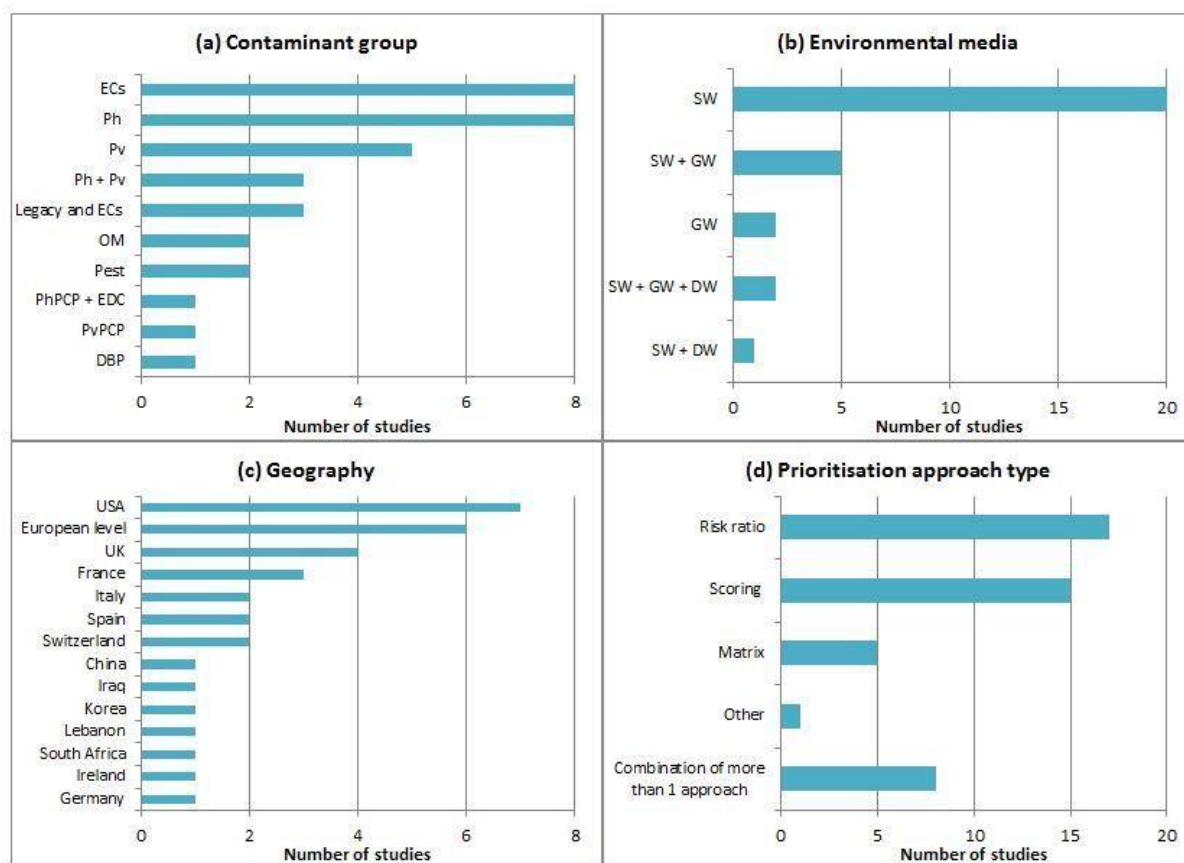
178 Following the screening of titles and abstracts, the remaining articles were examined in full to determine
179 their eligibility for inclusion in further assessment. This selection generated a more focused group of
180 studies to improve quality and the confidence of the analysis relating to the research question. A
181 predefined scoring system for relevance and quality was developed as part of the protocol
182 (Supplementary Information A). Studies were included if they had a relevant outcome (i.e. a prioritised
183 list of chemicals for water quality monitoring purposes) and were of sufficient quality. The quality was
184 determined through a process of critical appraisal to ensure only reliable studies were included. For
185 example, criteria included: the study having a clear aim and transparent methodology. For the eligible
186 studies, key information on the prioritisation approaches was extracted (see Supplementary Information
187 A).

188 **3 Prioritisation approaches for monitoring ECs in groundwater**

189 **3.1 Study characteristics from systematic review**

190 A total of 672 studies were identified and following the screening and eligibility assessment 33 studies
191 were deemed eligible for inclusion in the review. The primary reason for exclusion was the lack of a
192 relevant outcome, that is, the study did not include a prioritised list of chemicals for water quality

193 monitoring purposes. Summary results from this systematic review of published prioritisation studies
 194 are shown in Figure 2 (see Supplementary Information C (Table D) for details of the study
 195 characteristics). All studies were available in the English language and dated from 2003 to 2016. Many
 196 were published since 2014, accounting for 50 % of the studies included.



197
 198 **Figure 2. Summary results from review of studies of prioritisation approaches for ECs, a) key**
 199 **contaminant groups included in published prioritisation approaches, b) range of environmental**
 200 **media, c) geographical coverage of studies, d) types of approaches for prioritisation. SW=surface**
 201 **water, GW=groundwater, DW=drinking water. Ph=human pharmaceuticals, Pv=veterinary**
 202 **pharmaceuticals, Legacy=regulated legacy contaminants, Pest=pesticides, OM=organic**
 203 **micropollutants, PCP=personal care products, EDC=endocrine disrupting**
 204 **compounds, DBP=disinfection by-products.**

205 Eight of the studies focused on ECs as a general category, with a further three examining legacy
 206 contaminants and ECs together (Figure 2a). Two studies were aimed specifically at organic
 207 micropollutants, three related to pesticides and one to disinfection by-products. Half of the studies (n =
 208 17) focused on pharmaceuticals in the environment. Ten of these studies were for human
 209 pharmaceuticals, five for veterinary and two for both. Two of the studies focusing on pharmaceuticals
 210 also included personal care products.

211 Only a very small proportion of published prioritisation studies were found to have a groundwater focus
212 (Figure 2b). The majority of the studies were aimed at surface water (n = 21). A total of nine studies
213 related to groundwater, with only two focused on groundwater (see Supplementary Information C (Table
214 E) for full table of results). Five studies were aimed at both surface water and groundwater, and a further
215 two for surface water, groundwater and drinking water.

216 The selected studies were conducted in 13 different countries or regions (Figure 2c). Most of the studies
217 were undertaken in European countries (n = 21), six at a European scale and four based in the United
218 Kingdom. The USA also accounted for a significant number of the studies (n = 7). Five studies were
219 from other countries (Korea, China, South Africa, Iraq and Lebanon).

