

Journal Pre-proof



Emerging Contaminants: A One Health Perspective

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1 Emerging Contaminants: A One Health Perspective

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193 **GRAPHICAL ABSTRACT**



194

195 **PUBLIC SUMMARY**

- 196 • The current global development systems perpetuate the continuous creation
197 and release of new contaminants, posing ongoing environmental challenges.
- 198 • Pollution remains a significant global threat, impacting human and
199 environmental health at various levels, necessitating urgent action.
- 200 • Green production practices and sustainable environmental management play a
201 pivotal role in controlling pollution and promoting environmental
202 sustainability.
- 203 • This review provides an in-depth exploration of the sources and impacts of
204 emerging contaminants on planetary health, with a specific emphasis on
205 pollution control and prevention strategies.
- 206 • Adopting a One Health approach through interdisciplinary collaboration is
207 crucial for effectively addressing pollution and its complex impacts.

208

209

210 **ABSTRACT**

211 Environmental pollution is escalating due to rapid global development that often
212 prioritizes human needs over planetary health. Despite global efforts to mitigate legacy
213 pollutants, the continuous introduction of new substances remains a major threat to both
214 human and ecosystem health. In response, global initiatives are focusing on risk
215 assessment and regulation of emerging contaminants, as demonstrated by the
216 establishment of the UN's Intergovernmental Science-Policy Panel on Chemicals,
217 Waste, and Pollution Prevention. This review identifies the sources and impacts of
218 emerging contaminants on planetary health, emphasizing the importance of adopting a
219 One Health approach. Strategies for monitoring and addressing these pollutants are
220 discussed, underscoring the need for robust and socially equitable environmental
221 policies at both regional and international levels. Urgent actions are needed to transition
222 towards sustainable pollution management practices to safeguard our planet for future
223 generations.

224 INTRODUCTION

225 Before the Industrial Revolution, naturally occurring pathogens, including bacteria,
226 fungi, and viruses, were the primary contaminants of concern, presenting threats to both
227 human and ecosystem health (Wang et al., 2020b). However, industrialization brought
228 about significant changes in pollution patterns, introducing new contaminants into the
229 environment such as heavy metals, industrial chemicals, and particulate matter. With
230 the onset of the Anthropocene, humans have increasingly depleted natural resources
231 and developed new chemical molecules, or novel entities, in pursuit of global
232 development, resulting in waste streams transgressing planetary boundaries and
233 disrupting natural ecosystems (Matlin et al., 2022; Steffen et al., 2015), and inducing
234 changes in agricultural practices, which led to the evolution of wild-type pathogens
235 (Lebarbenchon et al., 2008). Various geogenic chemicals, encompassing metal(loid)s
236 and other hazardous substances, are consistently discharged into the environment
237 through diverse anthropogenic activities like mining, mineral processing, energy
238 production, construction, and agriculture (Naidu et al., 2021).

239 Beyond geogenic chemicals, the production of synthetic chemicals has surged
240 since the mid-20th century, marking what is often referred to as the second chemical
241 revolution, i.e., unprecedented development and use of novel synthetic chemicals
242 (Calvo-Flores et al., 2018). This surge is evidenced by the rapid growth of the Chemical
243 Abstract Service Registry, which grew from 20 million in 2002 to over 204 million by
244 2023, suggesting an addition of nearly 15,000 new chemicals daily (Escher et al., 2020).

245 Moreover, there has been a significant rise in efforts to genetically modify
246 microorganisms (Then, 2020; Hanlon and Sewalt, 2021; Rafeeq et al., 2023). While
247 synthetic chemicals and genetically engineered microorganisms have contributed
248 positively to human well-being by facilitating the development of new drugs and
249 advanced materials and enhancing agricultural productivity, concerns have been raised
250 over their risks to public health and the environment. Persson et al. (Persson et al., 2022)
251 recently highlighted that humanity has exceeded the planetary boundary, or safe
252 operating space, for anthropogenic chemicals, as the rate of chemical production
253 outpaces the rate of hazard assessments and the establishment of regulatory measures.
254 Similarly, Bernhardt et al. (Bernhardt et al., 2017) argued that synthetic chemicals are
255 agents of global change.

256 Emerging contaminants (ECs), also known as contaminants of emerging concern
257 (CECs), are newly identified synthetic or naturally occurring substances detected in the
258 environment, such as chemicals or biological agents, that are potentially harmful to
259 humans and the environment, or for which the risks have only recently become apparent.
260 They may include pharmaceuticals and personal care products (PPCPs), per- and poly-
261 fluoroalkyl substances (PFAS), emerging pathogens, cyanotoxins and other natural
262 toxins, pesticides, industrial chemicals, micro/nano plastics, nanomaterials, antibiotic
263 resistance genes, and other exogenous substances that are found in the environment but
264 are not yet well understood in terms of their impacts on humans and natural ecosystems
265 (Sauvé and Desrosiers 2014; Puri et al. 2023; Cousins et al., 2022). These contaminants

266 can enter the environment through various pathways, such as industrial discharge,
267 agricultural runoff, and improper waste disposal, leading to air, water, soil, and food
268 contamination. They can become part of complex mixtures of chemical pollutants and
269 biological hazards (Escher et al. 2020). Furthermore, these ECs have the potential to
270 undergo additional transformation and long-range transport, creating unforeseen and
271 uncharacterized chemicals and causing chemical pollution in areas distant from the
272 source (Kelly et al. 2007).

273 Pollution continues to pose a significant global threat, resulting in millions of
274 premature deaths annually (Fuller et al., 2022; Landrigan et al., 2018b) and widespread
275 environmental degradation (Naidu et al., 2021). Concurrently, thousands of species are
276 facing extinction (Framba 2019). These alarming challenges underscore the pressing
277 need for comprehensive strategies to address the interconnected environmental and
278 human health issues (Wu et al., 2023). Adopting a One Health perspective recognizes
279 the interconnectedness of human, animal, and environmental health, emphasizing the
280 need for collaborative efforts to address EC issues. By leveraging expertise from
281 various fields such as medicine, veterinary science, environmental science, and public
282 health, integrated approaches will reduce risks linked to ECs and enhance the well-
283 being of all organisms. While focusing on ECs is crucial, dealing with existing
284 pollutants is equally important. Innovative approaches such as green chemistry,
285 machine learning, and interdisciplinary cooperation are essential to overcome these

286 challenges. Moreover, educational reforms are crucial to preparing future generations
287 to effectively address environmental and health crises (Gao, 2024).

288 In this review, we provide a holistic perspective on ECs, which are recognized as
289 significant threats to human health and the sustainability of ecosystems. Through the
290 One Health approach lens, we acknowledge the intricate connections between the
291 health of people, animals, plants, and our shared environment. Our focus encompasses
292 the production, utilization, and dissemination of ECs in everyday life, emphasizing their
293 potential adverse effects, whether encountered individually or with other pollutants.
294 These effects span various environments, impacting human health and the well-being
295 of animals, plants, and microorganisms. We investigate methods for detecting and
296 analyzing ECs, critically assess regulatory frameworks and policies, and propose
297 innovative solutions to reduce their detrimental impacts on human and environmental
298 health. By adopting the One Health approach, we underscore the necessity for a
299 collaborative, multisectoral, and transdisciplinary response to effectively address
300 challenges posed by ECs and to promote a sustainable and healthy future for all forms
301 of life.

302

303 HISTORICAL PERSPECTIVE OF EMERGING CONTAMINANTS

304 Since the mid-20th century, the global socio-economic landscape has undergone a
305 profound transformation, marked by a surge in industrial activity and technological

306 advancement. This period has seen a dramatic rise in the extraction and utilization of
307 natural resources, particularly critical minerals and petrochemicals, which are
308 indispensable for expanding industrial sectors and the broader modernization process.
309 The repercussions of this intensified resource exploitation have been far-reaching,
310 leading to modifications in geochemical cycles and the distribution of metals (Borch et
311 al., 2010). Moreover, this era has been characterized by the synthesis, use, and release
312 of novel chemical compounds, many of which persist in the environment and have the
313 potential to accumulate biologically, thus emerging as new environmental contaminants
314 (Gibson et al., 2023a).

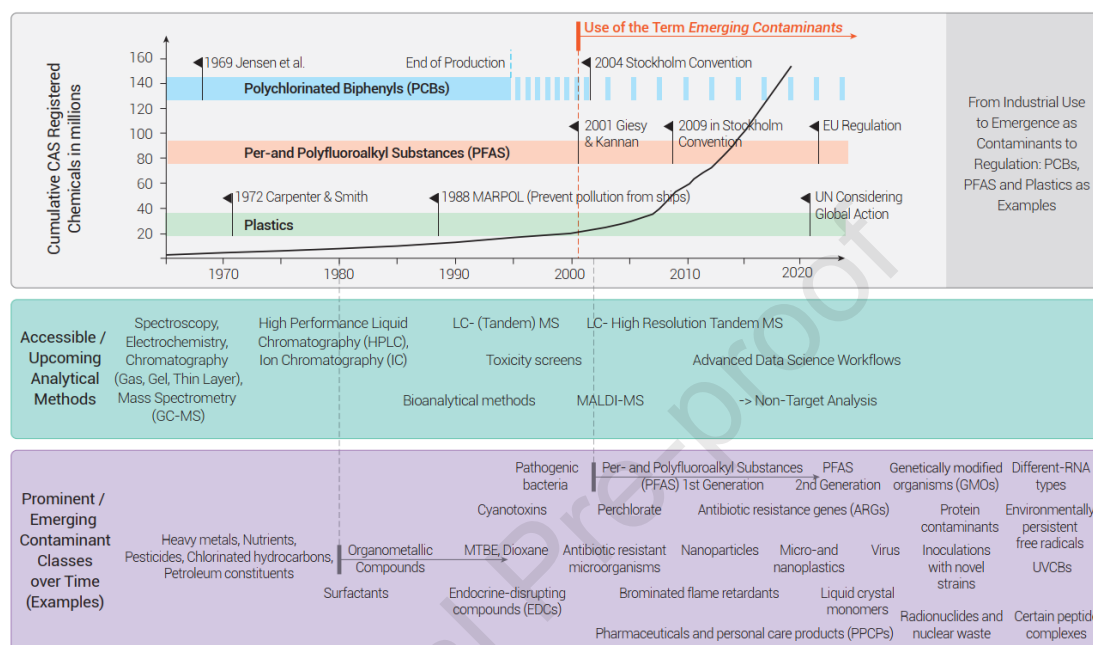
315 The toxicity of metal(loid)s, such as lead, mercury, cadmium, arsenic, cobalt, and
316 chromium, as well as organic pollutants like dichlorodiphenyltrichloroethane (DDT)
317 and polychlorinated biphenyls (PCBs), has long been recognized (Naidu et al., 2021).
318 Some of these pollutants have been banned or had limits imposed on their use due to
319 their adverse environmental and health effects, prompting efforts to regulate their
320 concentrations in water, soils, and other environmental media (Gibson et al., 2023b).
321 Whereas much is understood about legacy contaminants, ongoing advances in
322 analytical technology and toxicology continue to reveal new risks to human health and
323 the environment posed by ECs, enabling a better understanding of the sources,
324 persistence, bioaccumulation potential, mobility, and toxicity of such contaminants.

325 The increasing focus on environmental pollution has led to the identification of
326 substances that have transitioned from being celebrated as beneficial chemicals to

327 contaminants of significant concern. Examples of such evolving contaminants include
328 plastics and their byproducts, atrazine, triphenyl phosphate, tungsten, per- and
329 polyfluoroalkyl substances (PFAS), chlorofluorocarbons, neonicotinoids, glyphosate,
330 and many others (**Table 1**). This evolution is attributed to improved detection
331 capabilities for inorganic and organic contaminants at trace levels and a better
332 understanding of their wider ecosystem and health effects (**Figure 1**).

333 In recent years, significant attention has been devoted to addressing a wide array
334 of emerging contaminants, which nowadays extends beyond newly introduced
335 substances to include contaminants of emerging concern, which have been present for
336 some time but have recently garnered attention due to their potential impacts. As of
337 February 2024, the Environmental Protection Agency's (EPA) Toxic Substances
338 Control Act (TSCA) Chemical Substance Inventory contains 86,741 potentially
339 hazardous chemicals, with 42,293 currently commercially active (Us Epa, 2015).
340 Additionally, the NORMAN Network consortium has identified over 700 of the most
341 discussed ECs (NORMAN, 2024). Further, Wang et al. **Wang et al. (2020c)** identified
342 that over 350,000 chemicals and chemical mixtures have been registered for
343 commercial use around the world. The continuous expansion of these inventories is
344 expected due to the ongoing discovery of new substances and increased scrutiny of
345 existing ones. Herein, a One Health approach is particularly relevant to the assessment
346 and management of ECs (**Brack et al., 2022; Ogunseitan, 2022, 2023**). In the

347 subsequent sections, we will focus on prominent emerging contaminants categorized
 348 based on their current attention and potential concern (**Table 1**).
 349



350
 351 Figure 1. The evolution of emerging contaminants in relation to the advances in the
 352 detection and tracking of potentially toxic chemicals in the environment or biological
 353 systems, even at trace levels. Since the early 2000s the term “Emerging Contaminants”
 354 has been used to describe the discovery of new pollutant classes. Polychlorinated
 355 biphenyls (PCBs), perfluorinated substances (PFAS), and plastics exemplify
 356 problematic substances that were in use for decades (grey bars), but emerged as
 357 contaminants (pins) and were regulated and discontinued (faded-out shadow) with
 358 different lag times. Arrows in the lower panel indicate emerging contaminants that
 359 originated as replacements for other pollutants.

360

361 Table 1. List of prominent emerging contaminants categorized based on their current
 362 attention and potential concern

Categories	Secondary categories	Examples of emerging contaminants	
Organic emerging contaminants	Endocrine-disrupting compounds (EDCs)	17-Alpha-ethinylestradiol (EE2) (Union, 2015), 17-Beta-estradiol (E2) (Union, 2015), Estrone (E1) (Union, 2015) Steroid hormones (Canasius K. Kanangire, 2023), Phthalate acid esters (PAEs) , Bisphenols (Weiss et al., 2023)	
	Food and feed additives	2,6-Ditert-butyl-4-methylphenol (Union, 2015)	
	Persistent organic pollutants (POPs)	Brominated flame retardants (China, 2023), Polychlorinated biphenyls (PCBs) (Weiss et al., 2023) Weiss et al., 2023), Polycyclic aromatic hydrocarbons (PAHs) (Murnyak et al., 2011), Dichlorodiphenyltrichloroethane (DDT) (Sauvé and Desrosiers, 2014), Perfluorinated chemicals (Sauvé and Desrosiers, 2014), Polybrominated diphenyl ethers (PBDEs) (Naidu and Wong, 2013; Petrovic et al., 2004) Per- and Polyfluoroalkyl Substances (PFAS) (Agency, 2023)	
	Pharmaceuticals and personal care products (PPCPs)	Disinfectants: Disinfection (Byproducts, Chlorate, Formaldehyde) (Agency, 2023), Pentachlorophenol and its salts and esters (China, 2023), Diclofenac (Union, 2015); Cosmetics: 2-Ethylhexyl 4-methoxycinnamate (Union, 2015); Analgesics and anti-inflammatories (Rathi et al., 2021): Flumequine, Trimethoprim, Ketorolac, Pain reliever, Illicit drugs (Hernandez-Maldonado and Blaney, 2015), Pharmaceutically active compounds (PhACs) (Murnyak et al., 2011) Antibiotics (China, 2023) , Macrolide antibiotics (Union, 2015)	
	Surfactants (López-Mahía et al., 2005)		
	Organic solvents/plastic additives	Hexachlorobutadiene (China, 2023), Dechlorane plus (both cis and trans isomers), Dichloromethane (China, 2023), Chloroform (China, 2023), Nonylphenols (China, 2023)	
	Pesticides (Canasius K. Kanangire, 2023) and Herbicides	Methiocarb (Union, 2015), Neonicotinoids (Union, 2015), Oxadiazon (Union, 2015), Tri-allate (Union, 2015), Perchlorate (Agency, 2023), Dicofol (China, 2023)	
	Cyanotoxins (Agency, 2023)	Microcystin(s) (Agency, 2023) , Cylindrospermopsin (Agency, 2023) , Anatoxin(s) (Agency, 2023) , Saxitoxin(s) (Agency, 2023)	
	Inorganic emerging contaminants	Metal	Strontium, Manganese, Tungsten, Lithium (Agency, 2023)
		Nanoparticles (Canasius K. Kanangire, 2023)	
Radionuclides and nuclear waste (Ahearne, 1997)		H-3, Sr-90, Cs-137, Tc-99, I-129, Pu-239, Pu-240, (233, 234, 235, 238) U, Am-241	
Emerging biological contaminants	Pathogenic bacteria (Agency, 2023)		
	Antibiotic-resistant microorganisms (Rysz and Alvarez, 2004)		
	Antibiotic resistance genes (ARGs) (Rysz and Alvarez, 2004)		
	Virus (Fuhrman, 1999)		
	Protein contaminants (Johnson et al., 2006; Nichols et al., 2009; Saunders et al., 2009a, b)		
	Genetically Modified Organisms (GMOs) Inoculations with novel strains		

	Different types of RNA (e.g., RNAi and other Biologicals)
	Certain peptide complexes
Other emerging contaminants	Micro- and nanoplastics (Thompson et al., 2004)
	Liquid crystal monomers (Su et al., 2019b)
	Environmentally persistent free radicals
	Substances of unknown or variable composition, complex reaction products, or biological materials

363 The table categorizes emerging contaminants into three groups: those currently in the
 364 spotlight (highlighted in blue), those with potential concern but less current attention
 365 (highlighted in purple), and contaminants of the past that are now emerging with
 366 renewed concern. Some emerging contaminants have been identified for control by
 367 various environmental regulatory agencies, including the Ministry of Ecology and
 368 Environment of the People's Republic of China (China, 2023), the European Union
 369 (Union, 2015), and the United States Environmental Protection Agency (Agency,
 370 2023). It is important to note that this table provides only a selection of examples for
 371 each category, and there are many more emerging contaminants within each group.

372

373 PRODUCTION, USE, AND ENVIRONMENTAL RELEASE OF 374 EMERGING CONTAMINANTS

375 **Production and use of emerging contaminants**

376 Over the last century, global population growth, fueled by industrialization and
 377 urbanization, has spurred increased demand for consumer goods. Consequently,
 378 industries producing these goods, such as pharmaceuticals, household products, and
 379 plastics, have expanded significantly (Johnson and Bell, 2022). The extensive use and
 380 improper disposal of these products have led to their omnipresence in the natural
 381 environment, causing continuous contamination with potentially harmful chemicals
 382 from diverse sources (Tong et al., 2022). Taking plastics as an example, their global
 383 production has surged to 460 million tons (Mt) in 2019 from 234 Mt in 2000, resulting
 384 in a doubling of plastic waste generation over the past two decades (OECD, 2022). This

385 increase in plastic production and consumption has contributed to the proliferation of
386 micro/nano plastics in various ecosystems. While microplastics only account for 12%
387 of plastic waste in the natural environment, they are of significant concern because of
388 their potential long-term impacts on ecosystems and organisms (Kumar et al., 2020;
389 OECD, 2022). Over time, larger plastic particles can break down into micro/nano
390 plastics through mechanical action and biological fragmentation (including microbial
391 degradation and grind by metazoa during ingestion), leading to the continuous
392 accumulation of these particles (MacLeod et al., 2021; Martínez-Orgániz et al., 2023;
393 Zhao et al., 2023a). This pollution is considered irreversible due to the lasting
394 environmental impact long after the elimination of plastic emission sources (MacLeod
395 et al., 2021).