220 The examined studies represent several different approaches of combining exposure and hazard
221 assessments to determine risk, including the risk ratio approach, and scoring systems or matrices (Figure
222 2d). Seventeen studies followed the risk ratio approach which was used slightly more frequently than
223 the scoring system approach. The risk ratio approach relies on having the dose-response toxicological
224 data for the relevant trophic levels and receptors but is considered a simple to use method and it is easy
225 to communicate the results.⁵⁷ A value above one indicates risk and may activate the substance's inclusion
226 in monitoring programmes.^{10,44,58} The scoring approaches involved categorising and combining scores
227 for exposure and hazard. For example, for exposure leaching indicators can be used and for hazards,
228 classification data can be used instead of dose-response data. There were 15 scoring system approaches,
229 three of which also used a matrix approach for combining the scores. Six of the studies used a
230 combination of the risk ratio and scoring system approach. Examples were the EU WFD prioritisation
231 studies⁵⁸⁻⁶⁰, where their first stage screening involved scoring chemicals based on the persistence,
232 bioaccumulation and toxicity (PBT) approach and then the second stage prioritisation was based on the
233 risk ratio approach.

234 Only a very small proportion of published studies were found to have a groundwater focus and of those
235 only one covered ECs specifically (Figure 2). This highlights the limited attention that has been paid to
236 groundwater and groundwater receptors to date. The number of substances and groups of substances
237 covered so far for both surface water and groundwater is also very limited, and the geographical coverage
238 biased to Europe and USA. This emphasises the need for prioritisation approaches to now look beyond
239 traditional hotspots of surface water and wastewater systems and consider approaches that are
240 appropriate for the protection of groundwater bodies. A wider geographical scope is needed, and risk to
241 groundwater from ECs may be region or country specific in terms of substances used, quantities used,
242 as well as pathways for potential groundwater contamination. The tendency for prioritisation of
243 pharmaceuticals, could lead to some other ECs escaping scrutiny.⁵⁴ This may be referred to the “*Matthew*
244 *effect*” whereby “*the prominence of a few contaminants targeted for investigation is dictated largely by*
245 *the attention devoted to them in the past*”.⁵⁴ Some of the prioritisation studies^{10,57,61} which examined ECs
246 and some classical contaminants had only included few pharmaceuticals in their priority lists.

247 **3.2 Limitations of the study**

248 This review has several limitations including a risk of bias in the results because there were repetitions
249 in the prioritisation approaches included. About half of the studies only updated existing approaches or
250 applied them, and sometimes the same authors were involved in more than one study. This can result in
251 showing trends in the approaches used, just because they have been used previously. The same is also
252 true for the types of ECs studied due to the focus on pharmaceuticals. It was beyond the scope of this
253 review to consider unpublished prioritisation approaches and therefore other approaches for
254 prioritisation of ECs in groundwater may be applied in some countries that were not included. As
255 discussed in Section 6 there were limitations with comparing the results of different prioritisation
256 approaches and these should be addressed in future to help verify the results.

257 **4 Approaches for assessment of environmental exposure of ECs in groundwater**

258 This section describes the trends in the methods for exposure assessment, their applicability to the
259 groundwater environment and highlights the strengths and weaknesses. Table 1 provides an overview
260 of the characteristics of the exposure (and hazard) assessment in each of the studies.

Table 1 Summary approach to exposure and hazard assessment

Reference	Exposure									Hazard													
	Generic				Surface water		Groundwater			Receptors		Dose response					Classification						
	Chemical Property	Sales	Usage	Metabolism	Predict conc SW	Measured conc SW	Predict conc GW	Measure conc GW	Leaching Indicators	Ecology	Human	Algae	Daphnia	Fish	Mammalian	Human dose	Persistence	Bioaccumulation	Carcinogenicity	Mutagenicity	Teratogenicity	Endocrine disruption	Neurotoxicity
Boxall <i>et al.</i> ⁶²			•	•						•		•	•	•									
Capleton <i>et al.</i> ⁶³		•		•							•				•		•	•	•	•	•	•	•
Besse and Garric ⁶⁴		•		•	•					•		•	•	•		•	•						
Kim <i>et al.</i> ⁶⁵		•		•						•		•			•								
Kools <i>et al.</i> ⁶⁶	•				•					•					•								
USEPA ^{29,67}		•	•			•		•			•				•			•	•	•			
Götz <i>et al.</i> ²⁵	•	•				•																	
Hebert <i>et al.</i> ⁶⁸						•		•			•							•	•				
Kumar and Xagorarakis ⁶⁹						•				•	•	•	•				•	•	•	•	•	•	•
Murray <i>et al.</i> ⁷⁰						•		•			•				•								
Daginnus <i>et al.</i> ⁵⁹ (WFD)	•	•			•					•	•	•	•	•		•	•	•	•	•			
Diamond <i>et al.</i> ⁵⁷						•				•		•	•		•	•						•	
von der Ohe <i>et al.</i> ¹⁰						•				•		•	•										
Coutu <i>et al.</i> ⁷¹										•	•				•		•	•	•				
Sui <i>et al.</i> ¹¹		•			•					•		•	•				•	•	•				
Ortiz de García <i>et al.</i> ⁷²						•				•		•	•		•	•							
Bouissou- Schurtz <i>et al.</i> ⁷³	•				•	•				•		•	•										
Dabrowski <i>et al.</i> ⁵²	•	•	•						•		•							•	•	•	•	•	•
LaLone <i>et al.</i> ⁷⁴										•			•										
Maruya <i>et al.</i> ⁷⁵					•	•				•			•										
Carvalho <i>et al.</i> (JRC) ⁵⁸	•	•			•	•				•	•	•	•	•	•								

Reference	Exposure									Hazard													
	Generic				Surface water		Groundwater			Receptors		Dose response					Classification						
	Chemical Property	Sales	Usage	Metabolism	Predict conc SW	Measured conc SW	Predict conc GW	Measure conc GW	Leaching Indicators	Ecology	Human	Algae	Daphnia	Fish	Mammalian	Human dose	Persistence	Bioaccumulation	Carcinogenicity	Mutagenicity	Teratogenicity	Endocrine disruption	Neurotoxicity
(WFD)																							
Chirico <i>et al.</i> (JRC) ⁶⁰ (WFD)	•	•			•					•	•	•	•	•			•	•	•	•	•	•	•
Di Nica <i>et al.</i> ⁷⁶	•		•		•					•		•	•	•									
Ki <i>et al.</i> ⁵⁰	•		•						•														
Kuzmanović <i>et al.</i> ⁷⁷						•				•		•	•	•									
Al-Khazrajy and Boxall ⁷⁸			•		•					•	•	•	•	•		•							
Busch <i>et al.</i> ⁷⁹						•				•		•	•	•									
CIS WGGW ⁴³	•							•	•	•	•	•	•	•		•	•	•	•	•	•	•	•
Clarke <i>et al.</i> ⁵⁴	•				•		•			•				•									•
Donnachie <i>et al.</i> ⁶¹						•				•		•	•	•									
Guo <i>et al.</i> ⁸⁰		•			•					•	•	•	•	•	•	•							
Mansour <i>et al.</i> ⁸¹		•			•					•	•	•	•	•	•	•	•						
Sangion and Gramatica ⁸²										•		•	•	•									

262 Notes: a. Exposure assessment not included as part of this study. b. Hazard assessment not included as part of this study. Conc = concentration; SW = surface
263 water; GW = groundwater.