396 Pharmaceuticals and personal care products (PPCPs) represent one of the largest groups
397 of ECs, encompassing a wide array of compounds with diverse chemical and physical
398 properties. These substances are commonly used in daily life for various purposes,
399 including human and animal healthcare. With over 50,000 different types of PPCPs
400 currently produced and approximately 30 million metric tons used globally, the
401 prevalence of these compounds may be increasing annually (Liu et al., 2020).

402 Pharmaceuticals as the main components of PPCPs include numerous types of drugs
403 and their metabolites, such as antibiotics (for both humans and livestock), hormones,
404 non-steroidal anti-inflammatory drugs, anticancer drugs, antiepileptics,
405 antidepressants, and β -blockers (Wilkinson et al., 2022). Among these biologically

406 active substances, antibiotics have emerged as the most commonly reported PPCPs over
407 the past few decades (Berglund et al., 2023; Manaia et al., 2022), with the global
408 consumption rate increasing from 9.8 to 14.3 defined daily doses per 1000 population
409 per day between 2000 and 2018 (Browne et al., 2021). The increasing prevalence of
410 associated antibiotic-resistant genes (ARGs) is a well-documented health concern and
411 is now recognized as a prominent global threat to public health (Larsson and Flach,
412 2022). Besides pharmaceuticals, PPCPs also encompass various chemicals in body
413 lotions, disinfectants, eye care, hair care, handwash, insect repellent, lipsticks,
414 moisturizers, fragrances, shampoo, soaps, sunscreen creams, and plasticizers used in
415 product packaging and lining (Chakraborty et al., 2023) and PFAS compounds added
416 to cosmetics (Whitehead et al., 2021).

417 Over time, advancements in knowledge and analytical methods have led to the detection
418 of risks associated with various chemicals. During the recent COVID-19 pandemic,
419 64.7% of respondents never disinfect their hands using sanitizers before the COVID-
420 19 outbreak, but 91.0% disinfect their hands at least twice per day after the COVID-19
421 outbreak (Guo et al., 2021). Therefore, particular attention has been paid to biocides
422 found in disinfectants (Lu and Guo, 2021). With the implementation of advanced
423 analytical instruments such as high-resolution mass spectrometry (HRMS) and artificial
424 intelligence (AI) techniques, the potential risks posed by a broader range of PPCPs are
425 expected to be uncovered PPCPs in the future. After production and application, PPCPs
426 are primarily introduced to the environment directly or indirectly through the discharge

427 of raw sewage or treated effluents of various quality from wastewater treatment, animal
428 husbandry, animal manure, or municipal treatment plant sludge as fertilizer, and landfill
429 leachate (Carpenter and Helbling, 2018; Carpenter et al., 2019; Hu et al., 2023). In fact,
430 the presence of PPCPs in surface water has become an indicator of an urbanizing water
431 cycle (Brooks, 2014).

432 Engineered nanoparticles (ENPs), one of the most typical ECs, were included in the list
433 of ECs by EPA in 2010 (Li et al., 2022d). ENPs such as carbon NPs (De Volder et al.,
434 2013), TiO₂ NPs (Weir et al., 2012), and hydroxyapatite (Sadat-Shojai et al., 2010) are
435 widely incorporated in a diverse range of consumable goods, including commercial
436 cosmetics, sporting goods, sunscreen, and toothpaste. In terms of global production,
437 SiO₂ NP and TiO₂ NP were the largest, followed by AlO_x NP, CeO₂ NP, FeO_x NP, and
438 ZnO NP, carbon nanotubes (CNTs) (100-1000 t/a in 2010) and AgO NPs (55 t/a in 2010)
439 (Piccinno et al., 2012). The increasing application of ENPs in consumer products has
440 caused their increased occurrence in the natural ecosystems (Bathi et al., 2021).

441

442 **Pathways for environmental release of emerging contaminants**

443 To better understand and address ECs and their harmful impacts, it is crucial to
444 thoroughly analyze the characteristics of these substances, how they are released into
445 the environment, and how they can affect living organisms. For example, a number of
446 big research questions were identified by Boxall et al. (2012) to understand the risks of
447 PPCPs in the environment, and more recently, a synthesis of progress toward answering

448 most of these questions was provided, within which a number of timely research needs
449 remain unanswered (Boxall and Brooks, 2024). We can work towards a more
450 sustainable approach by using innovative technologies to identify these contaminants,
451 eliminate their sources, and apply green chemistry principles for designing safer
452 chemicals (Erythropel et al., 2018). This comprehensive understanding of problematic
453 substances and their pathways of exposure is essential for developing effective
454 strategies (Naidu et al., 2016; Tran et al., 2018). Figure 2 illustrates the release processes
455 and potential pathways of emerging pollutants in different environmental
456 compartments.

457 In both urban and rural areas, sources of ECs can be categorized as point source
458 discharges from wastewater treatment plants (WWTPs), which include effluents from
459 domestic, industrial, and hospital sectors and non-point sources such as stormwater
460 runoff from agriculture (including livestock and aquaculture) and urban areas (Aguilar-
461 Aguilar et al., 2023; du Plessis, 2022; Morin-Crini et al., 2022; Parida et al., 2021).
462 Additionally, ECs may originate from household products and leachates from landfills,
463 among other sources. Conventional WWTPs were not explicitly designed to remove
464 ECs effectively. As a result, many contaminants have been reported in treated effluents
465 at concentrations typically ranging from ng/L to $\mu\text{g/L}$ (Ramos et al., 2016; Subedi et al.,
466 2015; Tran et al., 2018). The continuous discharge of ECs in these effluents challenges
467 existing global chemical management approaches that identify chemicals as persistent
468 using cutoff values (Brooks et al., 2009) because effective exposure duration increases

469 when introduction rates from sewage or effluent discharge exceed the rate of
470 degradation (Ankley et al., 2007). Efficient treatment of wastewater containing various
471 chemical contaminants and pathogenic microorganisms remains a significant challenge
472 in environmental engineering (Majumder et al., 2021), particularly in low and middle-
473 income countries.

474 Food production has significantly increased in recent years to meet the growing global
475 demand. As a result, agricultural activities have become common contributors to
476 releasing emerging pollutants into the environment (Evans et al., 2019; Kumar et al.,
477 2020; Nguyen et al., 2023). This is often linked to the discharge of agrochemicals
478 (Morin-Crini et al., 2022), antibiotic residue from livestock wastes (Nguyen et al.,
479 2023), microplastic debris resulting from the extensive use of plastic mulching film
480 (Kumar et al., 2020), and pathogens introduced through the application of livestock
481 manure or WWTP biosolids as fertilizer (Buta et al., 2021). Without significant
482 alterations to existing practices, new pollutants produced by intensive farming are
483 expected to continue accumulating in soils, potentially polluting nearby water bodies
484 through surface runoff and infiltration (Morin-Crini et al., 2022). Additionally, there is
485 a risk for these pollutants to enter the atmosphere through agricultural spray drift or
486 volatilization following pesticide application (Wilkinson et al., 2017).

487 Beyond the discharge of effluents from WWTPs and agricultural activities, leachate
488 from landfills, where household wastes are deposited, constitutes a significant source
489 of emerging pollutants in terrestrial ecosystems (Figure 2) (Eggen et al., 2010; Naidu

490 et al., 2016; Qi et al., 2018; Qian et al., 2024; Rogers et al., 2021). PPCPs, endocrine-
491 disrupting chemicals, and ARGs have been identified in untreated landfill leachate at
492 concentrations ranging from ng/L to $\mu\text{g/L}$ (Qi et al., 2018; Yi et al., 2017), including at
493 levels (Chung et al., 2018) exceeding proposed predicted no effect concentrations for
494 development of antibiotic resistance (Bengtsson-Palme and Larsson, 2016). When
495 these potentially toxic leachates seep out or overflow into water bodies, they can
496 adversely affect aquatic organisms (Rogers et al., 2021). The construction industry is a
497 significant environmental concern as it generates various contaminants, including
498 construction and demolition waste, fly ash, plastic waste, and dust, during construction
499 (Hong et al., 2021; Zhong et al., 2022). These pollutants can potentially affect the living
500 conditions of nearby residents and construction workers (Kang et al., 2021). However,
501 the environmental fate of emerging pollutants associated with building sites remains
502 largely unknown, and the application of new building materials that are being
503 developed, such as engineered living materials (McBee et al., 2022), could also
504 exacerbate this problem.

505 Particulate contaminants, such as ultrafine particles, micro(nano)plastics, and ENPs,
506 may be released into the atmosphere through processes including volatilization, aerosol
507 formation, and diffusive exchange (Barroso et al., 2019; Enyoh et al., 2020). These
508 airborne pollutants could further be transported to surrounding or remote areas through
509 dry or wet deposition or wind events (Barroso et al., 2019; Yang et al., 2021). These
510 particles could also carry other PPCPs and move to a remote area. Fernandez et al

511 (Fernandez et al., 2021) found that polycyclic aromatic hydrocarbons (PAHs), PCBs,
512 and polybrominated diphenyl ethers are present in remote high-mountain European
513 lakes, indicating a long-range atmospheric movement of such pollutants from urban to
514 remote areas with the help of aerosol particles. Meteorological factors, including
515 temperature, precipitation, wind speed, and boundary layer mixing, play vital roles in
516 affecting the migration behaviour of airborne pollutants (Sridharan et al., 2021).
517 Atmospheric compartments, mainly consisting of outdoor and ambient air, atmospheric
518 fallout, and suspended or street/road dust, have become the transport medium of
519 airborne contaminants and a point source of emerging pollutants in terrestrial and
520 aquatic ecosystems (Mbachu et al., 2020; Yang et al., 2021).

521 Nanoparticles can be formed by anthropogenic activities such as combustion in
522 cooking, vehicles, thermal power plants, aircraft engines, chemical manufacturing, ore
523 refining, smelting, and welding (Jeevanandam et al., 2018). There are three potential
524 entry points for NPs into the environment over their lifespan: (i) during the manufacture
525 of raw materials and nano-enabled goods; (ii) during use; and (iii) after disposal of
526 items containing NPs (waste treatment) (Gottschalk et al., 2013). Lifecycle estimates
527 indicate that the majority of NP emissions occur during the use stage and after disposal
528 in landfills (Keller et al., 2013). However, emissions during manufacture account for
529 less than 2% of the total output (Gottschalk and Nowack, 2011). ENPs may be released
530 directly or indirectly into the environment via a built environmental system like
531 WWTPs or waste disposal facilities. As for direct ENP emission, ENPs can act as

532 fertilizers to remediate soil, control the release of plant growth-regulating substances,
533 detect pathogenic bacteria, and control plant diseases and pests. Potential secondary
534 emissions may occur through various pathways, including the discharge from WWTPs,
535 the utilization of biosolids as soil amendments, or leachates from landfill sites. These
536 engineered systems play a pivotal role in dictating the destiny of ENPs, influencing
537 whether they are discharged as effluent or incorporated into biosolids, and determining
538 their state (whether they remain bare, coated, or undergo chemical or physical
539 transformations) (Zuin et al., 2013). Sun et al (Sun et al., 2016b) reported that in the
540 European Union in 2014, the sinks of TiO₂ NP, ZnO NP, AgO NP, and CNTs were
541 mainly landfills (7000 t a⁻¹), sediments (7600 t a⁻¹), and soils (8400 t a⁻¹). The
542 predominant emission pathway of TiO₂ NP and ZnO occurs via wastewater and
543 ultimately accumulates in sewage. CNTs and AgO NPs are primarily discharged into
544 the environment during their manufacturing and application processes, where they are
545 subsequently deposited in landfill sites.

546

547



548

549 Figure 2. Schematic illustration of the multifaceted pathways of EC production,
 550 utilization, and environmental release. Sectors such as industries, agriculture,
 551 households, hospitals, and wastewater treatment plants all contribute to the distribution
 552 of these contaminants. From industrial processes to agricultural practices and everyday
 553 household activities to medical and treatment facilities to effluent discharges, these
 554 sources collectively disseminate ECs into the environment.

555

556 Additionally, concerns have been raised about the environmental and human health
 557 risks of emerging protein contaminants such as proteinaceous infectious particles
 558 (prions) and *Bacillus thuringiensis* (Bt) proteins (Saunders et al., 2008; Stanley et al.,
 559 1998). Prions are misfolded forms (PrP^{Sc}) of normal cellular prion proteins (PrP^{C}) that
 560 are capable of self-templating (thus their infectivity), and various prion strains can
 561 cause fatal neurodegenerative diseases in various hosts, such as Creutzfeldt–Jakob
 562 disease in humans, bovine spongiform encephalopathy in cattle, and chronic wasting

563 disease (CWD) in cervids. Take CWD prions as an example: Once released into the
564 environment, they can bind to soils and persist for years as contamination sources and
565 infect wildlife (Smith et al., 2011). Bt proteins are produced in genetically modified Bt
566 crops and are insecticidal, resulting in concerns over their ecotoxicity and
567 environmental residue levels (Clark et al., 2005; Liu et al., 2021). The prions and Bt
568 proteins may present unique challenges because their production and source are
569 associated with wildlife and agricultural crops (Saunders et al., 2008; Clark et al.,
570 2005). Therefore, their occurrence and distribution in the environment are often
571 associated with the population dynamics and migration of infected animals and the
572 production, cultivation, and distribution of Bt crops. Thus, prions can be magnified,
573 while Bt proteins can be continuously produced and released into the environment.

574 In summary, ECs could, directly and indirectly, enter the environment from various
575 sources, such as industrial and agricultural operations, mining and construction
576 activities, oil and chemical leaks, diffuse sources like stormwater drains, roads, and
577 parking areas, and wastewater treatment systems (Figure 2) (Pal et al., 2010; Tong et
578 al., 2022) and the use of a wide range of consumer products. Emerging contaminants in
579 soil or landfills can also seep into adjacent groundwater (Gogoi et al., 2018; Pradhan et
580 al., 2023). River networks and wind can transport these pollutants from residential,
581 industrial, and agricultural areas to remote regions and eventually into marine
582 environments (Tong et al., 2022). Understanding the environmental release processes

583 and transformation pathways of ECs is pivotal for evaluating their potential ecological
584 impacts and for developing efficient mitigation and remediation strategies.

585

586 ADVANCES IN THE DETECTION AND ANALYSIS OF EMERGING 587 CONTAMINANTS

588 The development of new analytical techniques and technologies has significantly
589 enhanced the detection and analysis of ECs. This progress has bolstered our capability
590 to extract, quantify, and detect ECs in environmental samples. Mass spectrometry (MS)
591 and bioanalytical techniques have been particularly effective in analyzing emerging
592 organic contaminants (Pérez-Fernández et al., 2017). Furthermore, electrochemical
593 detection methods, with a focus on green technology, have emerged to measure ECs,
594 especially pharmaceuticals (Hassan et al., 2022). These innovations have played a
595 crucial role in elucidating the sources, classification, fate, and transport of ECs and in
596 the development of treatment technologies for their removal (Shahid et al., 2021).

597

598 **Sampling and analytical methods**

599 *Advanced sampling and separation.* Recent global initiatives are reshaping the future
600 of analytical chemistry, focusing on sustainable technologies. This impact is
601 particularly evident in methodologies for sampling and sample preparation to detect
602 and characterize ECs. Among these advancements is the solid phase microextraction

603 (SPME) chemical biopsy approach, which offers a flexible format for high-throughput
604 quantification of ECs (Bojko et al., 2021). Enhanced by matrix-compatible thin film
605 coatings and balanced coverage phenomena, SPME effectively eliminates matrix
606 effects and extracts a wide range of compounds with diverse physicochemical
607 properties. It is effective not only with gas chromatography-mass spectrometry
608 (GC/MS) and liquid chromatography-mass spectrometry (LC-MS) but also with direct
609 MS coupling, showing versatility and effectiveness in analysis (Reyes-Garces et al.,
610 2017; Zhou and Pawliszyn, 2024; Zhou et al., 2023b). Extraction techniques for ECs
611 have evolved to enable on-site sampling using thin films, either through spot (Murtada
612 and Pawliszyn, 2022) or time-weighted average sampling methods (Ahmadi et al.,
613 2017). In-vivo sampling, employing a small needle format, allows for the direct
614 assessment of exposome effects in response to environmental pollution at the sampling
615 site (Yu et al., 2021). These designed probes conduct non-exhaustive sampling over
616 longer periods, accumulating sufficient analytes for sensitive detection via
617 chromatography or mass spectrometry. Additionally, a filter-incorporated needle-trap
618 device facilitates the simultaneous determination of free and particle-bound pollutants
619 in a single step when combined with solid-phase microextraction (SPME) and
620 measured directly with GC/MS. Portable GC-MS instruments enable gas sampling for
621 on-site analysis (Zeinali et al., 2022). These advancements promise to enhance
622 environmental protection efforts by generating large volumes of scientific data using
623 simple, cost-effective, and sustainable analytical instrumentation. Moreover, these tools

624 facilitate the untargeted characterization of samples, thereby aiding in the discovery of
625 new compounds, including ECs (Reyes-Garces et al. 2017, Yu et al. 2021)

626 Apart from mass spectrometric detection, chromatographic separation is also crucial in
627 analyzing ECs. Liquid chromatography (LC) or gas chromatography (GC) is typically
628 coupled to MS for analysis. However, very polar fractions are a problem for both. Being
629 nonvolatile, they cannot be analyzed by GC nor retained by the stationary phase of LC.

630 Alternative chromatographic separation methods are being explored to close this gap.
631 For example, a recent study combined supercritical fluid chromatography (SFC) with
632 HRMS to identify unknown disinfection by-products in drinking water (Nihemaiti et
633 al., 2023). Hydrophilic interaction chromatography (HILIC) is also commonly
634 employed in orthogonal analysis to analyze polar compounds. For example, HILIC-
635 HRMS was applied in disinfected water analysis, leading to the identification of a new
636 class of polar disinfection byproducts (DBPs) – halomethanesulfonic acids (Zahn et al.,
637 2016; Zahn et al., 2019). An alternative that has emerged in recent years is an extra
638 separation dimension (i.e., ion mobility spectrometry [IMS]) hyphenated to the
639 conventional GC- or LC-MS systems. IMS is a rapid gas-phase separation technique
640 that separates ions based on their size, shape, and charge. IMS is particularly useful for
641 the separation of isomeric analytes or coeluting matrix components. The collision cross
642 section (CCS) values provided by IMS analysis supplement the common identification
643 parameters like retention time and mass-to-charge ratio (m/z) for the screening and
644 structural elucidation of ECs. The inclusion of IMS in nontargeted analysis significantly

645 improves confidence in the elucidation of unknown chemical structures. For instance,
646 ion mobility-mass spectrometry (IM-MS) has been used to analyze ECs in human urine
647 samples (Belova et al., 2021). In another example, a nontargeted LC-IM-MS analysis
648 of emerging per- and polyfluoroalkyl substances in aqueous film-forming foams used
649 CCS to enhance confidence in identifying unknown chemical structures and improve
650 specificity in suspect screening (Luo et al., 2020).