263 The application of Measured Environmental Concentration (MECs) as a measure of environmental
264 exposure was found to be a common approach (n = 17). MEC values from surface water were utilised
265 in 13 of the included studies and four studies applied MEC values from groundwater. The use of MECs
266 for groundwater are discussed further in Section 4.1.

267 Calculating Predicted Environmental Concentrations (PEC) was also a common approach with a total
268 14 studies using this approach to characterise exposure. Only one study calculated PECs specifically
269 for groundwater. Sales or usage data was frequently used to estimate PECs (11 studies). It can be
270 difficult to obtain the data required on sales, usage and environmental releases of ECs relevant to
271 groundwater exposure. For example, it would be an enormous task to obtain usage data for all
272 pharmaceutical compounds in the United Kingdom, and this type of information is not currently
273 systematically reported or accessible.⁸⁰ Two studies did not use sales or usage data to calculate the PEC:
274 one study⁷⁵ used wastewater effluent data to calculate PECs in surface water and the other study⁶⁶ on
275 veterinary pharmaceuticals used estimates of the number of animals.

276 Five of the studies that calculated the PEC in surface water were for human pharmaceuticals using the
277 European Medical Agency (EMA) guidelines⁸³. Two of the studies calculated the PEC in surface water
278 for veterinary pharmaceuticals using another EMA guideline⁸⁴. The PEC in surface water was calculated
279 using a European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC) Targeted Risk
280 Assessment (TRA) Tool by the three WFD studies⁵⁸⁻⁶⁰, the first in 2011⁵⁹ and then in 2015^{58,60}. The
281 latter also applied the FOCUS model in addition to the PEC calculation of pharmaceuticals in
282 wastewater.^{58,60} PECs were therefore calculated mostly for surface waters using established methods for
283 specific contaminant groups such as human or veterinary pharmaceuticals, or pesticides. In addition,
284 none of these studies used MECs to validate the PECs. Only one study⁷³ compared PEC and MECs and
285 found a poor relationship that was not scrutinised as part of the study.

286 Five studies used neither MEC or PEC for characterisation of exposure in the water environment. Three
287 of the studies⁶²⁻⁶⁴, used sales or usage data as an indicator of exposure in surface water. Each of the
288 studies were for veterinary pharmaceuticals and all involved the same author which may bias the results.

289 Overall only four studies^{43,50,52,54} predicted concentrations in groundwater or the likelihood of a
290 contaminant entering groundwater (see Supplementary Information C). Two studies used neither the
291 MEC or PEC approach and instead used leaching indicators: one study used the extended Attenuation
292 Factor (AF)⁵⁰ and another used the Groundwater Ubiquity Score (GUS index)⁵². The Groundwater
293 Watch List (GWWL) study⁴¹ proposed a leaching indicator scoring system based on chemical properties
294 and also incorporated MECs of ECs where they are available. The fourth study⁵⁴ used a model which
295 incorporated the AF and an application rate for biosolids to calculate PEC. Two of the studies focused
296 on pesticides^{50,52} and two studies^{43,54} covered ECs; one of which considered only one source (spreading
297 of biosolids)⁵⁴ and the second^{43,42} considered all ECs but this methodology has yet to be implemented at
298 the EU level and will be done on a voluntary basis.

299 The review highlighted that there is no trend in the methodologies for predicting concentrations of ECs
300 in groundwater or the likelihood of a contaminant entering groundwater. Therefore, rationales and the
301 limitations of these methodologies have been examined in further detail in Sections 4.1 and 4.2.

302 **4.1 Measured Environmental Concentrations (MEC)**

303 The application of MECs as a measure of environmental exposure has been demonstrated as a common
304 approach. It is a reliable representation of environmental exposure because the results represent actual
305 occurrence rather than estimates. However, there is a dependency on availability of monitoring data
306 which there may be a lack of for ECs. The EU WFD surface water prioritisation studies⁵⁸⁻⁶⁰ used
307 monitoring data where possible and modelling was undertaken for substances where an insufficient
308 quantity of monitoring data was available.⁵⁸ The USEPA^{29,67} similarly used environmental release data
309 and production data in the absence of MECs.

310 There are further considerations when the MEC approach is used, which include how to summarise the
311 data to be representative of the risk, and dealing with results below the LOD. Studies that used MECs
312 commonly incorporated both the frequency of detection of a compound, as well as the magnitude of its
313 concentration. Frequency addresses regularity of occurrence and the magnitude addresses intensity.
314 Concentrations could change over time which is difficult to capture⁵⁷ with the paucity of monitoring
315 data of ECs in groundwater in particular. The magnitude can be represented by the mean concentration,
316 the maximum or both.^{29,43,67} Most studies opted for the conservative approach of using the maximum
317 concentration (e.g. ^{10,70,73,77}). One study¹⁰ calculated the 95-percentile concentration of the sites to help
318 account for spatial variations. Only a few studies reported whether the MECs were influenced by point
319 sources such as wastewater treatment plants.

320 The studies differed in their approaches to dealing with values below the LOD. Several studies^{10,29,67}
321 truncated the dataset by excluding data below the LOD. Alternatively, one study⁷¹ left censored data by
322 replacement with the highest LOD value to take a more conservative approach. Caution should be taken
323 when dealing with MEC datasets with a high proportion of censored results, (i.e. < LOD) and
324 substitution methods, such as replacing non-detects with half the detection limit or zero, are not
325 recommended for calculation summary statistics (mean, median, quartiles). Statistical approaches such
326 as Maximum Likelihood Estimation (MLE) and Regression on Order Statistics (ROS) should be used
327 for estimating summary statistics.⁸⁴

328 It can be argued that excluding less than values is appropriate in the context of prioritisation, because
329 highly toxic chemicals that are frequently monitored but not often detected would result in a high risk,
330 when in fact any risk is more likely to be low.¹⁰ Conversely, disregarding MECs below the LOD could
331 possibly lead to an underestimation of the real risk if the ECs are hazardous but present at low levels
332 that could still be harmful to human health or the environment.

333 4.2 Exposure assessments for the likelihood of a contaminant to enter groundwater

334 4.2.1 Physico-chemical properties of ECs

335 The likelihood of a contaminant entering groundwater is considered higher if the contaminants' sorption
336 coefficient is low (indicating higher mobility) and persistence is high,⁸⁶ where persistence is defined as
337 the long-term exposure to an organism and is based on the half-life data.⁸⁷ Two studies^{41,52} focussed on
338 physico-chemical properties of ECs in their prioritisation.