651

652 *Advanced mass spectrometry.* Mass spectrometry (MS) is among the most applied
653 techniques for the analysis of ECs. High-resolution mass spectrometry (HRMS)
654 instruments, like time-of-flight (TOF) and Orbitrap mass spectrometers, offer high
655 mass accuracy and resolution that are critical for identifying ECs through structural
656 elucidation (see Table S1). More recently, HRMS has been applied in identifying
657 transformation products and metabolites of ECs (Tian et al., 2021), and in the non-
658 targeted analysis/suspect screening of ECs (Liu et al., 2021). HRMS has revealed many
659 new ECs in the environment and elucidated their transformation products and
660 metabolites. Compared with other analytical techniques, the capability to conduct
661 nontargeted analysis is an invaluable advantage of HRMS in ECs' analysis. HRMS
662 enables the integration of nontargeted analysis with bioassays and in chemico methods
663 to identify bioactive and toxic chemicals in a sample. This combined approach enables
664 the precise identification and broad capture of bioactive/toxic chemicals (Hollender et
665 al., 2017). For instance, an estrogen receptor α (Er α) protein affinity assay combined

666 with HRMS has been applied to identify Er α -active compounds in source and drinking
667 water samples from major rivers in China (Li et al., 2023). In combination with effect-
668 directed analyses, ultrahigh-resolution MS (i.e., Fourier transform ion cyclotron
669 resonance mass spectrometry) was adopted to identify the toxicity drivers of unknown
670 disinfection byproducts in chlorinated and chloraminated drinking waters (Dong et al.,
671 2023a). In addition to *in vitro* bioassays, *in chemico* methods based on key chemical
672 reactions (i.e., molecular initiating events) have also been applied to identify and
673 measure the toxicities of environmental samples (Yeung et al., 2023). The combination
674 of *in vitro* and *in chemico* assays with nontargeted chemical analysis represents a novel,
675 more effective approach to identifying the bioactive/toxic contaminants in our
676 environment (Prasse, 2021; Tian et al., 2023).

677

678 ***Other advanced analytical chemistry techniques.*** Nuclear magnetic resonance (NMR)
679 spectroscopy is an advanced method for characterizing the chemistry of environmental
680 samples (Simpson et al., 2011). NMR has several advantages for the discovery of
681 contaminants, potential transformation products, and characterizing the reactivity of
682 contaminants over other techniques. The primary advantage is that structural
683 elucidation can be performed without an authentic standard because the molecular
684 profile from different NMR experiments can be used for complete structural
685 elucidation. Another advantage is that NMR can leverage different nuclei to explore the
686 structure of different metals and organic contaminants and their interactions with

687 environmental and biological media. However, NMR is less sensitive than the
688 previously described MS techniques, which can result in higher sample needs for
689 characterization. NMR is also less accessible than other instruments, which has created
690 a barrier in the broader application of this powerful and versatile technique for
691 characterizing metals and contaminants and their impacts on both environmental and
692 human health.

693 Electron paramagnetic resonance (EPR) can be used to detect environmentally
694 persistent free radical (EPFR) signals without the need to capture reagents, unlike
695 common short-lived free radicals. However, the presence of particles or colloids
696 associated with EPFRs, along with the co-existence of paramagnetic components such
697 as transition metals in the matrixes and varying environmental conditions like humidity
698 and temperature, can significantly interfere with EPR detection (Li et al., 2014;
699 Simpson et al., 2011). The interference of components makes it impractical to separate
700 them, as they likely contribute to the formation of EPFRs. Additionally, the diverse
701 chemical structures of EPFRs pose a challenge to their identification. Researchers have
702 categorized EPFR types based on g values and bandwidth, referring to them as oxygen-
703 centered and/or carbon-centered. However, studies have shown that both parent
704 chemicals and their degradation byproducts contribute to EPFR formation, potentially
705 playing simultaneous roles (Yi et al., 2019). The reactivity of EPFRs varies with their
706 structures, yet attributing signals to specific structures or quantifying the contributions
707 of different structures remains elusive.

708

709 **Suspected-target and non-target screening approaches**

710 The number of anthropogenic chemicals has grown beyond our capacity to study them
711 using traditional environmental monitoring approaches that rely upon the development
712 of targeted analytical methods tailor-made to individual chemicals (Muir et al., 2023a).
713 This challenge drives the need to develop suspect and nontargeted screening (NTS)
714 methodologies to identify ECs in complex environmental and biological media (Juliane
715 and Lee, 2017). The past three decades have witnessed the development of a wide range
716 of HRMS instruments that are capable of resolving hundreds or even thousands of
717 chemical compounds (M) by measuring the mass-to-charge ratio (m/z) of their
718 corresponding (quasi)molecular ions (e.g., M^+ , $[M+H]^+$, and $[M-H]^-$) with sub-part per
719 million ($<1\text{ppm}$) accuracy. The following sections provide a brief primer on the
720 methodologies employed in the NTS of ECs.

721

722 ***Suspect screening.*** Modern HRMS can gather both m/z and CCS data for numerous
723 compounds within a sample. However, sorting through this data and differentiating
724 between environmental contaminants (ECs) and the matrix is akin to finding a needle
725 in a haystack. Comparison of experimentally obtained mass spectra with those
726 compiled in spectral libraries (e.g. the NIST Mass Spectral Library) has been a time-
727 honored approach to identifying an unknown (Holmes et al., 2006; McLafferty and
728 Turecek, 1993). One drawback of spectral library searching is the finite size of the

729 library, which may not contain (bio)transformation products, by-products, or
730 proprietary compounds whose authentic standards may not be readily available
731 (Böcker, 2017). Another challenge is the reproducibility of collision-induced
732 dissociation spectra, which vary between laboratories depending on the instrument and
733 experimental conditions. Suspected screening practitioners increasingly rely on
734 structure databases (e.g., PubChem, CompTox Chemicals Dashboard) (McEachran et
735 al., 2017), which are orders of magnitude larger than spectral libraries. Current suspect
736 screening methods involve the creation of a list of structures whose computed/predicted
737 properties are then compared with those obtained by experiment. However, the
738 database's structural form does not always match the chemical structure observed by
739 HRMS (McEachran et al., 2018). The experimental measurements are compiled using
740 a peak-picking algorithm, the choice of which may influence the reliability and
741 reproducibility of results (Schulze et al., 2023). The analyst is also cautioned that no
742 single instrumental method is capable of detecting all chemical compounds and that
743 each step of the analysis could remove compounds present in the sample (Black et al.,
744 2023; Hulleman et al., 2023). This is particularly relevant when a large suspect list,
745 consists of compounds with a wide range of properties. For example, an instrumental
746 method suitable for the analysis of anionic PFAS may not be appropriate for emerging
747 brominated flame retardants. Black *et al.* (Black et al., 2023) have highlighted the
748 urgent need to develop predictive methods to assess which compounds will be
749 detectable using a given set of experimental and instrumental conditions. The identity

750 of a compound cannot be confirmed by its mass alone. This is why *in silico* (i.e.
751 computer modeling) methods are essential to predicting the dissociation of compounds
752 on the suspect list, their chromatographic retention time (RT), and, CCS to assist in
753 differentiating similar compounds. The application of harmonized values, such as the
754 unified retention time index (RTI), is also utilized in several wide screening workflows
755 in Europe (Aalizadeh et al., 2021; Alygizakis et al., 2023). With the help of RTIs, the
756 number of false positives can be reduced in the first screening step from suspect
757 screening and nontarget screening workflows. Quantum chemical (Koopman and
758 Grimme, 2021) and machine-learning-based methods (Wang et al., 2021b) are capable
759 of predicting ion ratios but at greater computational cost. Chromatographic retention
760 times (RT) (Bouwmeester et al., 2019) and CCS (Zhang et al., 2023a) can also be
761 predicted using machine learning models.

762

763 ***Nontargeted screening.*** A disadvantage of suspect screening is the fact that it requires
764 prior knowledge of the occurrence of impurities and transformation products that are
765 often unknown. Consequently, these compounds are absent from structure libraries,
766 leaving the analyst with the unenviable task of answering the question, “What organic
767 compounds are present in the environment that should not be there?” without knowing
768 their structure(s) beforehand. Consequently, the analyst must identify the structures of
769 the compounds detected in an NTS experiment using first principles interpretation of
770 their mass spectra. However, this is currently impractical for all compounds detected,

771 which number in the thousands. Therefore, practitioners of NTS have developed a range
772 of experimental and computational strategies to prioritize mass spectra for structure
773 elucidation. Environmental risk assessment efforts have shown that >60% of
774 compounds with the potential to persist in the environment and bioaccumulate contain
775 the elements chlorine, bromine, or fluorine (Mueller et al., 2023). Their mass spectra
776 also display characteristics unique to the presence of halogens, and NTS strategies to
777 identify ECs have largely focused on halogenated compounds (Ieda and Hashimoto,
778 2023; Jobst et al., 2013; Koelmel et al., 2020; Léon et al., 2019; Steeves et al., 2024;
779 Zhang et al., 2019). Emerging PFAS are more challenging to recognize since ^{19}F is a
780 single stable isotope. However, a previous study has shown that isotopic ratios (viz.
781 $^{13}\text{C}/^{12}\text{C}$) can still be used to discover PFAS, which are characterized by having relatively
782 fewer carbon atoms than other non-fluorinated compounds with the same molecular
783 weight (Zhang et al., 2019). Recently, Zweigle *et al.* (Zweigle et al., 2023) have
784 exploited this characteristic to develop a novel approach to PFAS discovery that
785 involves plotting the mass defect normalised to the number of carbons (MD/C) vs. mass
786 normalised to the number of carbon atoms (m/C). Cl, Br, and F-containing compounds
787 can also be revealed using ion mobility because halogenated compounds are
788 characterised by relatively small CCS compared to their molecular weight (Foster et
789 al., 2022; MacNeil et al., 2022). However, the most common approach to the discovery
790 of unknown pollutants involves monitoring a fragment ion that is common to an entire
791 class of pollutants. Machine learning is increasingly being used to guide NTS. Methods

792 that predict a spectrum from a structure, such as CFM-ID (Competitive Fragmentation
793 Modelling) (Wang et al., 2021b) are becoming more mature. However, the reverse
794 problem of predicting a structure from a spectrum has yet to be solved. Boiko *et al.*
795 (Boiko et al., 2022) have recently reported on an automated tool that can assign
796 elemental compositions in an unbiased, unconstrained way. It is anticipated that further
797 growth in the areas of machine learning and artificial intelligence will eventually enable
798 true, unsupervised NTS (Xu et al., 2021).

799

800 **Advanced bioanalysis**

801 *Bioanalytical techniques.* While chemical analysis-based methodologies offer
802 significant advantages, such as low detection limits, excellent accuracy, and good
803 selectivity for monitoring ECs, the steady growth in the development of biosensors,
804 also known as bioanalytical tools (Neale et al., 2021) for environmental analysis cannot
805 be overlooked. This growth is largely attributable to their superior capabilities in rapid,
806 specific analysis and real-time monitoring. Biosensors, which are analytical devices
807 that combine a biological recognition element with a transducer (Saxena et al., 2021),
808 have been developed to detect various ECs. Detectable ECs include antibiotics (Zhou
809 et al., 2021), pesticides (Tahirbegi et al., 2017), bisphenol A (Gao et al., 2022b; Tsekeli
810 et al., 2021), and microplastics (Tang et al., 2023b). Biosensors effectively detect ECs
811 in environmental samples (Haigh-Flórez et al., 2014) as well as in foodstuffs and
812 biological samples (Hejji et al., 2023; Prossner et al., 2022; Sanli et al., 2020; Sarkar et

813 al., 2023), particularly within an effects-directed analysis framework (Neale et al.,
814 2023).

815 Recent advancements in biosensor technology have seen the introduction of novel
816 biological recognition elements, such as aptamers, in sensor development. Aptamer-
817 based biosensors, or aptasensors, have emerged as robust and powerful analytical tools
818 for the detection of ECs. This is largely because of their high specificity for small
819 molecules, low fabrication cost, design flexibility, and high stability. For example,
820 specific aptamers have been developed to detect chloramphenicol in honey and
821 enrofloxacin in sewage water (Dong et al., 2022; Zhou et al., 2022). The possibility of
822 incorporating advanced engineered nanomaterials, such as carbon-based nanomaterials,
823 metal-organic frameworks, and noble metal nanoparticles, into biosensor systems is
824 being explored (Liu et al., 2022). With their good electrical conductivity, nanoscale
825 size, and compatibility with biological molecules, these nanomaterials could
826 significantly enhance biosensor performance. Indeed, nanomaterials have been found
827 to increase biosensor sensitivities and lower the limit of detection by several orders of
828 magnitude (Malhotra and Ali, 2018).

829

830 ***Advanced analytical techniques for biological contaminants.*** Recent advancements in
831 the detection of biological emerging contaminants (ECs), such as pathogens, ARGs,
832 and functional genes associated with the biosynthesis of cyanobacterial toxins, have
833 been facilitated by high-throughput quantitative polymerase chain reaction (qPCR) and

834 next-generation sequencing-based methods (Karkman et al., 2018; Stedtfeld et al., 2018;
835 Xie et al., 2023). A comprehensive study recently outlined the advantages and
836 disadvantages of these methods, including classical cultivation-based techniques, for
837 ARG detection (Liguori et al., 2022). One of the significant benefits of sequencing
838 methods is their ability to identify a wide range of pathogens or ARGs across diverse
839 microorganisms present in samples (He et al., 2022b). Despite their high-throughput
840 nature, the sensitivity of these methods relies heavily on the effectiveness of the analysis
841 pipelines (Han et al., 2019). In recent years, computational tools have played a pivotal
842 role in enhancing pathogen surveillance. Notably, the development of a comprehensive
843 pathogen database has empowered the MBPD pipeline to achieve holistic habitat
844 surveillance and coinfections of pathogenic bacteria (Yang et al., 2023). Moreover,
845 advancements in understanding the genomic signatures of pathogens through deep
846 learning approaches, such as DCiPatho, have enabled highly accurate identification of
847 pathogens on a genomic scale (Jiang et al., 2023). Despite the strides made in pathogen
848 detection through sequencing methods, monitoring the environmental dissemination of
849 high-risk ARGs, particularly originating from pathogen hosts, remains challenging and
850 requires novel tools.

851 The analytical methods for cyanobacterial toxins include biological (mouse bioassay),
852 biochemical (enzyme-linked immunosorbent assay; protein phosphatase inhibition
853 assay), chemical (HPLC; LC/MS; high-performance capillary electrophoresis; thin
854 layer chromatography; and GC), and molecular biological (conventional polymerase

855 chain reaction, PCR; quantitative real-time PCR, qPCR; biosensor method) (Massey et
856 al., 2020). The chemical method is the most researched and well-established and is by
857 far the most commonly used.

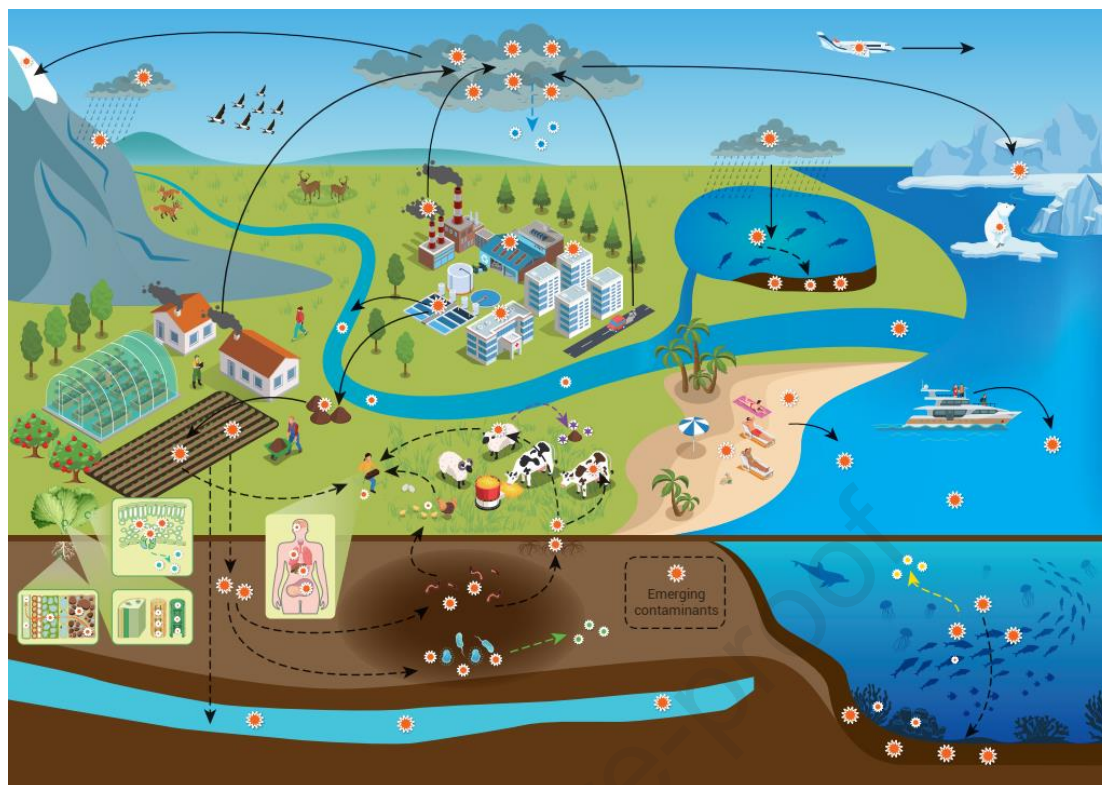
858

859 DISTRIBUTION AND FATE OF EMERGING CONTAMINANTS

860 **Emerging organic contaminants**

861 Terrestrial ecosystems face numerous challenges arising from introducing and
862 accumulating a range of potentially toxic organic substances (Figure 4). Synthetic and
863 naturally occurring emerging organic contaminants (EOCs) are widespread across
864 diverse environmental settings. Despite often existing in low concentrations, these
865 EOCs can exert significant and enduring effects, prompting extensive research into
866 their distribution and fate in recent years. EOCs originate from various sources,
867 including industrial waste, agricultural runoff, and household products. They can be
868 categorized based on their chemical properties and sources, with subsequent
869 subsections discussing some of the most prevalent types.

870



871

872 Figure 3 Pathways through which emerging contaminants (ECs) enter the environment

873 and their subsequent fate. ECs can originate from various sources, such as industrial

874 discharges, agricultural runoff, and wastewater effluents. Once released, ECs can

875 undergo transformation processes such as degradation, volatilization, and

876 bioaccumulation, influencing their distribution across different environmental

877 compartments, including water bodies, soils, and the atmosphere.