339 The GWWL methodology⁴³ used a simple scoring system to indicate the likelihood of an EC reaching
340 groundwater. The REACH guidelines⁸⁷ provide indicators for persistent chemicals based on the halflife
341 in water >40 days (P) and >120 days indicating very persistent (vP) chemicals. The GWWL scoring
342 methodology for persistence was consistent with this and the Pesticide Properties Database (PPDB).⁸⁶

343 The GWWL methodology⁴³ proposed two indicators for mobility: $\log K_{oc}$ and $\log K_{ow}$. K_{oc} is the ratio of
344 the concentration of the contaminant that is sorbed to the organic carbon in the soil versus that which is
345 in solution.⁸⁸ The K_{ow} relates to the equilibrium partitioning of a contaminant between octanol and water
346 phases and is a surrogate for K_{oc} .⁸⁸ The GWWL methodology⁴³ gave higher risk scores for contaminants
347 less likely to sorb to the soil and therefore more likely to reach groundwater. While this criterion is
348 reasonable, the actual thresholds for the scoring in the methodology were neither explained nor justified.

349 The second study⁵² to focus on physico-chemical properties of ECs utilised the GUS index as an
350 indicator of environmental exposure to prioritise pesticides in South African groundwater. The GUS
351 index applies the K_{oc} and the half-life in soil⁵² and is widely used as an indicator of pesticide
352 mobility^{52,89}. They scored the pesticides with a GUS index of greater than 2.8 as highly mobile and
353 those with a value of less than 1.8 as non-leachers. Again, this is consistent with the REACH
354 guidelines⁸⁷ and the PPDB⁸⁶.

355 Using EC physico-chemical properties has merits as a screening tool for determining the likelihood of
356 an EC entering groundwater relative to other substances. However, there are also some obvious
357 drawbacks and uncertainties. It is difficult to predict the half-life and mobility of chemicals in
358 environmental field conditions, and they are dependent on variables including temperature, pH,
359 moisture, microbial populations and the soil type.^{86,90,91} Many authors^{92,93} have illustrated that chemicals
360 can be neutral or ionic depending on the soil pH and therefore their sorption capacity changes, and as a
361 result $\log K_{ow}$ may not be the most universally appropriate indicator.⁹⁴ Therefore, these methods are
362 more appropriate for non-polar organic chemicals, such as pesticides, where they contribute to a better
363 understanding of environmental fate and transport dynamics.⁹⁵ However they may not be appropriate
364 for non-polar ECs such as pharmaceuticals. Other studies have demonstrated a relationship between the
365 frequency of detection of pesticides and the GUS index, but also revealed that some presumed "non-
366 leaching" pesticides were actually detected in groundwater.⁹¹

367 Neither study tested the sensitivity of their results for these leachability indicators. Also, the results were
368 not verified by comparing the higher risk ECs with environmental data. These findings highlight that
369 approaches that only use physico-chemical properties of ECs as leachability indicators can potentially
370 mask or overestimate risks.

371 **4.2.2 Pathway to groundwater**

372 The vulnerability of groundwater to ECs is also dependent on many other factors including the
373 physicochemical properties of the soil and subsoil, the depth to groundwater and the recharge rate. The
374 AF (attenuation factor) is a simple index for ranking the leaching potential of pesticides and has been
375 frequently used in the past (e.g. ⁹⁵⁻⁹⁷). It was proposed in 1985⁵³ and is based on the half-life of the
376 pesticide, depth of the soil, bulk density, organic carbon, sorption coefficient and recharge rate.

377 The extended AF was utilised in one study⁵⁰ as part of a geospatial leaching tool for agrochemicals in
378 the USA. It accounted for the properties of Volatile Organic Compounds (VOCs) as well as pesticides,
379 by adding in the dimensionless Henry's constant (Kh) (air partition coefficient) and the diffusion
380 coefficient in soil. They used digital mapping of annual pesticide usage, soil properties and recharge to
381 examine the variation in potential leaching loads over a regional scale, and found it could distinguish
382 between areas of high and low susceptibility.

383 The second study⁵⁴ to apply the AF adapted a model for estimating PECs of pesticides in groundwater
384 for sixteen organic ECs detected in biosolids in Ireland. It calculated the leaching quantity as a function
385 of the AF and the application rate, the fraction intercepted by the crop and the thickness of the
386 unsaturated zone.

387 Neither study attempted to verify their methods by comparing results with actual groundwater
388 monitoring data. However, both studies^{50,54} did undertake a sensitivity analysis on the parameters and
389 found that K_{oc} and soil organic carbon were the most sensitive. In research into uncertainty analysis on
390 the AF method it was found that a small variation in the retardation factor (i.e. retention in the mobile
391 phase) could lead to different prioritisation classifications⁹⁸. The authors of the study using the
392 geospatial leaching tool⁵⁰ did acknowledge issues with the spatial and temporal map resolution. They
393 emphasised the trade-off between the data availability and the accuracy of the predictions and concluded
394 that their tool should only be used as a first step rapid and large-scale tool.⁵⁰ Approaches that incorporate
395 geographical information at a regional scale are now common practice (e.g. ⁹⁹⁻¹⁰³). Soil and groundwater
396 models are considered to be less appropriate for generic risk assessments for determining monitoring
397 programmes, as they can be too site specific.⁴⁴

398 A better understanding of the fate and transport of ECs in groundwater is required to inform risk
399 assessments, particularly their sorption and degradation.^{16,104} In recent years, there have been several
400 studies on the leaching potential of certain ECs, predominantly pharmaceuticals. For example, one
401 research study¹⁰⁴ examined the irrigation of soil columns and irrigated fields to assess the leaching

402 potential of acidic pharmaceuticals (ibuprofen, gemfibrozil, naproxen, ketoprofen, and diclofenac). At
403 higher pH values (>8) these compounds tended to take their ionised more soluble state which increased
404 their leaching abilities. However, no contamination of these pharmaceuticals in groundwater was
405 observed.¹⁰⁴ Another study¹⁰⁵ found differing sorption of PPCPs with triclosan and octylphenol being
406 moderately to strongly sorbed and negligible for carbamazepine. These authors demonstrated that
407 microbial activity and soil organic carbon were important for the degradation. The relative persistence
408 (28 to 39 days in unsterilized soils) and poor sorption of carbamazepine indicated that it is more likely
409 to leach to groundwater.¹⁰⁵ Other studies have also highlighted carbamazepine as being relatively
410 persistent and being prone to accumulate in soil.^{104,106,107} Detections of carbamazepine have been
411 observed in groundwater possibly as a result of the long-time available for downward migration due to
412 its high persistence.¹⁰⁴ Consequently there are many factors that may determine the presence of ECs in
413 groundwater and research into their persistence and sorption capabilities in environmental conditions is
414 still on-going. In addition, the lag time between environmental releases and the potential occurrence in
415 groundwater needs to be considered when attempting to verify prioritisation approaches.

416 **4.3 Outlook for exposure assessments for the likelihood of an EC entering groundwater** The
417 review found that the use of MECs is the preferred method for surface water and groundwater and more
418 reliable more for representing environmental exposure especially for groundwaters where it is difficult
419 to estimate the concentrations. Careful consideration is required when summarising data and dealing
420 with results below the LOD so that the data is representative of the risk of exposure. Data should be
421 summarised using statistically sound methods that are appropriate for the particular MEC dataset.

422 However, there is still insufficient monitoring data for most ECs and therefore estimates will still be
423 required.⁴² It is important therefore to generate a comprehensive list of ECs that have the potential to
424 occur in groundwater that may not yet be measured. This initial list could be vast and therefore should
425 be drawn up with the involvement of stakeholders.⁵⁹ There is still a dependence on the availability of
426 sales and usage data and data on the physico-chemical properties of ECs which is not as accessible as
427 other contaminant groups that are regulated such as pesticides.⁴²

428 Unlike for surface water there are no standard methods for calculating PECs for ECs in groundwater.
429 Only four studies were found to estimate the likelihood of an EC reaching groundwater or calculate
430 PECs which all used slightly different approaches. Approaches that only use physico-chemical
431 properties of ECs as leachability indicators can potentially mask or overestimate risks. Nevertheless, it
432 should be acknowledged that these simple approaches can be useful as first steps in the development of
433 monitoring programmes.⁵² However, from the studies reviewed it is not clear that they are treated as
434 such, due to the lack of sensitivity testing of results, verification with monitoring data or other
435 prioritisation studies and no mechanisms to update the methods with new data and understanding as
436 they become available.

437 Depending on physico-chemical properties of the EC does not reflect real environmental
438 conditions.^{84,90,91} In theory the two studies which incorporate the vulnerability of groundwater to
439 contamination from ECs should provide a more accurate representation of the risk of exposure.
440 However, similar to the approaches that use only physico-chemical properties of ECs, these methods
441 that incorporate the pathway still do not verify the prioritised results with monitoring data. There is an
442 inherent difficulty in doing this because the fate and transport of ECs may vary in different
443 environmental conditions and there is also a lag time to consider for groundwater due to varying
444 contaminant velocities through in the unsaturated zone. Also, care needs to be taken in the application
445 of tools developed for certain organic contaminants to other ECs, such as acidic pharmaceuticals which
446 may have very different mobility. Therefore, it is not possible to determine a completely unified
447 approach for determining exposure of ECs in groundwater but it is clear that there is a requirement to
448 incorporate new data and research on the sorption and degradation of ECs into any prioritisation
449 approach to improve predictions of exposure.

450 **5 Approaches for hazard assessment of ECs in groundwater**

451 This section provides a review of the methods used to characterise the hazard in each of the studies
452 included (Table 1). Twenty-five of the studies dealt with aquatic ecology as the receptor and sixteen for
453 human health. The approaches for assessing the hazard were grouped into two different types: firstly
454 those that used dose-response data and secondly that used classification data in the scoring system
455 approach.

456 **5.1 Dose-response data hazard assessments**

457 Of the studies that used dose-response data (n = 29), 20 used ecotoxicological data for three trophic
458 levels. Only two studies used mammalian toxicology data. Most of the studies reported using
459 experimental data from existing databases and literature and eight studies reported using
460 Quantitative Structure-Activity-Relationship (QSAR) data, which estimate the effects based on
461 structural properties of chemical compounds.¹⁰⁸

462 Ten studies used human dosage information as indicators of toxicity in humans, applying either the
463 Acceptable Daily Dose (ADI) (n = 6) as “*a measure of the amount of a specific substance in drinking*
464 *water that can be ingested daily over a lifetime without an appreciable health risk*”¹⁰⁹ or Therapeutic
465 Dose TD (n = 4) as the amount required to have the desired therapeutic effect. Only one study⁶⁶, applied
466 the therapeutic dose as a surrogate for toxicity data for aquatic ecology.

467 For the nine studies that incorporated groundwater, six used dose-response data. Human health was the
468 main receptor considered in these studies (n = 7) and only two considered aquatic ecology. The
469 bioavailability of an EC was generally not accounted for in these approaches, with the exception of one
470 study¹⁰ in this review which corrected the MEC for bioavailability. The lack of experimental

471 ecotoxicological data is considered the norm rather than the exception for many compounds.^{10,59} Recent
472 studies have highlighted that ECs require further toxicological data to be developed.^{10,55}

473 Several authors^{10,64,72} emphasised that chronic toxicology data sets are the most appropriate to use for
474 hazard assessments of ECs because the main concern relates to long-term exposure at relatively low
475 concentrations. Availability of data for chronic exposure remains low and therefore a reliance on acute
476 data was also highlighted by the same authors.^{10,64,61} A conservative approach proposed was to use the
477 lowest available PNEC, even if it is an acute endpoint.¹⁰ Certain health effects cannot be predicted using
478 acute or chronic dose-response tests.¹⁰ In one study⁵⁷, different toxicological endpoints for ECs known
479 to have estrogenic activity were used instead. This was the only study where this approach was
480 undertaken, but few details were provided.

481 **5.2 Classification data hazard assessments**

482 Eleven studies used classification data to characterise the hazard. Only two of these studies did not use
483 any dose-repose toxicity data in addition to the classification data. A number of studies incorporated
484 specific long-term health effects data for carcinogenicity (n = 9), mutagenicity (n = 9), teratogenicity (n
485 = 7), endocrine disruption (n = 6) and neurotoxicity (n = 3). Several studies also used persistence (n =
486 6) and bioaccumulation (n = 11) properties of the EC for prioritising the hazard.

487 Due the focus on human health in groundwater studies (7 of the 9 studies), the long-term health effects
488 classification approach was used in five of the studies. Only two studies that incorporated groundwater
489 used persistence or bioaccumulation as part of the hazard assessment. The advantages and
490 disadvantages of these approaches for hazard assessment in groundwater are discussed in the following
491 sections.

492 **5.2.1 Classification based on the persistence, bioaccumulation, and toxicity (PBT) assessment**

493 It has been suggested that the reason persistence has often been disregarded in prioritisation approaches
494 is that it is less relevant when there is a continuous discharge into rivers.^{57,77} However, for groundwaters
495 persistence is an important factor because more persistent ECs are likely to leach and accumulate in
496 groundwaters. The widespread detection of atrazine in groundwater today, several decades after it
497 ceased being used, is an example of the importance of chemical persistence in groundwater.²⁸ The PBT
498 assessment is considered useful for circumstances where the risks are difficult to quantify⁴⁴, which
499 makes it relevant to the groundwater context. The PBT approach is also used in the United Kingdom to
500 determine if substances are defined as hazardous in groundwater under the WFD and GWDD.¹¹⁰

501 For the assessment of persistence, REACH guidelines⁸⁷ definitions of the vP and P was used in the EU
502 WFD prioritisation studies⁵⁸⁻⁶⁰. The USA study⁵⁷ used a higher threshold of >180 to indicate persistent
503 chemicals. The BIOWIN programme for organic substances can be used to estimate the
504 biodegradability in environmental conditions.^{59,72} This was used in the EU WFD prioritisation
505 studies⁵⁸⁶⁰ and a Spanish study⁷². For the assessment of toxicity in the PBT approach the studies

506 generally used the classification under the REACH guidelines⁸⁷ or dose-response data, sometimes
507 alongside the risk ratio approach.