878

879 **Pharmaceuticals and Personal Care Products.** Pharmaceuticals and personal care

880 products (PPCPs) represent substances utilized for personal health or cosmetic purposes

881 that can find their way into the environment through multiple pathways, including

882 excretion post-consumption (Chen et al., 2023). Among PPCPs, pharmaceuticals,

883 especially antibiotics, raise significant concerns due to their widespread use and

884 potential environmental impact. Antibiotics, primarily administered orally for bacterial
885 infection treatment in humans and animals, undergo enzyme-mediated metabolism
886 before excretion, involving phase I and II processes (Berkner and Thierbach, 2014).
887 Phase I metabolism involves oxidation, reduction, and hydrolysis, transforming parent
888 compounds into various metabolites, while phase II metabolism entails conjugation
889 with molecules like glucuronic acid or sulfate, further altering their chemical structure.
890 Consequently, resulting metabolites may enter the environment at higher
891 concentrations than their parent compounds due to these metabolic processes (Monteiro
892 and Boxall, 2010). Some pharmaceuticals resist biochemical transformation during
893 metabolism and are excreted unchanged, entering the environment in multiple forms
894 (Adeleye et al., 2022). Understanding these metabolic pathways is pivotal for
895 identifying the diverse forms of pharmaceuticals in the environment and assessing their
896 potential ecological and human health impacts.

897 Pharmaceuticals and other PPCPs enter the environment through various pathways,
898 such as wastewater discharge from sewage treatment plants and animal farms, excretion
899 from humans and animals, and improper disposal practices (Adeleye et al., 2022).
900 Despite efforts in wastewater treatment, PPCPs are not effectively targeted for removal,
901 often persisting due to treatment conditions (Liu et al., 2017). National surveys, such
902 as one conducted in the United States, have shown that final effluents from WWTPs
903 receiving discharges from PPCP manufacturers may contain concentrations of PPCPs
904 10–1000 times higher than those typically found in WWTPs without such inputs

905 (Phillips et al., 2010). This trend was also observed globally, particularly for commonly
906 used PPCPs like antibiotics (Adeleye et al., 2022). Advanced analytical techniques have
907 enabled the detection of PPCPs in sewage, groundwater, surface waters, drinking water,
908 soil, and aquatic organisms across numerous countries, even at low concentrations
909 (Aydın et al., 2022; Richardson and Ternes, 2020; Wu et al., 2021b). For instance, a
910 comprehensive survey conducted in 2015 identified over 600 different pharmaceutical
911 substances and their transformation products across more than 70 countries on all
912 continents (aus der Beek et al., 2016).

913 Once in the environment, PPCPs undergo various processes determining their fate.
914 Some PPCPs can degrade over time through microbial action, although the rate of
915 biodegradation varies based on the compound's chemical structure. PPCPs can also
916 adsorb onto soil particles or sediment in water bodies, influencing their mobility and
917 bioavailability. Aquatic organisms, such as fish, mollusks, and algae, can take up PPCPs
918 from water through direct exposure or diet. It was evident that $\log K_{ow}$, rather than $\log K_{ow}$
919 K_{ow} , is a better indicator of their bioaccumulation and trophic magnification for a
920 marine food web (Guo et al., 2023). However, the apparent volume of distribution
921 represents a promising proportionality constant to understanding the bioaccumulation
922 of ionizable chemicals (Zhang et al., 2022a). Once in the water bodies, most PPCPs
923 remain in the water phase because of their hydrophilic nature, such as sulphonamide
924 antibiotics, whereas some hydrophobic ones (e.g. estrogens) might sorb to sediments
925 or be accumulated by organisms (Chaves et al., 2022). The presence of antibiotic

926 residues in the environment might increase the risk of antibiotic resistance
927 dissemination in environmental settings and consequently transfer to the human
928 microbiome. Terrestrial organisms, including plants and insects, can also be exposed to
929 PPCPs through the contaminated soil. Antibiotics are usually the most abundant PPCPs
930 in plants originating from soils that were amended with biosolids and animal manure
931 applications. For plants, hydrophobic compounds may partition into lipids and will be
932 predominantly retained by roots, while most hydrophilic compounds will move to the
933 xylem (in equilibrium with the water) (Bartrons and Peñuelas, 2017). Further studies
934 are needed to understand the bioaccumulation of ionizable PPCPs in aquatic and
935 terrestrial organisms (Carter et al., 2024).

936

937 ***Cyanotoxins and other algae toxins.*** Risks of toxins produced during harmful blooms
938 of algae, cyanobacteria, and other organisms represent a classic One Health topic
939 (www.cdc.gov/habs/ohhabs.html). Cyanobacterial blooms stimulated by multiple
940 factors, such as global warming and eutrophication of water bodies, have led to a
941 significant increase in the frequency, distribution range, intensity, and duration of
942 cyanobacterial blooms, thus further exacerbating the risk of algal toxin poisoning
943 (Huisman et al., 2018; Zhang et al., 2022d). Cyanotoxins can be classified into three
944 groups based on their chemical structure: cyclic peptide, alkaloid, and
945 lipopolysaccharide (LPS). Depending on the mode of toxicity to animals, toxins can be
946 classified as hepatotoxic cyclic peptide toxins (represented as microcystin and

947 nodularin), neurotoxic alkaloidal toxins (anatoxin, saxitoxin), cytotoxic alkaloidal
948 toxins (cylindrospermopsin), dermatotoxic alkaloidal toxins (aplysiatoxin;
949 lyngbyatoxin), irritant toxins (LPS), and some other biologically active substances
950 (Xie, 2006). Globally, microcystin-LR is the most common cyanotoxin in freshwater,
951 brackish water, and marine habitats (Massey et al., 2022). Lakes and reservoirs differ
952 in morphology and trophic status, which can impact the dispersal and distribution of
953 cyanotoxins (Wood et al., 2017). At the same time, cyanotoxins are subject to transport
954 and diffusion at the sediment-water interface, with different types of sediments
955 exhibiting different adsorption capacities (Liu et al., 2019). Notably, algae,
956 cyanotoxins, and toxins present in a variety of freshwater, marine, soil, and terrestrial
957 species can be wind-driven to float in the air and transported over greater distances
958 (Wisniewska et al., 2019). Moreover, cyanotoxins in the atmosphere may, under certain
959 conditions, settle on the ground or in water bodies and impact the surrounding
960 environments (Wisniewska et al., 2022). The accumulation of cyanotoxins involves a
961 complex process of gradual accumulation and transfer in ecosystems. The process can
962 be manifested primarily through the cascading of cyanotoxins through the food chain
963 and their progressive enrichment in organisms. For example, fish and shellfish,
964 organisms that consume food rich in cyanobacterial toxins, accumulate the toxin in their
965 tissues, resulting in a gradual build-up of cyanotoxins in the upper levels of the food
966 chain (Ferrao and Kozlowsky-Suzuki, 2011).

967

968 **Emerging inorganic contaminants**

969 **Engineered nanoparticles.** ENPs that accumulate in the environment will undergo a
970 series of physical, chemical, and biological processes such as chemical transformation,
971 aggregation, and dissolution. The interplay between these processes and the ENP
972 transport ultimately determines the potential fate of ENPs (Peijnenburg et al., 2015).
973 The chemical transformation process mainly includes the dissolution and sulfidation of
974 ENPs. In a series of studies, it has been found that the dissolution of NP is triggered by
975 particle-inherent factors (e.g., surface coating, particle size, shape, and aggregation
976 state) and environmental parameters such as solution pH, dissolved organic carbon, and
977 temperature (Bundschuh et al., 2018). Thereinto, the most commonly occurring
978 passivation process, that is, the sulfidation of nanoparticles, makes their surface appear
979 to be almost inert, thus affecting the reactivity.

980 The colloidal stability of ENPs is a crucial factor that influences their fate and
981 environmental effects (Lowry et al., 2012). The homo-aggregation (interactions
982 between the same ENPs) of NP is positively correlated with the NP concentrations. The
983 aggregation characteristics are often explained by the classical Derjaguin-Landau-
984 Verwey-Overbeek theory. Owing to the low predicted ambient concentrations of ENPs
985 (e.g., in the range of pg/L to low $\mu\text{g/L}$ for surface water), homo-aggregation is less
986 likely to happen and is affected by ionic strength. The aggregation rate of NP increases
987 with the surrounding medium's ionic strength, and multivalent cations are more
988 efficient than monovalent cations (Adam et al., 2016; Baalousha et al., 2013). However,

989 heteroaggregation of ENPs with mineral particles is more common in natural
990 environments (Zhao et al., 2015), which ultimately affects the environmental fate of
991 ENPs and their risk to ecosystems and organisms (Zhao et al., 2021). The majority of
992 the studies on ENP transport in porous media used water-saturated artificial columns
993 often packed with quartz sand, while only a few involved natural soils (Solovitch et al.,
994 2010). Key environmental factors controlling ENP transport processes are solution
995 ionic composition, pH, and natural organic matter (NOM) chemistry, while the degree
996 of water saturation in porous media such as soils is an additional physical factor. The
997 impact of ionic composition, NOM, and solution pH on the NP fate is similar in aquatic
998 systems and saturated and unsaturated porous media. For plants, an increasing number
999 of studies related these factors to plant uptake. For instance, size-exclusion limits that
1000 range from < 10 nm to the uptake of cells exceed 20 nm for the uptake of leaves and
1001 can reach 100 nm in exceptional cases (Eichert et al., 2008; Jia et al., 2023; Wang et al.,
1002 2016). Assimilation of elements from larger particles is possible if they dissolve, while
1003 low zeta potentials usually favor direct particle uptake.

1004

1005 ***Radionuclides and nuclear wastes.*** Whether released from nuclear power plants,
1006 medical facilities, or sites where radioactive material was improperly disposed of,
1007 radionuclides pose considerable challenges to environmental quality and human well-
1008 being (Santhanabharathi et al., 2023). Radionuclides undergo radioactive decay,
1009 emitting radiation over time (Santhanabharathi et al., 2023). Nuclear wastes threaten

1010 ecosystem health. Strict regulations govern the handling and disposal of nuclear waste
1011 to prevent environmental contamination (Natarajan et al., 2020; Shan and Ding, 2024).
1012 Consideration should extend beyond physical and chemical interactions to encompass
1013 biological uptake and long-term ecological consequences of radionuclides and nuclear
1014 waste.

1015

1016 **Biological contaminants**

1017 ***Pathogenic bacteria.*** The intricate interplay between pathogenic bacteria and various
1018 environmental sources, particularly in agricultural settings, underscores the complexity
1019 of this challenge (Banerjee and van der Heijden, 2023; Zhang et al., 2023c).
1020 Agricultural soils are often underestimated as reservoirs of human and animal
1021 pathogens and can give rise to a spectrum of diseases affecting air, water, and food
1022 (Singh et al., 2023). For example, bacterial species like *Bacillus anthracis*, *Vibrio*
1023 *cholera*, and *Burkholderia pseudomallei* have the potential to cause severe infection
1024 and, in some cases, death through direct contact (Limmathurotsakul et al., 2016; Steffan
1025 et al., 2020). Foodborne pathogens such as *Escherichia coli* O157:H7 and *Salmonella*
1026 *enterica* can also enter the food chain, triggering epidemics with severe health
1027 consequences (Gonzalez-Martin et al., 2014; Scott et al., 2017).

1028

1029 ***Antibiotic resistant bacteria and resistance genes.*** Antibiotics and antibiotic-resistant
1030 bacteria (ARB) carrying ARGs have existed for hundreds of thousands of years before

1031 the discovery of antibiotics by humans (D'Costa et al., 2011; Waglechner et al., 2021).
1032 However, the industrialization and widespread use of antibiotics in both human and
1033 animal populations have exerted unprecedented selective pressure on bacteria across
1034 various interconnected niches, including human, animal, and environmental
1035 microbiomes. This has led to the accelerated development of antibiotic resistance traits
1036 within these communities on a global scale (Levy and Marshall, 2004; Zhu et al., 2022).
1037 Thus, anthropogenic activities could increase the emergence of ARB, their resistance
1038 genes, and their dissemination between the human, animal, and environmental
1039 compartments, aggravating the existing antibiotic resistance crisis (Fu et al., 2023). For
1040 example, the extensive use of antibiotics and the intensive agricultural practices
1041 prevalent in modern farming have transformed soil ecosystems into potential reservoirs
1042 of pathogens and ARGs (Zheng et al., 2022). Within this soil environment, the
1043 biopollutome emerges as a complex network of pathogens and ARGs, creating a
1044 prevalent threat to ecosystems (Wang et al., 2023a). Although multiple barriers restrict
1045 the flow of both bacteria and genes, pathogens recurrently acquire new resistance
1046 factors from other species, thereby reducing our ability to prevent and treat bacterial
1047 infections (Larsson and Flach, 2022), which demands urgent and effective measures to
1048 control the formation and dissemination of ARB.

1049 Antibiotic resistance has been referred to as a silent pandemic and has emerged as a
1050 significant concern in the realm of biological ECs (Mah, 2021). Hence, the increasing
1051 number of antibiotic-resistant microbes poses threats to human health. Over the last

1052 decade, ARGs have been detected in all habitats, including the natural environment and
1053 human industrial habitats (Zhang et al., 2022e). Anthropogenic activities play a key role
1054 in selecting genes from environmental and cellular sources, facilitating their subsequent
1055 co-option to confer antibiotic resistance. With increasing human activities,
1056 microorganisms and their genetic material move more often between humans, animals,
1057 and the environment, which collectively increases opportunities for the transmission
1058 and evolution of ARGs (Danko et al., 2021; Larsson et al., 2023b; Zhang et al., 2022e).
1059 Once these drug-resistant genes are transferred to human-associated pathogenic
1060 bacteria, such as ESKAPE (*Enterococcus faecium*, *Staphylococcus aureus*, *Klebsiella*
1061 *pneumoniae*, *Acinetobacter baumannii*, *Pseudomonas aeruginosa*, and *Enterobacter*
1062 species) pathogens and plant pathogens, it may further exacerbate the clinical
1063 pathogenic risks (Zhang et al., 2021a). These pathogens are not only present in the
1064 bodies of humans and animals, but can also enter the water through excretions such as
1065 feces, urine, and saliva, and spread through respiratory secretions into the air. The threat
1066 posed by pathogenic bacteria also presents a significant challenge within the One
1067 Health framework (Fu et al., 2023). Over the past two decades, infectious diseases have
1068 been accountable for approximately 15 million global deaths annually (Cowie and
1069 Dore, 2012). Meanwhile, plant diseases contribute to the loss of up to 30% of global
1070 food production each year (Savary et al., 2019).

1071 Antibiotic-resistant bacteria and ARGs originating from human activities are
1072 recognized as emerging biological contaminants that can potentially impact

1073 environmental ecosystems (Karkman et al., 2019; Pruden et al., 2006). Apart from
1074 antibiotics, a range of non-antibiotic pollutants like heavy metals, disinfectants,
1075 biocides, and non-antibiotic drugs can alter bacterial behavior and contribute to the
1076 development of antibiotic resistance (Lu et al., 2018; Lu et al., 2020; Luo et al., 2023;
1077 Pál et al., 2015; Wang et al., 2019). Furthermore, ARB and ARGs can disseminate back
1078 to the human and animal microbiomes (Vaz-Moreira et al., 2014) through food
1079 ingestion, drinking water, and direct contact while swimming in contaminated water
1080 and while in contact with contaminated crops, thus creating a loop between the human,
1081 animal and environmental microbiomes. Nevertheless, future research should provide
1082 quantitative information about the dissemination routes of ARB and ARGs from the
1083 environment to the human microbiome by considering human exposure and the
1084 probability of successful colonization of the human microbiome by these biological
1085 pollutants. There is an urgent need to move from descriptive, qualitative, or semi-
1086 quantitative research to quantitative risk assessments of the drivers of antibiotic
1087 resistance proliferation in the environment and its dissemination to the human
1088 microbiome (Larsson et al., 2023a).

1089

1090 **Viruses.** Among microorganisms, viruses are most prone to becoming emerging
1091 pathogens because they can infect their hosts and adapt to new environments through
1092 mutation, genetic recombination, and reassortment (Du et al., 2022). The pathogenicity
1093 of many bacteria is due to the virulence factors they carry encoded by lysogenic phages

1094 (Jansson and Wu, 2023). Soil plays a significant role in the distribution and transmission
1095 of viruses in natural environments (David Walter et al., 2011). Research indicates that
1096 viruses can survive in soil for varying durations depending on factors like temperature,
1097 moisture content, pH, and the presence of an envelope. Enveloped viruses like SARS-
1098 CoV-2 can survive for up to 90 days in soils with 10% moisture content (Anand et al.,
1099 2021). Additionally, enteric viruses can persist on surfaces like door handles, banisters,
1100 and food, contributing to their transmission (Steffan et al., 2020). The abundance of
1101 viruses in soil is higher in environments with high organic matter and moisture content
1102 (Anand et al., 2021). Changes in soil moisture levels can impact the composition and
1103 activity of soil DNA and RNA viruses, potentially affecting soil ecology (Wu et al.,
1104 2021a). Understanding how viruses interact with soil is crucial for assessing their
1105 environmental impact and potential transmission pathways. Because the size of the host
1106 is tens to thousands of times larger than the size of the virus, viruses are more flexible
1107 than bacteria in terms of transport and dispersal by animals, wind, or rain (Prosser et
1108 al., 2023). Influenza viruses (Wood et al., 2010), hepatitis A viruses, coronaviruses
1109 (Carlson et al., 2020; Zhu et al., 2022), and others, can survive in the soil for a long
1110 time, leading to human exposure.

1111

1112 **Protein contaminants.** Prions and Bt proteins are considered two important classes of
1113 emerging protein contaminants. Prion proteins can bind to soils and suspend in water,
1114 thus persisting in the environment for years and serving as a significant environmental

1115 reservoir for disease propagation (Johnson et al., 2006; Nichols et al., 2009; Saunders
1116 et al., 2009a, b). Our understanding of the fate and transport of prion proteins in the
1117 environment is very limited. Using sand or soil columns, previous studies found that
1118 recPrP and purified PrP^{Sc} had limited mobility, where the migration of recPrP was
1119 smaller than 1 cm in the quartz sand column and purified recPrP was primarily retained
1120 near the point of contamination in soil columns (Cooke and Shaw, 2007; Jacobson et
1121 al., 2010). Bt proteins were found to persist in soils for two months, 180 days, and up
1122 to 234 days, respectively, and were found to have the potential to be transported through
1123 the landscape by sediments and crop residue debris in surface runoff (Feng et al., 2011;
1124 Strain and Lydy, 2015; Tapp and Stotzky, 1998). Nonetheless, significant knowledge
1125 gaps remain in understanding the fate, transport, and environmental risks of protein
1126 contaminants (e.g., prions and Bt proteins).