508 For the assessment of bioaccumulation, European guidance recommends that the bioconcentration
509 factor (BCF) for aquatic species is used, mostly from fish.^{59,87} The BCF is the ratio of a substance's
510 concentration in an organism and its quantity freely dissolved in ambient water.⁵⁹ This approach was
511 used in only three of the studies in this review, with differing thresholds for risk. The logK_{ow} is also
512 used to estimate a contaminants potential to bioaccumulate within an organism.⁶⁴ Two studies^{59,64} used
513 a threshold of a logK_{ow} > 4.5 to indicate a risk of bioaccumulation. This threshold originates from EMA
514 guidelines^{66,87} which required pharmaceuticals to be screened for further assessment. The USA study⁵⁷
515 used a similar threshold of logK_{ow} >5, and another study⁶⁹ used a threshold of 3, to indicate
516 bioaccumulation potential. One of the studies⁶⁴ did highlight the weaknesses of using logK_{ow} as an
517 indicator of bioaccumulation for pharmaceuticals as they are mostly polar and ionisable. For ECs such
518 as pharmaceuticals there has been little research on their bioaccumulation potential in biota.¹¹¹

519 **5.2.2 Classification based on long-term health effects**

520 Studies that used long-term health effects data for hazard assessment did so to assess the risk to human
521 health. One study⁵² scored ECs based on their potential to cause carcinogenic, teratogenic, mutagenic,
522 endocrine disruption and neurotoxic effects. Its authors suggested that this method is more appropriate
523 due to chronic exposure and endpoints such as carcinogenicity and endocrine disruption being realistic
524 hazards. Another advantage of this method is that MECs or PECs are not necessarily required. Another
525 study⁶⁹ prioritised the hazard using seven categories for human health effects, which incorporated
526 doseresponse ecotoxicology data for PPCPs and endocrine disrupting compounds for human health.

527 Both of these studies^{52,69} used intermediate scores when there was no data to ensure that they were
528 deemed higher risk than an EC classified as having no effect. It was emphasised by one of the studies⁶⁹,
529 that an important issue with these prioritisation approaches was lack of data for many of the health
530 effects categories. The study found that 62% of data in the carcinogenicity category and 82% in the
531 fertility impairment were missing, which resulted in a high uncertainty of results. The lack of an official
532 definition of endocrine disrupting compounds also makes scoring ECs based on this criterion inherently
533 difficult.⁶⁰

534 Weightings used to assign importance to different criteria are subjective.⁷¹ It therefore is a complex task
535 and the easiest option can be to assign equal weightings to all different categories.^{69,72} For example, a
536 study⁶⁹ gave equal weight to health effects categories, whereas others such as^{52,63}, weighted the scores
537 to give more importance to carcinogenicity and mutagenicity. Expert judgement is used to assign
538 weightings and can allow decision makers to set priorities; even the importance of different receptors,
539 i.e. human health or aquatic ecology.^{69,71}

540 **5.3 Outlook for approaches for hazard assessment of ECs in groundwater**

541 The review highlighted that the use of dose-response toxicity data to characterise the hazard of ECs was
542 the most common approach and only two studies did not use it. However, there is a paucity of toxicity
543 data for many ECs and data is often not accessible due to protection from ‘commercial-in-confidence’.⁴²

544 The main concern of ECs in groundwater relates to long-term exposure at relatively low concentrations.
545 In this context there are some issues with the prioritisation approaches reviewed. In particular the
546 reliance on acute toxicological data rather than chronic toxicological data could misrepresent the risk.
547 Only few studies considered chronic exposure endpoints such as carcinogenicity and endocrine
548 disruption (approximately 28%) but there was a higher portion of the groundwater studies (55%) that
549 did. There are also significant gaps in this type of toxicological classification data which can create high
550 uncertainty in the hazard assessment results.

551 Unlike surface waters the main source of ECs is not through rapid continuous discharges and therefore
552 the accumulation of ECs is an important consideration. Only two groundwater studies used persistence
553 or bioaccumulation as part of the hazard assessment. There is no standard approach for the assessment
554 of bioaccumulation, and for ECs such as pharmaceuticals the evidence in the literature on their
555 bioaccumulation potential in biota is still limited but is a growing research area.¹¹²⁻¹¹⁴

556 When using the classification approach based on long-term health effects, weightings are generally used
557 to assign importance to a criterion. These weightings are subjective and therefore sensitivity testing
558 should be built into any prioritisation approach to understand the uncertainties and the robustness of the
559 results.

560 It is clear that greater accessibility and generation of toxicity data for ECs is required and that there are
561 many uncertainties in the hazard assessment approaches. Future approaches for assessment of the
562 hazard of ECs in groundwater should incorporate flexibility to update prioritisation results as new data
563 becomes available, and research on the most appropriated approaches for groundwater are determined
564 and refined.

565 **6 Comparison of prioritisation approaches**

566 Two subsets of prioritisation studies (ECs and pharmaceuticals) were analysed, to compare the
567 chemicals on the prioritised lists to provide an indication of the impact of using different approaches on
568 the results. Only substances that were classified as ECs by the NORMAN network (and not ‘classical’
569 contaminants) were included in the analysis. The selection process for studies and substances included
570 are described in Supplementary Information A.

571 The first subset of studies included five studies that prioritised ECs (see Supplementary Information D).
572 There were 37 ECs included in this analysis. Only three ECs were prioritised in more than one of the

573 studies: diazinon, triclosan and estrone. Diazinon is a pesticide and is regulated in some countries so is
574 not typically considered an emerging contaminant.

575 The second subset of studies included six studies that prioritised human pharmaceuticals (see
576 Supplementary Information D). There were 64 pharmaceuticals included in this analysis. The studies
577 had been carried out in several different countries: United Kingdom⁸⁰, two from France^{73,64}, Iraq⁷⁸,
578 Lebanon⁸¹ and China¹¹. Three pharmaceuticals were prioritised in five of the six studies: carbamazepine,
579 diclofenac and ibuprofen. Three others were prioritised in four studies: amoxicillin, ciprofloxacin and
580 clarithromycin. Overall a total of 20 of the 64 pharmaceuticals were prioritised in more than one study
581 (31%).

582 The comparison of prioritisation results for the two subsets of studies, has shown that there were more
583 similarities between the prioritisation studies for pharmaceuticals. This can be attributed to the
584 similarities between the initial lists of chemicals. The initial lists of pharmaceutical studies were
585 generated from similar sources such as prescription and usage data but in several different countries.
586 All the studies used the PEC and dose-response data. One study⁷³ was an exception, its authors used the
587 MECs and it did have fewer pharmaceuticals in common with the other studies.