1127

1128 **Microplastics and nanoplastics**

1129 As one of the world's most prominent emerging pollutants, microplastics (MPs) are
1130 ubiquitously distributed across the atmosphere, pedosphere, hydrosphere, and
1131 biosphere. Micro- and nanoplastics (MNPs) could be widely detected in the terrestrial
1132 ecosystem and human body (Jiang et al., 2020). Microplastic fragmentation by rotifers
1133 in aquatic ecosystems has been reported to contribute to global nanoplastic pollution
1134 (Zhao et al., 2023a). Plastic particles enter the environment from ubiquitous sources,
1135 posing a potential threat to aquatic organisms, soil, the atmosphere, and human health

1136 (McIlwraith et al., 2021; Piehl et al., 2018). Atmospheric microplastics are found in
1137 both indoor and outdoor air. Indoors, concentrations in residential homes can be as high
1138 as 1.96×10^4 particles/(m².day), while in schools, they can be as low as 6.20×10^3
1139 particles/(m².day), and in dormitories [9.9×10^3 particles/(m².day)] they are 5.5 times
1140 higher than in offices [1.8×10^3 particles/(m².day)]. The abundance of MPs in outdoor
1141 air showed regional differences, with higher abundance of MPs in urban air than in rural
1142 air, and higher levels of MPs in cities in northern China than in southern cities (Feng et
1143 al., 2023b). Some studies have shown that atmospheric deposition of MPs ranges from
1144 0.5 to 1,357 MP m⁻² d⁻¹(outdoors) and 475 to 19,600 MP m⁻² d⁻¹(indoors). During
1145 deposition, microplastics can utilize plant stomata (20 - 40 µm long and 5-10 µm wide),
1146 with 20 - 200 nm of microplastics accumulating in the stomatal lumen and passing
1147 through the stomata into leaf tissue. Research has validated the capability of polystyrene
1148 (PS) nanoplastics to infiltrate leaves and migrate to plant roots, demonstrating their
1149 ability to penetrate plant leaves through foliar exposure (Wang et al., 2022d). Within
1150 the phloem, nanoplastics can travel alongside bulk water or sap, a process influenced
1151 by sap's composition and flow rate within the stem (Su et al., 2019b). Furthermore, the
1152 downward movement of nanoplastics within vascular tissues requires traversal through
1153 various physiological barriers, including intercellular plasmodesmata, vesicles, and
1154 conductive cells (Sun et al., 2021b). Consequently, the continuous aggregation of
1155 nanoplastics could potentially obstruct the vascular system, impeding the downward
1156 translocation of smaller nanoplastics (Sun et al., 2021b). The average abundance of

1157 microplastics in fish in the oceans was 3.5 ± 0.8 particles/stripe, but in highly polluted
1158 waters, in contrast, oysters had the highest abundance of 99.9 particles/individual
1159 (Wang et al., 2023d).

1160 Micro- and nanoplastics accumulate in many organisms in the environment, which
1161 leads to food chain pollution impacting the life and health of all organisms in the food
1162 chain. Micro- and nanoplastics are not easy to degrade after being ingested by animals
1163 so they accumulate continuously in the body. Studies have shown that $0.2\sim 0.3 \mu\text{m}(2.5$
1164 $\text{mg}\cdot(100 \mu\text{L})^{-1})$ PS labelled with radioactive isotope Cu-DOTA was given to mice by
1165 gavage, and it was found that plastic particles were absorbed into the blood, liver, brain,
1166 spleen, testis, bladder and other tissues through the intestinal tract, resulting in various
1167 organ toxicity (Im et al., 2022). Micro- and nanoplastics can be detected in human feces,
1168 which indicates that the intake of micro- and nanoplastics is high (Zhang et al., 2021c).
1169 After micro- and nanoplastics enter the gastrointestinal tract through food, the
1170 undigested micro- and nanoplastics are excreted with feces, but smaller micro- and
1171 nanoplastics will enter the systemic circulation. Some studies have found that there are
1172 micro- and nanoplastics in human blood, so micro- and nanoplastics may be transported
1173 to various organs through blood, but the mechanism of micro- and nanoplastics entering
1174 the blood circulation is still unclear and needs further study (Leslie et al., 2022). The
1175 maximum particle diameter of micro- and nanoplastics uptake by organisms is
1176 determined by the morphology of species' feeding and digestive organs (Lambert et al.,

1177 2017). Micro- and nanoplastics mainly enter the respiratory and gastrointestinal tract
1178 and can then be transferred to other secondary organs according to their size and shape.

1179

1180 5.5 Other emerging contaminants

1181 **Liquid crystal monomers.** Liquid crystal monomers (LCMs) are a class of synthesized
1182 organic chemicals that are key materials for liquid crystal displays (LCDs), which can
1183 undergo phase transitions between liquid and solid states at specific temperatures.

1184 LCMs are typically diphenyl-based compounds that contain functional groups like
1185 cyano, fluorine, chlorine, or bromine (Li et al., 2018). The production output of LCMs
1186 for LCD panels is approximately 500 tons per year (Zhang et al., 2017). However, the
1187 environmental release of LCMs during the use and dismantling of waste LCDs is a
1188 concern, and global estimates range from 1.07 to 107 kg/year (Liang et al., 2021).

1189 Numerous studies have indicated the widespread presence of LCMs in the environment,
1190 and projections suggest a significant increase in their prevalence in the near future (Su

1191 et al., 2019a). These LCMs exhibit environmental persistence, long-range migratory
1192 capabilities, and potentially harmful impacts on various species (Feng et al., 2023a).

1193 Consequently, LCMs have gained attention as ECs because of their distinctive
1194 properties, including persistence, bioaccumulation, toxicity, and extensive
1195 environmental distribution (Liang et al., 2021).

1196 LCMs have been found in various environmental matrices, indicating their widespread
1197 distribution and potential exposure risk to organisms. Air is considered a significant

1198 transport medium for LCMs, allowing their migration from e-waste recycling sites to
1199 the surrounding environment. Investigations into waste LCD panel dismantling
1200 revealed atmospheric concentrations of LCMs at 68,800-385,000 pg/m³ (Shen et al.,
1201 2022). LCMs have also been observed in indoor and outdoor dust, sediment, landfill
1202 leachate, sewage sludge, and soil samples. LCMs median levels in dust collected across
1203 China ranged from 41.6 to 171 ng/g (Zhang et al., 2022c), depending on the sampling
1204 region. LCM concentrations in urban soils from different functional zones ranged from
1205 0.774 to 12.9 ng/g dw (Li et al., 2022c). In biota samples, LCMs were found in wild
1206 aquatic invertebrates and fishes (Wang et al., 2022c). LCMs were also detected in the
1207 hands, forehead skin wipes, and serum of e-waste dismantling workers (Cheng et al.,
1208 2022). The LCM concentrations in the serum samples of the occupational workers were
1209 significantly higher than those in the reference serum samples, indicating a high
1210 exposure risk in the occupational population (Boiko et al., 2022). These studies have
1211 provided direct evidence of LCMs in the environment, indicating their widespread
1212 pollution and highlighting the importance of understanding their distribution and fate.

1213

1214 ***Environmentally persistent free radicals.*** Unlike traditional free radicals with lifetimes
1215 spanning milliseconds and microseconds, EPFRs are stabilized on or in specific
1216 particles, with lifetimes extending beyond days and even months. EPFRs exhibit
1217 stability and ubiquity in various environmental matrices such as atmospheric
1218 particulates, soil, biochar, and microplastics (Yang et al., 2017b; Zhu et al., 2020). Their

1219 presence is potentially implicated in diverse environmental and biological processes.
 1220 Notably, EPFRs have been observed to mediate the generation of a significant amount
 1221 of reactive oxygen species (ROS) (Kelley et al., 2013), recognized for their involvement
 1222 in chemical degradation (Yang et al., 2016) and the induction of oxidative stress, which
 1223 can adversely affect organisms, leading to DNA damage and diseases such as lung and
 1224 cardiovascular diseases (Mahne et al., 2012). Ongoing research is addressing various
 1225 aspects of EPFRs, each presenting substantial challenges.

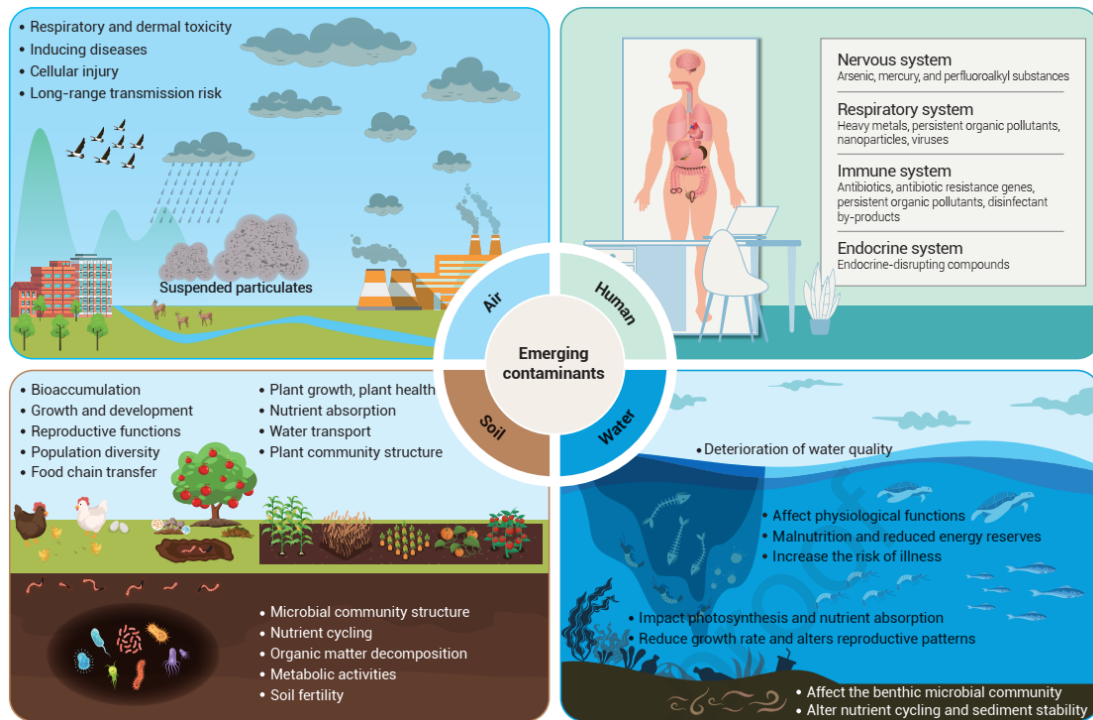
1226

1227 RISKS OF EMERGING CONTAMINANTS TO PLANETARY HEALTH

1228 **Environmental quality implications**

1229 *Bj bodfkd»`l kq`j fk^kq»mobpbkq»pr`pd`kq`i»ofph»d`mi^kbq`ov»eb`iqe»_v»afpor mfdkd»*
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 1231 *^i»» /- . 2&» Qebpb»`l kq`j fk^kq» buef`fq»`e^o``qofp`p»pr`e»`p»nbopfpdk`b»*
 1232 *_fl`^`rj ri^ql k»»kaj l`_fifq»»ml`pkq`iiv»d oj`fkd»bkar ofkd»bksfol kj`bkq`id l`qofkq»*
 1233 *q^`q`bl m`oafvb»b`l pvpqj p»»b`a`s»bq`i»» /- . &»Qebv»`k»nbopfpqf»»xep»bksfol kj`bkq»*
 1234 *d o»budpkaba»nbofl ap»»t f`el r`q`abd o`a`ql k»»ib`afkd»d`_fl`^`rj ri^ql k»fk»l od`kfpj p»*
 1235 *^ka»xep»pr`pbnr`bkq`ofph»l`oxob`^efkd»e`oj`a`i»`lk`bkq`ql`kp»»J`^kv»B@»abj l`kpp`q`d»*
 1236 *b`l`q`uf`fq»»ml`pfkd»xepob`q»d`»nr`q`»ifcb»»mi^kq»»ka»l`q`bo»l`od`kfpj`p`d`d`o»f`k`p`k`b»*
 1237 *me`oj`^`br`q`^ip»ifhb»»kq`_fl`q`p»^ka»el`oj`l`kbp»`^k»afpor`mq»xep»bkal``ofkb»pvpqj`p»l`o»*
 1238 *q`oob`p`q`i»»ka»»nr`q`»pnb`fbp»»`r`pfkd»ob`ml`ar`q`sb»»ka»abs`bil`nj`bkq`i»fj`m`foj`bkq»*
 1239 *%b»Obwbkab»»ka»J`l`rk`q`bo»» / 0&»k`k`q`o`i»p`b`q`k`d`p»b`l`pvpqj`p»l`q`pk`e``bj`fuq`obp»*

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- 1241 *ml qbkq`iiv»obpr iqkd»fkd»pvk bodsfq` »l o»`kq`dl ksfq` »bacb`q»q`q`j nif»»b`l il df`^i»ofph»*
- 1242 *%Bp`ebo»bq`i`»/-/- &»J l obl sbo)»pl j b»B(@)»pr`e»`p»mi`pq`p»`ka»j f`ol mi`pq`p)»`k»*
- 1243 *pbosb»`p»`^oofbop»d o»l qeb»`l kq`j fk`kq)»c`^fifq`qkd»q`bfo»``rj ri`ql k»fk»`nr`q`»*
- 1244 *l od`kfpj p»`ka»ml qbkq`i»bkq»»fkd »q`b»d l a»`e`fk»»Hfkd l ml ril r »bq`i`»-// &T`^kd»bq»*
- 1245 *^i`»-/.` &R kabopq`kafkd»q`bj l sbj bkq`l oB(@)»q`ol rde»q`b»bksfol kj bkq`p»sfq`i»d o»*
- 1246 *^ppppfk d»q`bfo»»ofph»»e``q op»ifhb»sl i`qifq)»pl ir`_fifq)»`ka»`apl omq`l k»d »pl fi»m`oq` ibp»*
- 1247 *fk`ar bk`b»`l kq`j fk`kq` q`k`pml oq` q`ol rde»`fo)»t`^qo)»`ka»pl fi)»fj m``qkd»`q`bfo»*
- 1248 *afpq`_r`ql k»`ka»bunt pr`ob»m`q`t`^vp»»Hksbpq`d`qkd»q`b»bacb`q`l oB(@)»l k»pl fi)»t`^qo)»`ka»*
- 1249 *^fo»b`l pvpq`j p»fp»`or`f`i»d o»`lj mobe bkpf sbiv»bs`ir`^qkd»`q`bfo»`bksfol kj bkq`i»*
- 1250 *fj nif`^ql kp»E bob»t b»`l kpfabo»pl j b»bksfol kj bkq`i»nr`ifq)»fj nif`^ql kp»l oB(@)»fk»*
- 1251 *^q`l prebof`»)»p`oobpq`f`i»`ka»`nr`^q` »pvpq`j p+*
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1253

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1256

1257 **Soil ecosystems.** Emerging contaminants, such as PPCPs, pesticides, and industrial

1258 chemicals, have been increasingly detected in soil environments worldwide (Snow et

1259 al., 2017). These contaminants threaten soil organisms, including bacteria, fungi,

1260 earthworms, insects, and plants. Exposure to ECs can adversely affect soil organisms,

1261 disrupting their physiological functions, reproductive capabilities, behavior, and overall

1262 health (Figure 4). Among these, PFAS and MPs have garnered much attention for their

1263 potential to alter the composition and functionality of soil bacteria and fungi (Bolan et

1264 al., 2021; Ren et al., 2018; Riveros et al., 2023; Wang et al., 2023c). Studies indicate

1265 that exposure to such ECs can lead to shifts in microbial community structures (Jiang

1266 et al., 2018; Wang and Hou, 2023), affecting the abundance and diversity of key
1267 microorganisms involved in nutrient cycling and organic matter decomposition (Ma et
1268 al., 2023; Pagel et al., 2016; Wang et al., 2022a). On the other hand, exposure to ECs
1269 can lead to the selection of bacteria and fungi that can catabolize these pollutants (Wang
1270 et al., 2021e). Cyanotoxins can enter the soil through runoff and rainfall leaching.
1271 Accumulation of cyanotoxins in the soils can adversely affect plant health, animal
1272 health, microorganisms, and consequently, soil health (Bouaïcha and Corbel, 2016).
1273 Furthermore, cyanotoxins affect aerobic microbial communities at the sediment-water
1274 column interface, which may affect nitrogen transformation (Li et al., 2020). The
1275 repercussions of these disruptions extend beyond the immediate microbial community,
1276 with potential consequences for soil health and ecosystem functioning. The metabolic
1277 activities of soil microorganisms, essential for maintaining soil fertility, are particularly
1278 vulnerable to ECs (Tang et al., 2023c; Tran et al., 2013). The interference with microbial
1279 functions can hinder nutrient cycling processes, leading to imbalances in the availability
1280 of essential elements for retaining soil productivity (Khan et al., 2023; Xiang et al.,
1281 2023). Additionally, the disruption of microbial communities may compromise the
1282 soil's ability to resist pathogens and maintain resilience in the face of environmental
1283 stressors and climate change (Hou et al., 2023; Sunyer-Caldú et al., 2022). The
1284 relationships between soil microorganisms and ECs necessitate further research to
1285 unravel the mechanisms underlying these effects and develop strategies for mitigating
1286 their impact on soil health.

1287 The effects of ECs on plants reverberate through the entire ecosystem, influencing the
1288 structure and dynamics of plant communities (Pullagurala et al., 2018; Rizwan et al.,
1289 2021; Zhou et al., 2023a). While the contaminants encompass a broad range, their
1290 overarching impact on plant health remains a common theme. Emerging contaminants
1291 in soils can impede plant growth and development, posing challenges to individual
1292 species and the overall biodiversity of plant communities. One notable consequence is
1293 the alteration of nutrient uptake mechanisms in plants. Emerging contaminants like
1294 ENPs, PFAS, and MPs have been shown to interfere with the physiological processes
1295 that govern nutrient absorption (Jiao et al., 2021; Moreno-Jiménez et al., 2022; Rizwan
1296 et al., 2021). This disruption can lead to nutrient deficiencies, compromising the health
1297 and vigour of plant populations. Furthermore, contaminants may accumulate in plant
1298 tissues, potentially entering the food chain and posing risks to organisms feeding on
1299 contaminated plants (including human beings) (Lesmeister et al., 2021; Wang et al.,
1300 2023b). Water transport mechanisms within plants are also vulnerable to the presence
1301 of ECs in soils. Certain contaminants can impede the movement of water through plant
1302 tissues. This disruption can cause reduced growth, altered reproductive patterns, and
1303 overall compromised resilience in plant communities (Khalid et al., 2020; Martínez-
1304 Fernández et al., 2016; Wang et al., 2022b). As we strive to understand the broader
1305 implications of ECs on soil plants, exploring the connections between soil, plants, and
1306 the myriad ECs that shape their interactions becomes imperative.