588 Three of the pharmaceutical studies also compared their ranking outcomes to results from other
589 publications. In the first it was found that carbamazepine and ibuprofen were the most prioritised
590 pharmaceuticals among the eight studies they examined.⁸¹ They also highlighted that six (out of 26) of
591 their prioritised pharmaceuticals were not prioritised elsewhere.⁸¹ The second⁷⁸ found that amoxicillin,
592 which they ranked highest, also ranked highly in earlier studies in the United Kingdom and Korea (^{58,64}).
593 The third study¹¹ compared its priority list to a previous review of prioritisation results for
594 pharmaceuticals.¹¹⁴ Nine of the high priority pharmaceuticals had been identified in the previous
595 review.¹¹ The study's authors also examined previous prioritisation research in France⁶⁴ and
596 Switzerland¹¹⁶ and found that there were similarities to their own list, despite the use of different
597 methodologies.¹¹

598 The two EC studies that had more than one prioritised EC (triclosan and estrone) in common employed
599 quite different methodologies. The initial lists of ECs were generated by different means and from
600 different sources. The studies also had significantly different numbers of substances on their initial lists
601 ranging from 34 to 2024 ECs (including classical chemicals prior to filtering), and were carried out in
602 Europe and the USA. It is not surprising that the prioritisation results from EC studies reviewed here
603 are variable. These studies can include a complex mixture of types of contaminants with different
604 sources and pathways to the aqueous environment. The substances (Table F of the Supplementary
605 Information) included pesticides applied to agricultural land that reaches water via runoff or infiltration
606 through the soil (such as cyanazine or diazinon), pharmaceuticals and industrial fragrances (such as
607 galoxalide) which probably enter the environment via wastewater, as well as plasticisers (bisphenol A)
608 and flame-retardants (perfluorooctanoic acid).

609 One of the other studies⁵⁷ in this review applied two hazard assessment approaches for ECs in surface
610 water: a scoring system that incorporated persistence and bioaccumulation scores (PBT approach); and
611 the risk ratio. The ECs identified by each approach were markedly different. The risk ratio approach
612 yielded the lowest number (n = 41) compared with the PBT approach which used the risk ratio for
613 toxicity (n = 60). Nearly half of the ECs identified by the first approach had relatively low half-lives
614 (<60 days).

615 It is apparent that comparing the prioritisation results to determine any commonalities is unsatisfactory
616 without first analysing the initial lists (which unfortunately have rarely been provided) and assessing
617 the substance type. Although most studies are therefore not directly comparable, it has been helpful to
618 provide an indication of the parallels between the priority lists for pharmaceuticals.⁸¹ Given the
619 uncertainties with developing any prioritisation approach,⁶¹ it is useful to make an attempt to evaluate
620 the results through comparison with other similar prioritisation approaches. This has been undertaken
621 in some studies (e.g. ^{11,78,81}), but there was still a lack of analysis of the initial lists and differences
622 between prioritisation methodologies. There is also merit in carrying out more than one prioritisation
623 using different methods, or sensitivity testing results to understand the uncertainty surrounding the
624 prioritised lists. This would minimise the risk of prioritising ECs that are lower risk or missing ones that
625 could be higher risk in the groundwater environment e.g. persistent chemicals.

626 **7 Framework for prioritisation approaches and future outlook**

627 This review has demonstrated that a common approach for prioritising ECs in groundwater has not been
628 developed and verified. Two main issues were revealed by the review. Firstly, the groundwater
629 exposure tools and models examined in this study all had merit, however they need to be confirmed
630 using actual groundwater quality data⁵⁰, whilst still considering the lag times. The level of detail
631 required to provide realistic estimates of loading or concentrations in groundwater therefore remains
632 unknown. For example, soil organic carbon was found to be important for sorption of ECs (e.g. ^{50,54})
633 but some of the simpler approaches depend on the physico-chemical properties of the EC which often
634 do not reflect real environmental conditions.^{84,90,91} There will always be trade-offs between complexity,
635 accuracy and data requirements.¹¹⁷ The use of MECs is the preferred method for surface water and
636 groundwater when adequate data is available. It is a more reliable method for representing
637 environmental exposure especially for groundwaters where it is difficult to predict concentrations.
638 Careful consideration is required when summarising MEC data and dealing with results below the LOD
639 so that the data is representative of the risk of exposure.

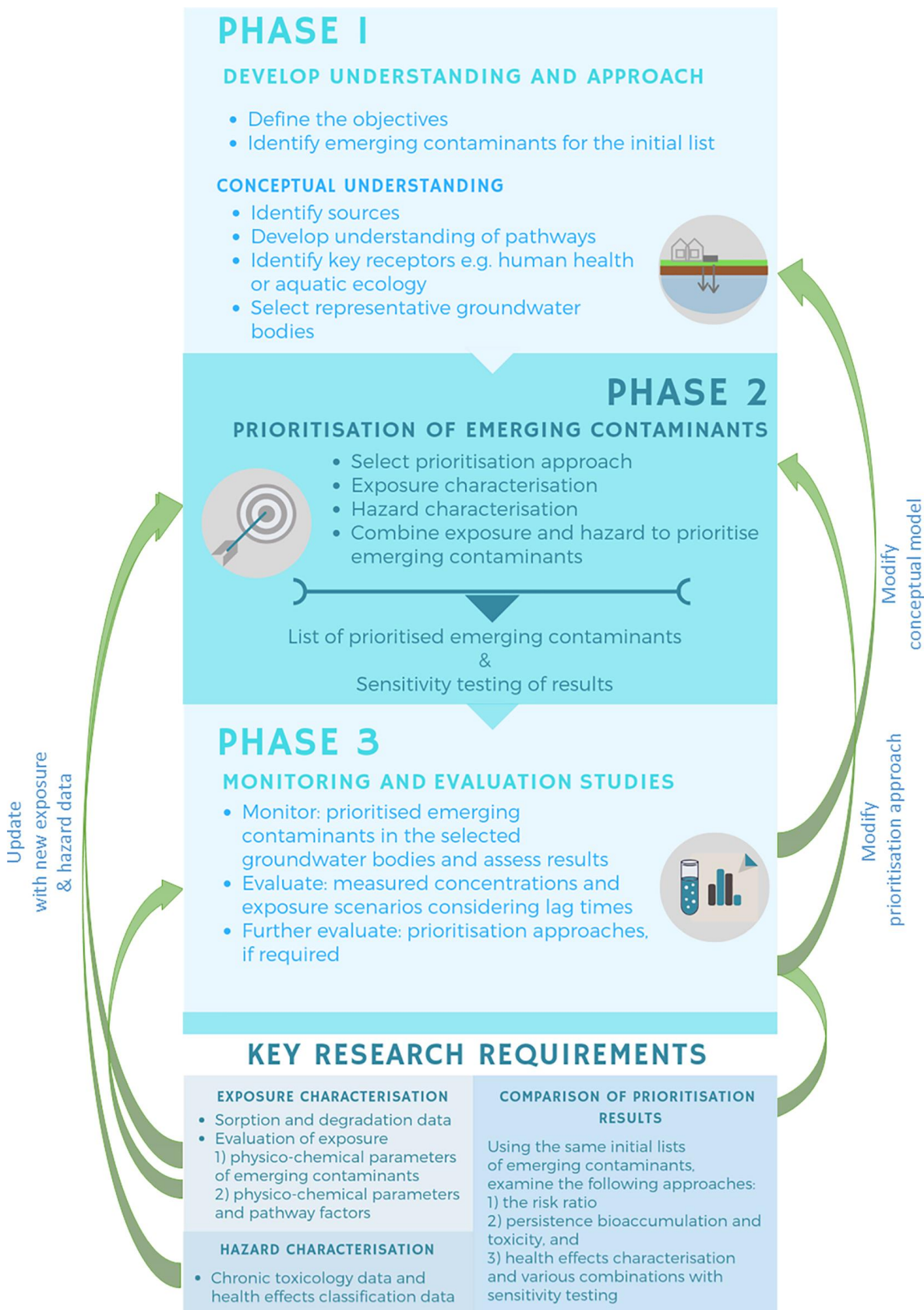
640 Secondly, the review has highlighted the paucity of toxicity data and physico-chemical data for ECs
641 and issues with access to available data. Due to the risk of ECs accumulating and the potential chronic
642 effects, the long-term health effects classification data will be important to incorporate.^{52,81} However,