1307 The impact of ECs on soil animals encompasses a wide range of organisms like
1308 protozoa, earthworms, nematodes, and arthropods. The broad category of ECs,
1309 including but not limited to PFAS, POPs, and microplastics, have been reported to
1310 influence the ecological dynamics of soil animals, with cascading effects on the entire
1311 soil food web (Burkhard and Votava, 2023; Dummett et al., 2023; Su et al., 2022).
1312 Bioaccumulation is a common phenomenon observed in soil-dwelling organisms
1313 exposed to ECs. Contaminants accumulate in the tissues of these organisms, leading to
1314 elevated concentrations that can disrupt physiological functions and compromise
1315 overall health. This bioaccumulation introduces complexities to soil food webs,
1316 potentially affecting higher trophic levels that rely on soil animals for sustenance
1317 (Hopkins et al., 2023; Okeke et al., 2022). Furthermore, soil animals can also act as
1318 carriers, leading to the migration of ECs (Sobhani et al., 2021; Wang et al., 2020a).
1319 Nevertheless, the toxicity mechanisms of ECs in soil animals remain poorly
1320 understood. Ongoing research efforts should aim to elucidate how ECs impact soil
1321 animal populations, paving the way for informed conservation and management
1322 strategies to safeguard soil biodiversity.

1323 In summary, the effects and impact of ECs on soil ecosystems are complex and
1324 multifaceted. The overarching influence of these contaminants on soil microorganisms,
1325 plants, and animals underscores the need for comprehensive research to unravel the
1326 complex web of interactions within soil ecosystems. By examining the broader category
1327 of ECs without fixating on specific types, scientists can better comprehend the

1328 interconnected challenges posed by these pollutants. Continued investigation is
1329 essential to inform sustainable soil management practices that mitigate the adverse
1330 effects of ECs and preserve the health and functionality of soil ecosystems.

1331

1332 *Aquatic systems.* As a vital component of various ecosystems, the aquatic environment
1333 faces increasing challenges due to the presence of diverse ECs. For example, EDCs in
1334 water bodies can impact aquatic ecosystems (Carnevali et al., 2018). These compounds
1335 interfere with the endocrine systems of aquatic organisms, leading to disruptions in
1336 reproductive, developmental, and physiological processes (Carnevali et al., 2018; You
1337 and Song, 2021). Recent studies highlighted the widespread occurrence of EDCs in
1338 water bodies, emphasizing their potential to disrupt the health of fish and amphibians
1339 (Carnevali et al., 2018; Celino-Brady et al., 2021; Langston, 2020; You and Song,
1340 2021). The bioaccumulation of EDCs in aquatic organisms underscores the need for
1341 continuous monitoring and regulatory measures to mitigate their impact. POPs,
1342 including PCBs, PFAS, and organochlorine pesticides, have long-lasting effects on
1343 water and sediment quality (Hagemann et al., 2020; Krithiga et al., 2022).
1344 Bioaccumulation of POPs in fatty tissues of aquatic organisms poses ecological risks
1345 (Krithiga et al., 2022). As noted above, PPCPs also enter water bodies through various
1346 pathways, raising concerns about their potential impact on aquatic organisms (Chaves
1347 et al., 2022; Corcoll et al., 2014; Osuoha et al., 2023). Cyanotoxins provide a
1348 competitive advantage for cyanobacteria and drastically reduce the populations of

1349 certain species in aquatic ecosystems, upsetting the ecological balance (Chia et al.,
1350 2019; Holland and Kinnear, 2013). At the same time, cyanotoxins can cause water
1351 pollution problems and directly threaten drinking water quality (Bhatt et al., 2023).
1352 Cyanotoxins may drastically reduce the populations of some species in water bodies,
1353 upsetting the original ecological balance. Secondly, the toxic effects of cyanotoxins
1354 may also affect the variety and abundance of microorganisms in water bodies, thereby
1355 interfering with aquatic ecological processes. In some locations at some times,
1356 cyanotoxins and other toxins produced by harmful algae blooms can represent the
1357 greatest EC water quality threat to public health and ecosystems (Brooks et al., 2016,
1358 2017).

1359 To allow for ENP-tailored risk assessment, the developers and regulators must know
1360 the most important parameters governing the behavior and toxicity of ENPs.
1361 Engineering nanomaterial wastes in the environment are not easy to degrade and will
1362 accumulate and remain in the soil and higher plants through transport, which is bound
1363 to have a significant impact on the growth of higher plants (Rico et al., 2011). The
1364 biological effects of ENPs on higher plants can directly affect ecosystems' health,
1365 stability, and sustainable development (Rico et al., 2011). On the one hand, the presence
1366 of ENPs (such as TiO₂ NPs, ZnO NPs, Fe₃O₄ NPs, and carbon nanotubes) can have a
1367 catalytic interaction on plant growth by increasing root activity, increasing water
1368 absorption, enhancing photosynthesis, or improving rhizosphere soil microbial
1369 communities and increasing metabolic enzyme activity. Several recent reviews have

1370 discussed the ENP accumulation in terrestrial plants, which can induce physiological
1371 and biochemical responses in plants (Du et al., 2017; Marslin et al., 2017; Tripathi et
1372 al., 2017). Cao et al. documented impacts on carbon fixation and water use efficiency
1373 during photosynthesis in response to CeO₂ NP exposure (Cao et al., 2017), which may
1374 indirectly influence soil organisms via the effect on soil moisture. On the other hand,
1375 ENPs (such as ZnO NPs, AgO NPs, CuO NPs, and CeO₂ NPs) may be potentially
1376 harmful to biota via reducing seed germination, generating reactive oxygen species,
1377 enhancing membrane permeability, inhibiting antioxidant enzyme activity, or damaging
1378 root hairs through physical friction. Mechanism and mode of toxicity vary among ENPs
1379 (von Moos and Slaveykova, 2014). Oxidative stress is a frequently reported
1380 phenomenon (Mwaanga et al., 2014). At present, research on the biological effects of
1381 ENPs mainly includes the mechanism of toxicity of ENPs to plants under different
1382 conditions and the role of ENPs in environmental systems from the perspective of
1383 organisms. Although the research has enhanced the theoretical value of nanobiology
1384 effects and toxicity research to a certain extent, there are often many contradictions in
1385 related research results. This is due to differences in the physical and chemical
1386 properties of ENPs themselves (such as composition, shape, surface coating, and
1387 charge), or differences in culture substrates, treatment methods, and plant species,
1388 resulting in different stability and biocompatibility in the environment. This then affects
1389 the interaction between ENPs and plants (Zuverza-Mena et al., 2017). ENPs

1390 accumulated in plants may also spread through the food chain to higher trophic
1391 organisms, causing certain ecological risks.

1392 In recent years, several independent studies have shown that AgNPs exhibit certain
1393 cellular or systemic toxicity to cells and body systems under both in vitro and in vivo
1394 conditions (Ahamed et al., 2010; Dhawan and Sharma, 2010). Ag^+ mainly exerts
1395 cellular/bacterial toxicity through the following toxicological mechanisms: (1) Interfere
1396 with the normal Na^+ and K^+ ion channels on the cell membrane, resulting in the
1397 imbalance of the membrane potential inside and outside the cell (Sun et al., 2016a), or
1398 bind to the sulfhydryl-containing (-SH) proteins on the cell membrane to inactivate
1399 them, destroy the barrier function and material exchange function of the cell membrane,
1400 and directly lead to cell necrosis (Sun et al., 2016a); (2) Enter the cytoplasm of cells,
1401 interact with sulfhydryl-containing proteins, and destroy the protein structure, resulting
1402 in the inactivation of biologically active enzymes, the imbalance of intracellular
1403 REDOX reaction, and the generation of a large number of ROS leading to cell damage
1404 (Sharma and Dietz, 2009). Nano-copper, a prominent metal nanomaterial, finds
1405 widespread use across various domains (Hu et al., 2022; Zhao et al., 2022). However,
1406 concerns have been raised regarding the significant harm nano-coppers can pose to
1407 human health and environmental safety. The liver is the main organ that is influenced
1408 by nanomaterials because it is the main organ involved in the metabolism of CuNPs
1409 (Jani et al., 1990). Tang et al. also found that the liver was the target organ for the
1410 accumulation of copper nanoparticles through gavage (Tang et al., 2018). Lei et al. (Lei

1411 et al., 2008) found that CuNPs could significantly increase triglyceride and
1412 phospholipid levels in the body through nuclear magnetic resonance technology and
1413 pattern recognition methods. Oral administration of CuNPs can cause hepatomegaly,
1414 hepatocyte necrosis, and hepatic insufficiency in rats and mice (Manna et al., 2012). In
1415 addition, Cu exposure can also produce significant toxic effects on the kidney, spleen,
1416 nerve, and gastrointestinal tract (Lei et al., 2008; Meng et al., 2007; Xu et al., 2012;
1417 Zhou et al., 2019).

1418 Biological contaminants influence the microbial composition of sediments. The
1419 introduction of ARGs and drug-resistant bacteria into sediments can alter the balance
1420 of microbial communities, potentially affecting nutrient cycling, sediment stability, and
1421 other crucial ecological processes (Kong et al., 2024). Viruses and pathogenic bacteria
1422 contribute to microbial contamination, affecting water quality in aquatic environments
1423 (Fong and Lipp, 2005; Pandey et al., 2014). Elevated microbial loads can compromise
1424 the safety of water for both aquatic life and human consumption, leading to the spread
1425 of waterborne diseases and impacting overall ecosystem health (Leclerc et al., 2002;
1426 López et al., 2009). Biological contaminants can also be toxic to aquatic plants. Viruses,
1427 pathogenic bacteria, and other biological agents may induce stress on plants, affecting
1428 their uptake of nutrients, growth rates, and overall health (Ashbolt, 2015; López et al.,
1429 2009). These effects can lead to changes in the abundance and distribution of aquatic
1430 vegetation. Aquatic plants can serve as vectors for transmitting pathogenic bacteria and
1431 viruses (Mehle and Ravnkar, 2012; Sime-Ngando, 2014). The presence of drug-

1432 resistant bacteria in plant tissues may contribute to the dissemination of antibiotic
1433 resistance in aquatic environments (Sime-Ngando, 2014; Yuan et al., 2023). This
1434 transmission pathway can have cascading effects on the health of associated aquatic
1435 fauna. Aquatic fauna are susceptible to infections caused by biological contaminants.
1436 Viruses, pathogenic bacteria, and antibiotic-resistant organisms can compromise the
1437 immune systems of aquatic organisms, increasing their vulnerability to diseases (Pipe
1438 and Coles, 1995). This heightened disease susceptibility may lead to declines in the
1439 population of aquatic organisms and disruptions in the ecological balance of aquatic
1440 ecosystems (Balbi et al., 2021; Mishra et al., 2023; Sun et al., 2023a). Emerging
1441 biological contaminants can impact the reproduction and development of aquatic
1442 animals (Balbi et al., 2021; Mishra et al., 2023; Sun et al., 2023a). Genetically modified
1443 organisms (GMOs) and RNA-based technologies, such as RNAi, can introduce novel
1444 genetic material into aquatic ecosystems. RNAi and other biological contaminants may
1445 interfere with the normal reproductive processes of aquatic organisms, potentially
1446 leading to reduced reproductive success, developmental abnormalities, and altered
1447 population dynamics (Kim et al., 2015; Mishra et al., 2023).

1448 Microplastics act as carriers of various pollutants, such as PCBs, PAHs, and heavy
1449 metal(loid)s (Barletta et al., 2019). These contaminants can leach from the surface of
1450 microplastics, leading to chemical contamination of water and sediments (Ahmed et al.,
1451 2021). This process introduces a new dimension of pollution to aquatic environments,
1452 affecting the overall quality of these habitats (Li et al., 2024). Microplastics can also

1453 negatively impact the physiology of aquatic plants, affecting processes such as
1454 photosynthesis and nutrient uptake (Ceschin et al., 2023; Ge et al., 2021). This can lead
1455 to reduced growth rates, altered reproductive patterns, and diminished aquatic plant
1456 health (Ceschin et al., 2023; Ge et al., 2021). Moreover, microplastics are often
1457 mistaken for food by aquatic organisms, leading to ingestion at various trophic levels
1458 (Egbeocha et al., 2018). This ingestion can cause physical harm, including internal
1459 injuries, blockages, and interference with digestive processes. The presence of
1460 microplastics in the digestive tracts of aquatic animals can also lead to malnutrition and
1461 reduced energy reserves (Alak et al., 2022; Harmon et al., 2024; Rakib et al., 2023).
1462 The toxicological consequences of microplastic-associated contaminants include
1463 disruption of endocrine systems, suppression of the immune system, and increased
1464 susceptibility to diseases. These effects can have profound implications for the health
1465 and survival of aquatic fauna (Ašmonaitė, 2019; Sreelakshmi and Chitra, 2021).
1466 Other ECs, such as liquid crystals, oil spills, prions, and a class of ECs called unknown
1467 or variable composition, complex reaction products, or biological materials (UVCBs),
1468 can also introduce hazardous substances into aquatic environments. The discharge of
1469 liquid crystal contaminants can disrupt water quality and affect the health of aquatic
1470 organisms (He et al., 2024). The presence of these compounds may alter nutrient
1471 cycling and cause ecological imbalances (He et al., 2024). Organometals, such as
1472 organomercury and organotin compounds, exhibit high toxicity to aquatic organisms.
1473 These contaminants can interfere with cellular functions, impair reproduction, and

1474 cause behavioural changes in fish and invertebrates (Gojkovic et al., 2023; Li et al.,
1475 2019). Accumulation of organometals in sediments may have long-term implications
1476 for benthic communities. Oil spills and organic solvents, including methyl tertiary-butyl
1477 ether (MTBE), can contaminate habitats (Bashir et al., 2020; Li et al., 2019). These
1478 contaminants can form slicks on the water surface, impact light penetration, and reduce
1479 oxygen exchange. The effects include the smothering of aquatic vegetation and
1480 disruption of feeding behaviours in aquatic animals (Bashir et al., 2020; Li et al., 2019).
1481 Prions associated with neurodegenerative diseases can enter aquatic environments
1482 through various pathways (de Motes et al., 2008). The presence of prions may pose a
1483 risk to the health of aquatic animals, potentially leading to neurological disorders. The
1484 effects on fish and other aquatic organisms are not fully understood but warrant further
1485 investigation (de Motes et al., 2008; Rickard et al., 2023). The UVCBs may also have
1486 unpredictable impacts on water and sediment quality and the health of aquatic plants
1487 and animals (Lai et al., 2022). Therefore, much research is needed to understand the
1488 specific effects of individual UVCBs.

1489

1490 ***Air quality.*** While the Industrial Revolution was a great success in technology, society,
1491 and services, it also introduced a significant quantity of harmful pollutants into the
1492 atmosphere (Huang et al., 2023a). These air pollutants can penetrate the respiratory
1493 system through inhalation. Meanwhile, for certain compounds direct air-to-skin dermal
1494 uptake is comparable to the inhalation intake, imposing a significant burden on human

1495 health (Cai et al., 2023; Garrido et al., 2018; Khan et al., 2024; Lao et al., 2018;
1496 Manisalidis et al., 2020; Wu et al., 2016; Xu et al., 2024; Zhang et al., 2023b).

1497 Numerous animal and human studies have shown that exposure to air pollutants,
1498 including ECs (e.g. PAHs, perfluoroalkyl sulfonate, organophosphorus ester, PBDEs,
1499 and paraben), can contribute to respiratory (He et al., 2022a), dermal (Pan et al., 2015),
1500 cardiovascular (Al-Kindi et al., 2020), immune disease (Wang et al., 2021d), and
1501 mortality (Fischer et al., 2015). Early exposure to these pollutants in humans tends to
1502 trigger and exacerbate multiple diseases in their later life (Shimpi et al., 2017; Wang et
1503 al., 2021d). It is confirmed that these air pollutants contribute to the production of ROS
1504 in mitochondria, cell membranes, and endoplasmic reticulum, ultimately leading to cell
1505 injury and adverse outcomes (Ghio et al., 2012; Zhang et al., 2022b). Furthermore, these
1506 airborne pollutants can greatly impact ecology and human health because of their long-
1507 range transport, persistence, and toxicity (Barroso et al., 2019). Importantly, complex
1508 airborne ECs can cause unpredictable toxic effects and health risks by interfering with
1509 transport, metabolism, and bioavailability after entering the human body (Zhang et al.,
1510 2020). For example, triphenyl phosphate levels on the skin surface of e-waste
1511 dismantlers were negatively correlated with the levels of three thyroid hormones used
1512 to evaluate thyroid function (Tang et al., 2023a). Human exposure to pollutants from
1513 coking contamination, including aromatic compounds mixture, metabolites of PAHs
1514 and their derivatives, chlorophenols, and nitrophenols, could increase DNA damage and
1515 lipid peroxidation, which is associated with increased disease risks (Jiang et al., 2023;

1516 Yang et al., 2023). Unexpectedly, residents near coking plants faced a 1.4 times higher
1517 risk due to coking contamination (Jiang et al., 2023). In addition, concentrations of ECs
1518 in the atmosphere reached thousands of picograms per cubic meter in emission sources
1519 or urban air (Barroso et al., 2019). The presence of ECs also appeared in remote areas,
1520 such as the Arctic region, because of their persistence and long-range atmospheric
1521 transport (Shoeib et al., 2006; Wallington et al., 2006).

1522 Notably, bioaerosol is another air pollutant of concern, which is a subset of atmospheric
1523 particles composed of bacteria, fungi, viruses, and their products, ranging in size from
1524 0.001nm to 100 μ m. Cyanotoxins may enter the atmosphere in the form of aerosols and
1525 spread further afield, posing a potential threat to atmospheric safety and contributing to
1526 the ecological risk of “air eutrophication” (Plaas et al., 2023). Bioaerosol is commonly
1527 released into the atmosphere from soil, water, vegetation, and animals (including
1528 humans), composting, sewage treatment plants, landfills, farms, and healthcare sites
1529 (Han et al., 2020; Rai et al., 2021; Rossi et al., 1991; Stockwell et al., 2019). Due to the
1530 diffusion of plant pollen, spores, and reproductive units of microorganisms, bioaerosols
1531 can be transported over long distances across geographical barriers (Després et al.,
1532 2012), posing a high public health risk. The occasional epidemiological spread of
1533 bioaerosol components can be highly disruptive to societies and economies, as
1534 demonstrated by the COVID-19 global pandemic (Leung, 2021). A previous study
1535 summarized the size-dependent particle deposition law of bioaerosols in different areas
1536 of the respiratory tract, showing that particles with a particle size larger than 0.5 μ m

1537 mainly deposit in the head airway through natural sedimentation and impact, while
 1538 particles with a particle size smaller than 0.5 μm can reach the lower respiratory tract
 1539 through further diffusion (Fröhlich-Nowoisky et al., 2016). It further leads to health
 1540 complications, such as allergic reactions, infectious diseases, acute toxic effects,
 1541 respiratory diseases, neurological effects, and toxic reactions to cancer and non-specific
 1542 symptoms (King et al., 2020).

1543

1544 **Risks to human health**

1545 *S[^]ofl r pB@ppqj j fkd xol j pl ro` bpr` e» p fkar p qf[^] i xfp[^] e[^] odbp)» dof[^] r iq[^] o[^] i x r kl a)»*
 1546 *^ka» fj mol nbo» t ^p q» a f p m l p[^] i» ^k» nboj b[^] q» q b» p l fi)» t ^q o» _ l a f b p)» ^ka» q b» ^f o)»*
 1547 *b p q[^] _ i f p e f k d f k q f[^] ^q b u m l p r o b m[^] t q e t ^v p d o x t f i a i f c b» k a x e r j ^k p» C[^] k d b q[^] i)» - / . &»*
 1548 *Q e b p b)» p r _ p q[^] k[^] b p)» j ^v» b k q o» q e b» e r j ^k» _ l a v» q e o l r d e» s[^] o f l r p)» b u m l p r o b)» o l r d p p)»*
 1549 *f k[^] i r a f k d f k d b p q f k d)» l k q j f k[^] q a x t ^q o x l o x d l a)» f k e[^] i f k d)» f o m l i i r q k q)» k a x a b o j ^i»*
 1550 *` l k q[^] ` q t f q» ` l k q j f k[^] q a x p r o c[^] ` b p)» % e f g q e b q[^] i)» - / 1 8)» b f b q[^] i)» - . 2 8)» M[^] - » k a»*
 1551 *?[^] o[^] b i[^])» - / 0 &» Q e b f o)» m b o p f p q b k q k[^] q o b)» j l _ f i f q)» ^k a m l q k q[^] i x d » ^` r j r i[^] q f k x e b»*
 1552 *b k s f o l k j b k q e b f d e q k x e b)» o f p h p l o b u m l p r o b)» f k q k p f c v f k d x e b f o f j n t ` q l k x e b[^] i q e)» b f b q*
 1553 *^i)» - . 2 8)» T[^] k d b q[^] i)» - / . ^ &» T[^] b x o b ` l d k f v b x e b)» a f s b o p b i f q o[^] q r o b x e[^] q e[^] p x u[^] j f k b a»*
 1554 *q e b)» m r _ i f[^] » e b[^] i q e» b a c b ` q » l o b j b a d f k d)» ` l k q j f k[^] k q)» ^k a)» f k p q[^] a)» l o m l s f a f k d)» ^»*
 1555 *` l j m o b e b k p f s b)» o f q[^] ^i x o b s f b t)» e b o b x t b)» f j x d x e f d e i f d e q p l j b l o x e b x o b i[^] q a x b a d o p f k»*
 1556 *q e f p x[^] p q j[^] l s f k d)» o b[^] l o _ ^ p f[^] » k a x p[^] k p i[^] q l k[^] i x o b p b[^] o[^] e +*

- 1557 Qeb» l kpbq» l o» s^ofl rp» lj f» » ^mmol^`ebp)» fk`irafkd» dbklj f`p)» mol qplj f`p)»
- 1558 q^kp`ofnqj f`p)»^ka»j bq`l il j f`p)»e^p»bk^_iba»qeb»abq`ql k»l o»j lib`ri^o`ibsbi»
- 1559 nboqo_^ql kp»ar b»q » bksfol kj bkq`i»bunl pr ob»^ka»_b`lj b»fk`ob`pfkdiv»rpba»q »
- 1560 fksbpqd^`q»el t »bksfol kj bkq`i»l kq`j fk^kq»`iqo»qeb»_fl il df`^i»rk`ql k»l ol od^kfpj p»
- 1561 %Hfj »kaH`kd)»-/. &We^kd»bq`i)»-/. _&L apk»qebpb»fkafkd»obfkdod`qat f`qfk»
- 1562 qeb»absbil nj bkq`ka»`nmif`^ql k»l o`asbop»l r q`lj b»m`qet`^vp)»t ef`e»`ob»`ebj f`^iiv»
- 1563 ^dkl pq` »`l k`bnq`^ij l abip»q`^qifkh»j lib`ri^o»fkdq`ql k»bsbkq»q »efdebo»ibsbi»p»l o»
- 1564 _fl il df`^i»obpnl kpbpl o»bibs^k`b»q »`ebj f`^i»ofph»`ppb»pj bkq`%`khib»bq`i)»- . - &
- 1565 ?b`rpb»qeb»unbofj bkq`i»abpfdk»l o»j bq`l il j f` »mmol`^`ebp»`efdeiv»sbop`qib)»f`q`^k»
- 1566 _b»^`nmifba»q »pq`av»j riq`mb»p`bk^ofl p»t f`q`»s^ofl rp»bksfol kj bkq`i»`l kafql kp»^ka»
- 1567 afabobkq`l od^kfpj p)»p` bii»p»`lj nibu»`l kq`j fk^kq` fuq`obp»`ka»`^pqt`^qob`cair bkq»
- 1568 %Hfj »kaH`kd)»-/. &Hl s`^bsf` »ka»Pffj npl k)»-/- &Sf`kq)»-- 6&W`^kv»pq`afbp»e`sb»
- 1569 abj l kpp`q`a»qeb»efde`r`qifq»l o»j bq`l il j f` »mmol`^`ebp»q` »`nfai»v»abq`q`r`ka`^j bkq`i»
- 1570 pefaq»fk»l od^kfpj »`rk`ql k»d o»`^»el pq`l o»bksfol kj bkq`i»j l abi»l od^kfpj p»^ka»
- 1571 abj l kpp`q`a»el t »qebpb»^`mmol`^`ebp»`^k»`lj nibj bkq`q`afql k`i»q`uf`fq»`fkaf`^q`op»
- 1572 %Arj`^p»bq`i)»-// &D`l`bq`i)»-// _&I`^_fkb»bq`i)»-// 0&Q`kd»bq`i)»-// - &W`kd»bq`
- 1573 ^i)»-/. &Abpnf`q»t`fabp`nob`a»`l k`bok)»`r`kabop`q`kafkd»qeb»erj`^k`eb`iq`»ofph»^ka»
- 1574 q`uf` »j b`e`kfpj p»obj`^fkp»`e`iibkdfkd»_b`rpb»l o»qebfo»avk`^j f` »k`q`ob)»`lj nibu»
- 1575 `lj ml`pfql kp)»^ka»`fkq`o`^`ql kp»l o»`l kq`j fk^kq»^ka»qebfo»j fuq`obp)»t ef`e»`mobpbkq`
- 1576 afaf`riq`bp»d o»`l ksbkql k`^ij l kfq`ofkd»`ka»j l abiifkd»x`j bt l ohp)»%bf»bq`i)»- . 2&

1577 *Kl kbq bibpp)»bsfabk`b)»ql r de»dbkbo`iiv»kl q)t bii»bpq`_ifpeba)»e^p»pr ddbpqa)»q^q»*

1578 *bunl pr obp»q`»B@q)»ob)»ppl`f`qat fq»qeb»d iil t fkd»afpb`pbp+*

1579

1580 ***Antibiotic resistance and infectious diseases.*** One of the pressing and increasing health

1581 threats posed by ECs is the rise of antibiotic resistance. PPCPs (e.g., antibacterial

1582 creams and ointments), when improperly used, disposed of, or inadequately treated,

1583 could contribute to the development of ARB (Anwar et al., 2020; Polianciuc et al.,

1584 2020; Zhang et al., 2023c). This outcome poses a significant threat to public health as

1585 conventional treatments become less effective, leading to an increased prevalence of

1586 infectious diseases (Polianciuc et al., 2020). For example, symptoms of infectious

1587 diseases, particularly those related to airway infections (e.g., lung infections), were

1588 much more common among individuals with compromised health or chronic conditions

1589 who used antibacterial medications.(Caioni et al., 2023). It has also been suggested that

1590 antibiotic resistance could amplify the mortality risks during pandemics of bacterial

1591 diseases, including tuberculosis and cholera, and even viral diseases, particularly in the

1592 case of influenza, where a significant proportion of deaths often is caused by bacterial

1593 pneumonia coinfections (Yang et al., 2022).

1594

1595 ***Endocrine disruption and reproductive disorders.*** Endocrine-disrupting chemicals,

1596 such as bisphenol A (BPA) and phthalates in plastics, represent a class of ECs that

1597 mimic or interfere with the endocrine hormones, often acting as agonists or antagonists.

1598 Endocrine-disrupting chemicals primarily target the female reproductive system. They
1599 can increase the risk of various reproductive disorders, including fertility issues,
1600 developmental abnormalities, and hormone-sensitive cancers (e.g., breast cancer)
1601 (Cantonwine et al., 2013; Laws et al., 2021; Matuszczak et al., 2019). For instance,
1602 individuals with polycystic ovarian syndrome (PCOS), a condition affecting nearly
1603 10% of women of childbearing age with unclear etiology, have been found to have
1604 higher BPA in their serum, urine, and follicular fluid compared to those without PCOS,
1605 suggesting that BPA exposure is an important contributor to the pathogenesis of PCOS
1606 (Laws et al., 2021).

1607

1608 ***Cardiopulmonary diseases.*** Airborne particulates can carry various ECs, including
1609 heavy metals (loids), POPs, nanoparticles, and even viruses (Dong et al., 2023b). The
1610 respiratory and cardiovascular systems become the primary targets, with potential
1611 consequences ranging from irritations (e.g., coughing) to chronic cardiopulmonary
1612 diseases (e.g., hypertension and chronic obstructive pulmonary diseases) (Qi et al.,
1613 2023; Sun et al., 2023b). A most recent meta-analysis comprising 13 studies showed
1614 that higher exposure levels of PFASs, especially for PFOS, perfluorooctanoic acid
1615 (PFOA), and perfluorononanoic acid, were significantly associated with a higher risk
1616 of hypertension (Pan et al., 2023). Notably, particulates with smaller sizes are much
1617 more harmful than larger particles because of the longer residence time and greater
1618 capacity for deeper penetration in the respiratory tract (Enyoh et al., 2020;

1619 Schraufnagel, 2020). Therefore, the airborne fine particulates could further amplify the
1620 health risks of the ECs contained. For instance, the interaction between airborne fine
1621 particles and viruses, such as H1N1, has been shown to extend viral distribution and
1622 aggravate respiratory tract infection (Dong et al., 2023b).

1623

1624 **Neurotoxicity.** Substantial evidence suggests that certain ECs, such as heavy
1625 metal(loid)s (e.g., arsenic and mercury), cyanotoxins (Stewart et al., 2006), and
1626 persistent organic pollutants (e.g., perfluoroalkyl compounds), possess neurotoxic
1627 properties (Kothapalli, 2021; Park et al., 2021). Chronic exposure to these substances
1628 is associated with an increased risk of neurological disorders, including cognitive
1629 impairments, developmental delays, and neurodegenerative diseases (Chen et al., 2016;
1630 Kodavanti, 2006). Even at low concentrations, these substances could exhibit great and
1631 long-lasting neurotoxicity (Lee, 2018). Early-life exposures are identified as a critical
1632 causal factor for the later development of Alzheimer's and Parkinson's diseases (Li et
1633 al., 2022b). Regions contaminated with PFAS in the drinking water exhibited a 33%
1634 higher mortality rate from Alzheimer's disease compared with uncontaminated areas
1635 (Mastrantonio et al., 2018).

1636

1637 **Immune system impacts and allergic reactions.** Emerging contaminants may influence
1638 the immune system, potentially leading to compromised immunity or triggering allergic
1639 reactions. Studies have reported that these substances can affect the activation and

1640 survival of immune cells, potentially contributing to allergic rhinitis and other allergic
1641 responses (Sollome and Fry, 2015). For example, epidemiological studies have
1642 demonstrated the immunosuppressive effects of PFAS on pediatric vaccination and
1643 other immune-related responses for both children and adults (e.g., diminished
1644 antibodies after vaccinations, increased risk of asthma) (Grandjean et al., 2012; Lee,
1645 2018; von Holst et al., 2021). A most recent study showed that prenatal exposure to
1646 PFOS and PFOA increased the risk of non-atopic asthma at the age of six by up to
1647 twofold (Sevelsted et al., 2023).

1648

1649 ***The description of EPFR reactivity and risks.*** Recent research has focused on
1650 understanding the properties and potential hazards of EPFR-containing particles. These
1651 particles have been found to display significant reactivity and toxicity, which is a cause
1652 for concern (Li et al., 2022a; Lieke et al., 2018). As a result, it is crucial to establish
1653 parameters to describe their reactivities to better understand their potential impact on
1654 human health and the environment. One potential parameter to describe the reactivity
1655 of EPFR-containing particles is the intensity of EPFR signals. However, this approach
1656 has limitations, as the detected EPFR signals are associated with various structures with
1657 different reactivities (Zhao et al., 2023b). Additionally, the captured ROS may not fully
1658 explain the reactivity of EPFRs, as their reactivity may occur through direct contact
1659 with target reactants without the generation of ROS, and the instantly captured ROS
1660 signals may not represent the reactivity of long-lasting EPFRs (Yang et al., 2017a).

1661 Further research is necessary to develop a proper parameter that correlates with the
1662 reactivity of EPFRs, which differs from the detected electron paramagnetic resonance
1663 signals, to evaluate their environmental implications accurately. Additionally,
1664 researchers should consider that EPFRs coexist with other chemical components, such
1665 as the parent chemicals, their degradation by-products, and reactive inorganic particles.
1666 The impacts of these coexisting components should be considered when identifying the
1667 reactivities or risks of EPFRs.

1668 The reactivities of EPFRs can lead to both adverse and beneficial effects, making their
1669 manipulation highly context-dependent. When EPFRs have detrimental environmental
1670 impacts, efforts should be made to mitigate or eliminate them. Conversely, if EPFRs
1671 play a positive role in pollution control, their influence should be enhanced and utilized,
1672 as seen in applications like biochar for organic contaminant degradation (Fang et al.,
1673 2015). Although EPFR formation has been studied in various processes (Liu et al.,
1674 2023; Tao et al., 2020), understanding the preferred or unpreferred conditions for EPFR
1675 formation and quantitative descriptions of their generation and decay kinetics remains
1676 limited. EPFRs differ from common contaminants, being highly dynamic and
1677 composed of various structures, necessitating studies on their environmental behavior
1678 and risks and the development of standardized experimental protocols and standard
1679 reference samples.

1680 In summary, the health risks associated with ECs will continue to be a major public
1681 health concern. More high-quality evidence and comprehensive strategies are urgently

1682 needed to better understand and mitigate their health effects. This requires
1683 interdisciplinary efforts, from establishing standardized contamination and public
1684 health surveillance systems to employing advanced epidemiological and molecular
1685 modelling and implementing evidence-based strategies. As we navigate this complex
1686 terrain, prioritizing research, regulatory measures, and public awareness will be
1687 paramount to curbing the adverse health effects of ECs and ensuring a healthier future
1688 for all.

1689

1690 MODEL-BASED ASSESSMENT OF FATE AND TOXICOLOGICAL RISKS 1691 OF EMERGING CONTAMINANTS

1692 **Modeling migration and environmental impacts of emerging** 1693 **contaminants**

1694 The development of mathematical models to understand the migration and impacts of
1695 ECs in water, soil, and air ecosystems is a current focal point in environmental pollution
1696 research (Arneeth et al., 2012). These models serve as valuable complements to
1697 monitoring networks, enriching our comprehension of EC sources, distributions, and
1698 life cycles. They also offer insights into the influencing mechanisms and environmental
1699 factors shaping EC dynamics. By facilitating comprehensive risk assessments for both
1700 human health and ecosystems, EC models play a pivotal role in providing early
1701 warnings, projecting outcomes under future climate scenarios, and evaluating the
1702 efficacy of remediation technologies.

1703 Quantitative structure-activity relationships (QSARs), one class of numerically
1704 analytical models that are developed highlighting the intrinsic correlations with or
1705 dependency on a pool of topologically, spectrally, and physicochemically interpretable
1706 structural information can be used as an alternative approach to unravel the
1707 toxicologically relevant or environmental influencing mechanism, and the structural
1708 requirements for transfer, migration, and toxicity of ECs. Furthermore, QSARs
1709 developed using advanced statistical methods, such as machine learning techniques,
1710 along with comprehensive datasets encompassing not only structural descriptors but
1711 also environmental factors, can effectively predict the environmental fate of emerging
1712 contaminants, including volatilization, photodegradation, and bioaccumulation.
1713 (Dracheva et al., 2022; Xiong et al., 2023). Though QSARs were classically applied to
1714 the virtue-screening of novel effective drugs for human health, the application of
1715 QSARs in environmental research arouses new vitality and greatly facilitates
1716 understanding the cause for the variance of toxicology and behaviour of pollutants and
1717 even provides basic data guiding risk management and remediation administration.
1718 Nevertheless, the development of QSAR models is typically hindered by several
1719 limitations. These include a scarcity of experimental training data, issues related to
1720 over-fitting and noise in statistical techniques, and a lack of consideration for
1721 environmental factors. These environmental factors play a crucial role in influencing
1722 the transport, precipitation, adsorption, and desorption processes in environmental
1723 matrices. On the contrary, the stability, reliability, and predictability of QSARs would

1724 be enhanced if meta-learning big data were involved in development (Schlender et al.,
1725 2023). The integration of environmental and structural factors of ECs is likely to
1726 aggravate the uncertainty of QSARs because they are hardly accommodated with the
1727 significant correlation in one model, whereas it is of particular interest for augmentation
1728 of the QSAR applicability domain. Given the numerous limitations of QSARs, high
1729 uncertainty or application factors are applied to QSAR modeling outputs during early
1730 tiers of risk assessment.

1731 Various modelling approaches have been developed to study the transport and impacts
1732 of ECs, including fate and transport models, multimedia models, and pharmacokinetic
1733 models. Fate and transport models simulate the movement and transformation of
1734 pollutants in different environmental compartments, such as air, water, soil, and biota
1735 (Wania and Mackay, 1996). Multimedia models integrate the fate and transport
1736 processes across multiple compartments to assess the overall environmental behavior
1737 of pollutants on regional to global scales (Liu et al., 2023). Pharmacokinetic models
1738 focus on the uptake, distribution, metabolism, and elimination of pollutants within
1739 organisms. These models draw from the findings of laboratory and field experiments to
1740 represent the physicochemical, mineralogical, and hydraulic properties of ECs,
1741 adsorption-desorption, chemical/biological transformation, and their retention in and
1742 exchange across environmental compartments.

1743 Numerical models that integrate multiple components, multiphase flow, and multiple
1744 reaction mechanisms have become the mainstream for simulating ECs in soil-

1745 groundwater systems. Notable examples include TMVOC (Pruess and Battistelli,
1746 2005), TOUGHREACT (Xu et al., 2004), RT3D (Clement, 1999), PFLOTRAN
1747 (Hammond et al., 2014), and PHT3D (Prommer et al., 2003). For ECs in ecosystems,
1748 bioaccumulation models have been developed to integrate ecological principles,
1749 dynamic processes, and complex environmental conditions to describe and predict
1750 contaminants accumulation and migration processes within ecosystems, such as
1751 CalTOX (Mckone and Enoch, 2002), KABAM (USEPA, 2009). However, due to the
1752 complex toxic mechanisms and biological effects involved in the transport processes of
1753 ECs in organisms (Muir et al., 2023a), there is currently a lack of universal, process-
1754 based models for the migration of ECs in ecosystems.