643 there are still significant gaps in chronic dose-response toxicological data and long-term health effects
644 classification data for ECs.

645 Lastly this review has indicated that no prioritisation approach is perfect, and it has not demonstrated
646 that one approach is superior to any other, but has highlighted some important advantages and
647 disadvantages. There is an indication that the most comprehensive prioritisation approaches are ones
648 that use a combination of approaches, for example, the risk ratio and scoring methods for hazard
649 assessment (e.g. ^{57,81}). It has also been shown that the persistence of the EC is important in the
650 groundwater context with the example of carbamazepine accumulation in soil and leaching to
651 groundwater.¹⁰⁴ The dose-response hazard classification can omit highly persistent ECs⁵⁷ and the
652 possibility of bioaccumulation of ECs.

653 The uncertainties with the results of any prioritisation approach require greater effort in scrutinising the
654 results, sensitivity test them and comparing them with other similar studies. Further research is required
655 to analyse the advantages of different prioritisation approaches to optimise the best one for ECs in
656 groundwater. Prioritisation of ECs should not be a static process and improvements in the approaches
657 should be sought and incorporated. Future prioritisation approaches should incorporate flexibility to
658 update prioritisation results as new data becomes available.

659 Therefore, a broad framework is proposed, that facilitates the incorporation of research on the
660 occurrence, hazards and prioritisation of ECs and an evaluation process. A phased approach adapted for
661 groundwater from Maruya *et al.*⁷⁵ is proposed as outlined in Figure 3. The figure also highlights the key
662 priority research areas of: 1) sorption and degradation of ECs in the environment; 2) evaluation of
663 different exposure characterisation approaches to confirm the level of detail required to provide
664 estimates of loading or concentrations in groundwater; 3) the chronic toxicity of ECs and health
665 classification data; 4) comparison of prioritisations approaches for groundwater. For example, the effect
666 of combining prioritisation approaches such as the risk ratio and scoring approaches could be
667 researched, as well as the influence of including persistence and bioaccumulation as factors.



669 **Figure 3 A phased framework for prioritisation of ECs in groundwater**
 670 **incorporating key**

670 **research requirements**

671 This framework and future research will hopefully enable the prioritisation methodologies to be
672 improved by feeding back results from the evaluations of the prioritisation approach and allowing the
673 incorporation of new data. This phased approach could also be verified with existing monitoring data
674 for ECs in groundwater.

675 The first phase involves developing the conceptual understanding and approach. The first step is to
676 define the objectives of the prioritisation approach. This ought to be done by both scientists and policy
677 makers or decision makers,² determining the priorities (human health, aquatic ecology or both). In
678 addition, it would be important to consider the scale of occurrence to be considered. The WFD, for
679 example, would require that both human health and ecology are considered and the occurrence to be
680 examined at a groundwater body scale.^{42,43}

681 The next step would be to develop the initial conceptual model for the source, pathway and receptors
682 of ECs in groundwater. Given the wide variety of ECs and difference in source types, it is considered
683 that a pragmatic approach would be to develop scenarios that focus on certain sources and groups of
684 substances that can then be tested.^{42,75} Such scenarios for groundwater could be designed around the
685 current understanding of the sources of ECs (see Figure 1¹⁷). One exemplary scenario could relate to
686 the ECs found in wastewater discharges from septic tanks and other private treatments works which
687 discharge to groundwater. It would also be important to monitor in areas with high and low groundwater
688 vulnerability to be representative of the risk spectrum⁴³ and allow different groundwater vulnerability
689 settings to be tested.

690 The second phase involves the actual prioritisation process. A prioritisation approach that is appropriate
691 for groundwater and the identified receptors needs to be selected. An initial priority list of ECs to be
692 monitored can be developed based on the characterisation of environmental exposure and hazard. The
693 results of the prioritisation of ECs should be sensitivity tested to understand the level of uncertainty
694 around the data used and any scores or weightings. Carrying out more than one prioritisation approach
695 using the same initial list and a further analysis of the resulting priority lists would help to ensure that
696 results are robust and that the decision makers are informed of the uncertainties that require
697 consideration.

698 The third phase involves monitoring the prioritised ECs in groundwater and verifying the conceptual
699 models and exposure characterisation by relating the MECs to the exposure scenario.⁷⁵ The monitoring
700 can then be adapted as needed based on the monitoring results and evaluation studies (see Figure 3).⁷⁵
701 The lag times between environmental release and occurrence in groundwater needs to be reflected. This
702 evaluation step can also be used to adapt the prioritisation approach if required and reassess
703 prioritisation results. Additional feedback loops are proposed to incorporate new physico-chemical data
704 and hazard classification and toxicity data.

705 The framework addresses the problem of the lack of knowledge on occurrence and fate of ECs, and
706 uncertainties surrounding prioritisation results. The prioritisation process needs to be dynamic and
707 responsive as new information becomes available, for example, through the proposed voluntary
708 European GWWL process, refinements can also be made to the conceptual models and subsequent
709 priority lists. The framework will ultimately enable further groundwater monitoring data to be gathered
710 for ECs that pose the highest risk to groundwater receptors, while paving the way for an optimised
711 approach for prioritising ECs in groundwater.

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715 **9 Supporting Information**

716 The Supporting Information (SI) available includes: Systematic review search protocol (A); Search
717 strings used for database and web searches (B); Study characteristics from systematic review (C); and
718 results tables of results from comparison of prioritization studies (D).

719

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