1755 Research efforts have increasingly focused on exploring the potential of atmospheric
1756 transport as a significant mechanism for redistributing ECs across various
1757 environmental compartments on both regional and global scales. To study this
1758 phenomenon, scientists have developed trajectory models as well as regional and global
1759 three-dimensional chemical transport models. These models aim to simulate the
1760 transport and evolution of a wide array of ECs, including microplastics, POPs, PFOSs,
1761 and PAHs. For instance, certain POPs undergo long-range atmospheric transport,
1762 leading to their subsequent deposition onto the Earth's surface and potential re-emission
1763 (Mackay, 1993). This process, commonly referred to as "hopping," facilitates the rapid
1764 transport of POPs to Northern high latitudes at rates approximately ten times faster than
1765 in tropical regions (Wania and Mackay, 1996). Studies also reveal that, despite global

1766 reductions in PAH emissions in recent decades, the concentrations of airborne PAHs in
1767 the Arctic region have not shown a significant decline because of the offset from
1768 increased volatilization from surfaces (e.g., ocean, snow, ice, permafrost, and soil)
1769 because of climate warming (Yu et al., 2019).

1770 Despite recent progress, important challenges remain in modelling ECs to understand
1771 their fates and impacts. The scarcity of observations is a key limiting factor in
1772 evaluating the models of most ECs, which calls for the design of multi-scale
1773 observation networks guided by models. Additionally, in the case of many ECs, there
1774 is still a lack of comprehensive understanding of transport and fate processes and
1775 toxicology within and across environmental compartments. In particular, researchers
1776 have increasingly highlighted the complex impacts of multi-pollutant interactions.
1777 Finally, the framework to represent ECs through different environment compartments
1778 may see a revolution catalyzed by the rapid development of Earth system models.

1779

1780 **Advancing evaluation and management of emerging contaminants** 1781 **through artificial intelligence**

1782 In recent years, there has been a significant increase in the use of machine learning to
1783 understand and predict the chemical reactivity, toxicity, transport, and remediation of
1784 environmental contaminants (Zhong et al., 2021). Among the various environmental
1785 contaminants being explored by these computational methods, PFAS has garnered
1786 particular scientific attention (Biswas et al., 2022; Yamijala et al., 2020). The majority

1787 of machine learning studies on PFAS have focused on supervised learning techniques,
1788 with only a handful of studies using unsupervised learning approaches. Within the
1789 former, Wong Group carried out the first machine learning study on PFAS to predict
1790 and rationalize carbon-fluorine (C-F) bond dissociation energies to aid in their efficient
1791 treatment/removal (Raza et al., 2019). Using Random Forest, Least Absolute Shrinkage
1792 and Selection Operator Regression, and Feed-forward Neural Networks, accurate
1793 predictions for C–F bond dissociation energies within chemical accuracy of the PFAS
1794 reference data were obtained (deviations less than 0.70 kcal/mol). In addition, this
1795 pioneering study demonstrated the efficiency of the machine learning approach, which
1796 required less than 10 min to train the data and less than a second to predict a new
1797 compound's C–F bond dissociation energy.

1798 Within the area of unsupervised machine learning, new unsupervised/semi-supervised
1799 machine learning models have been created to automatically predict the bioactivities of
1800 PFAS in various human biological targets, including enzymes, genes, proteins, and cell
1801 lines (Kwon et al., 2023). The semi-supervised metric learning models were used to
1802 predict the bioactivity of PFASs found in the recent Organisation of Economic Co-
1803 operation and Development (OECD) report list, which contains 4730 PFASs used in a
1804 broad range of industries and consumers. Other studies have also used machine learning
1805 to predict the bioconcentration of organic contaminants by plants, the ecotoxicity of
1806 chemicals, and the dissipation of organic contaminants in plants (Gao et al., 2022a;
1807 Watts, 2012). Together, these studies highlight the capabilities of machine learning to

1808 understand the reactivity of PFAS, which other researchers can leverage to predict and
1809 screen other environmental contaminants.

1810 Artificial intelligence is poised to revolutionize pollution control at the source,
1811 sustainable remediation of contaminated sites, and the implementation of sustainable
1812 management practices to prevent contamination (Figure 5). Through the utilization of
1813 AI technologies, such as machine learning and deep learning, significant progress can
1814 be achieved in addressing environmental challenges (Xu et al., 2021). AI can improve
1815 the efficiency and effectiveness of pollution control measures by analyzing intricate
1816 datasets, forecasting contaminant behavior, and refining remediation strategies (Xu et
1817 al., 2023). Furthermore, AI can play a pivotal role in monitoring air and water quality,
1818 pinpointing pollution sources, and predicting the dispersion of pollutants to enable
1819 prompt and targeted remediation actions. In addition, AI-driven digital simulations and
1820 digital twins can replicate environmental scenarios, assess remediation approaches, and
1821 monitor the success of mitigation efforts to enhance decision-making and resource
1822 allocation in pollution management (Wang et al., 2023e). Overall, AI serves as a potent
1823 tool for enhancing environmental sustainability by offering data-driven insights,
1824 optimizing remediation endeavors, and advocating proactive measures to safeguard the
1825 environment.

1826 GLOBAL EFFORTS TO CONTROL EMERGING CONTAMINANTS

1827 **Pollution prevention**

1828 The increasing recognition of ECs has led to global efforts to devise efficient strategies
1829 for their prevention, detection, and remediation (Figure 5). Governments worldwide
1830 have initiated policies to encourage industries and economic sectors to reduce source
1831 pollution by changing their production processes, operations, and material usage. For
1832 instance, the European Union has implemented a series of policies and regulations to
1833 ensure the protection of the environment and reduce pollution. One of the key
1834 components of this environmental framework is the Integrated Pollution Prevention and
1835 Control (IPPC) directive, which came into effect in 2008 to prevent and reduce
1836 pollution from industrial operations (Ramos Peralonso 2024). This directive applies to
1837 various sectors, including energy, mining, and manufacturing, and requires industries
1838 to adopt Best Available Techniques (BAT) to reduce emissions and waste generation
1839 (Daddi et al. 2014). The IPPC directive complements other regulations such as the
1840 Registration, Evaluation, Authorisation, and Restriction of Chemicals (REACH), the
1841 Zero Pollution Action Plan, and the “polluter pays” principle (European Commission
1842 2021). These regulations hold industries and businesses accountable for their
1843 environmental impact, promote sustainable practices, and ensure the long-term health
1844 and well-being of people and ecosystems. Similarly, the United States Congress enacted
1845 the Pollution Prevention Act (PPA) to promote industry pollution prevention and
1846 reduction efforts (Gad 2024). The act aimed to encourage businesses to adopt practices

1847 that would minimise or eliminate pollution at the source through changes in production
1848 processes, operation methods, and the use of raw materials.

1849 To balance economic development and environmental stewardship, the Chinese
1850 government has implemented diverse laws and regulations to address pollution and
1851 enhance the country's environmental conditions (Yang, Gao, and Li 2022). The
1852 Environmental Protection Law (EPL), initially enacted in 1989 and revised in 2014,
1853 stands as a cornerstone of legislation governing environmental protection in China
1854 (Zhang et al. 2017). Beyond the EPL, the country has introduced specific laws and
1855 regulations focusing on distinct facets of environmental protection, encompassing the
1856 Water Pollution Prevention and Control Law, Air Pollution Prevention and Control
1857 Law, and Soil Pollution Prevention and Control Law (Feng and Liao 2016; Liu et al.
1858 2023; Wu et al. 2015) and recently the Action Plan for Controlling Emerging
1859 Contaminants in 2022 issued by the state council. Several other countries have also
1860 enacted numerous regulations to prevent pollution and minimize environmental
1861 contamination across different industries. The United Nations Environment Programme
1862 has reported a 38-fold surge in environmental legislation implemented from 1972 to
1863 2019 (UNEP 2019). As of 2017, 176 countries possess legislative frameworks for the
1864 environment, and 150 countries have incorporated environmental protection or the
1865 entitlement to a healthy environment in their constitutions (IISD 2019). Additionally,
1866 164 countries have instituted government-level entities tasked with overseeing
1867 environmental protection.

1868 Despite these advancements, enforcing these laws faces challenges, as weak
1869 enforcement is a global trend exacerbating environmental threats. The difficulties in
1870 enforcing global environmental law stem from the reluctance of individual states and
1871 the lack of effective enforcement mechanisms on the international level (Sago 2019).
1872 While there has been a rise in cooperative international efforts to protect the
1873 environment, the enforcement of these laws remains a common issue. The disparity in
1874 environmental protection legislation between high-, middle-, and low-income countries
1875 may result in outsourcing production-linked emissions to low-income countries. In
1876 some developing nations, the execution and enforcement of pollution control policies
1877 are hindered by underfunded and politically weak government bodies responsible for
1878 implementation, which hampers effective enforcement (Bell and Russell 2018). The
1879 focus on economic growth over environmental protection during the transition phase
1880 has resulted in inconsistent and incoherent environmental laws and regulations (Gupta,
1881 Saksena, and Baris 2019). Additionally, weak property rights, poor access to credit, and
1882 limited technology choices distort the costs of improvements to environmental quality,
1883 further hindering effective pollution control (Ekstrom 2015). The inadequacy of current
1884 pollution prevention measures necessitates more concrete actions to address pollution
1885 on a global scale. Several strategies can be implemented to achieve this, including
1886 enforcing regulatory frameworks, adopting sustainable practices, promoting
1887 technological innovation, and engaging the public actively. These multifaceted
1888 approaches are essential for reducing pollution levels and ensuring the preservation of

1889 the environment for future generations. Herein, green chemistry presents particularly
1890 important opportunities for innovation and pollution prevention as we strive to achieve
1891 the Sustainable Development Goals (Lou et al., 2022). However, as identified by
1892 Erythropel et al. (Erythropel et al., 2018), two green chemistry principles of particular
1893 relevance to ECs, design benign chemicals (principle 4) and design for degradation
1894 (principle 10), have received relatively less attention, and thus represent timely research
1895 opportunities for pollution prevention.

1896



1897

1898 Figure 5. Strategies for controlling emerging contaminants encompass various
1899 measures, including pollution control at the source, sustainable remediation to clean up
1900 contaminated sites, and sustainable management practices to prevent contamination.

1901

1902 Pollution remediation technologies

1903 Many remediation technologies have been developed to tackle the urgent global
1904 problem of the environmental accumulation of anthropogenic pollutants (Singh and
1905 Ram, 2022). These technologies are vital in cleaning up contaminated sites and
1906 restoring them to environmentally acceptable conditions. Remediation methods span a
1907 spectrum of approaches, including physical techniques like excavation, soil vapour
1908 extraction, and chemical and biological treatments designed to degrade or immobilize
1909 contaminants in both soil and water (Hamadani et al., 2020). The choice of a specific
1910 environmental remediation method is contingent on the type and extent of
1911 contamination, with each method having its own set of advantages and disadvantages.
1912 Physical remediation techniques employ various processes and technologies to extract
1913 pollutants from the soil, restoring its usability. These encompass physical engineering
1914 measures, soil heat treatment technology, and adsorption technology (Baldissarelli et
1915 al., 2019; L. Li et al., 2023). Soil heat technology, conventionally used for pollutant
1916 removal via soil heating-induced volatilization, also emerges as an alternative for
1917 enhancing soil conditions (Lee et al., 2024; Sun et al., 2024). Additionally, adsorption,
1918 a conventional physical remediation method, relies significantly on the robust
1919 adsorptive capacities of activated carbon and biochar materials (Liu et al., 2021; Qi et
1920 al., 2022; Zhao et al., 2023). The large specific surface area, porous structure, and
1921 various forms of activated carbon enable efficient absorption of a broad spectrum of
1922 pollutants (Fan et al., 2023). Biochar, recognized as an environmentally friendly

1923 material, not only plays a pivotal role in alleviating soil contamination but also
1924 enhances the properties of degraded soil, serving as an ideal habitat for beneficial
1925 microbes (Blenis et al., 2023; Cabral Mielke et al., 2022). Ultrasonic waves are effective
1926 in destroying the structure of algae cells through the mechanical vibration effect
1927 (Dehghani, 2016). Additionally, physical methods such as manual salvage or
1928 mechanical algae removal equipment can be used to prevent the accumulation of
1929 cyanobacteria. Furthermore, the photocatalytic degradation of cyanotoxins can be
1930 achieved through the use of ultraviolet or visible light irradiation (Khadgi and Upreti,
1931 2019).

1932 The handling of environmental pollutants like agricultural film and other plastic waste
1933 could be effectively addressed through physical recycling methods followed by the
1934 reuse of processed materials (Picuno, 2014; Picuno et al., 2012). Physical recycling
1935 involves systematically sorting, cleaning, shredding, and melting of plastic waste to
1936 create new raw materials. These materials find application in producing diverse items
1937 such as fertilizer bags, garbage bags, and agricultural recycling water pipes (Civancik-
1938 Uslu et al., 2021). This approach not only mitigates the environmental repercussions of
1939 plastic pollution by diverting waste from landfills but also contributes to diminishing
1940 the need to produce new plastic. However, it is essential to acknowledge that
1941 mechanical recycling processes, including sorting, grinding, washing, drying, and re-
1942 granulation, may introduce pollution, such as volatile organic compounds and

1943 microplastic emissions (Fuller et al., 2020; Süß and Fischer, 2023). The economic
1944 viability of the recycling technology is also a major consideration.

1945 In the realm of chemical remediation, the focus is on transforming and reducing the
1946 mobility, effectiveness, and toxicity of pollutants in the environment using various
1947 chemical technologies. These include photolysis, Fenton processes, photocatalysis, and
1948 motorized repair processes (Brillas, 2021; Qu et al., 2023a, 2023b). Photolysis
1949 leverages light radiation to decompose contaminants in soil, water, or air (Curran et al.,
1950 1992). When contaminants are exposed to light radiation, the energy from the light can
1951 initiate chemical reactions that break down the contaminants into less harmful
1952 substances. Photolysis is particularly effective for degrading organic compounds, such
1953 as industrial chemicals, that are difficult to remove using other methods (Carena et al.,
1954 2020).

1955 Fenton technology is a chemical remediation method that uses the oxidation of iron
1956 ions (Fe^{2+}) in the presence of hydrogen peroxide to generate hydroxyl radicals (Ribeiro
1957 and Nunes, 2021). These hydroxyl radicals are highly reactive and effectively oxidize
1958 pollutants, transforming them into less toxic substances. This process has been widely
1959 studied and applied to treat various types of contaminated water and soil (W. Li et al.,
1960 2023; Xu et al., 2024). Photocatalysis is another commonly used chemical remediation
1961 method that involves using catalysts to produce hydroxyl radicals, which then facilitate
1962 the rapid oxidation and decomposition of pollutants (Ahmad et al., 2020). This method
1963 has shown promise in treating organic pollutants and has been extensively researched

1964 for its potential applications in environmental remediation (McCullagh et al., 2011;
1965 Mohammed et al., 2023). Electric remediation, also known as electrokinetic
1966 remediation, uses direct electric current to remove organic and inorganic contaminants
1967 from contaminated soils (Felter et al., 2021) by enriching contaminants to either the
1968 cathode or anode zone through electroosmosis, electromigration, and electrophoresis
1969 under an electric field (Cameselle, 2014). This technology is considered
1970 environmentally friendly and can be used to migrate and remove pollutants from the
1971 soil and sediment matrix.

1972 While physical and chemical remediation methods have played crucial roles in
1973 combatting environmental contamination, they come with inherent limitations,
1974 including the necessity for advanced infrastructure, skilled personnel, high processing
1975 costs, increased reagent requirements, and the potential generation of secondary
1976 pollutants. For instance, *in situ* chemical oxidation is considered a rapid and effective
1977 means of eliminating organic pollutants from contaminated areas (Rosas et al., 2013;
1978 Suanon et al., 2020). However, it is expensive and can yield undesirable harmful
1979 oxidation by-products, further harming the environment. Additionally, potent oxidizing
1980 agents pose substantial health risks to those handling them, underscoring the ongoing
1981 need for research and innovation in developing more sustainable and efficient
1982 remediation strategies (Xiang et al., 2022).

1983 Bioremediation is a remediation approach that uses a biological system, such as
1984 bacteria, fungi, microalgae, or plants, to eliminate or neutralize pollutants from a

1985 contaminated site (Huang et al., 2023b). This method is considered cost-effective
1986 because of the relatively low cost of implementing and maintaining bioremediation
1987 systems compared with other remediation techniques (Line et al., 1996; Watanabe,
1988 1997). Additionally, bioremediation is viewed as an eco-friendly approach because it
1989 relies on natural processes and does not involve the use of harsh chemicals that may
1990 further harm the environment. Furthermore, bioremediation is socially acceptable as it
1991 aligns with the growing emphasis on sustainable and environmentally conscious
1992 practices(Xiang et al., 2022). While bioremediation is a promising approach for
1993 managing pollutants in the environment, its full potential has yet to be realized because
1994 of several challenges associated with its implementation in natural environments
1995 (Borchert et al., 2021). One of the primary challenges is the poor colonization and
1996 performance of inoculated microbes in natural environments. When introduced into
1997 contaminated sites, these microbes may struggle to survive and effectively degrade
1998 pollutants due to competition with native microorganisms, limited availability of
1999 nutrients (including trace concentration of micropollutants well below KM (Kundu et
2000 al., 2019; Sun et al., 2021a), and adverse environmental conditions (Radwan et al.,
2001 2019). Additionally, the use of plants in bioremediation can be time-consuming, as they
2002 require sufficient time to grow and establish themselves before they can effectively
2003 remove pollutants from the environment. Furthermore, high concentrations of mixed
2004 pollutants in contaminated sites can inhibit the growth of both plants and microbes,
2005 limiting their ability to remediate the environment (Harindintwali et al., 2024). The

2006 environmental heterogeneity of contaminated sites also poses a challenge, as different
2007 areas within a site may have varying levels and types of contamination, requiring a
2008 tailored approach for effective remediation. To address these challenges, researchers
2009 have proposed integrating plants, adsorbents (such as biochar), and microbes into a
2010 single system for remediating contaminated sites (Harindintwali et al., 2020; Xiang et
2011 al., 2022). This integrated approach aims to leverage the complementary abilities of
2012 plants, adsorbents, and microbes to enhance the overall remediation process. By
2013 combining these elements, researchers seek to create a synergistic system that can more
2014 effectively mitigate the challenges associated with bioremediation and improve its
2015 overall performance in diverse environmental settings. Microbiome management is also
2016 an interesting development perspective in bioremediation (Kour et al., 2021).

2017

2018 **Sustainable management strategies**

2019 In addressing the challenges of ECs, sustainable management plays a pivotal role in
2020 their control and governance. Emphasis should be directed to advancing technologies
2021 for the management of ECs and undertaking critical research on environmental risk
2022 assessment and management of toxic and hazardous chemicals. Further research on the
2023 ecological and environmental harm mechanisms of ECs should be accelerated, and
2024 investments should be made in research on new theories and technologies for
2025 sustainable management strategies related to ECs. An environmental risk management
2026 information system for chemical substances should be established, and a platform for

2027 calculating toxicology and exposure prediction of chemical substances should be built.

2028 The early assessment and identification of key pollutants are essential for efficient

2029 control. Besides, innovation and education in green and sustainable chemistry,

2030 technology, and engineering can promote the generation of greener and more

2031 sustainable products and processes (Constable, 2021; Kümmerer and Clark, 2016).

2032 Enterprises associated with emerging pollutants should actively implement their

2033 primary responsibility, increasing national and corporate investment in scientific

2034 research is imperative for effective governance of emerging pollutants. In recognizing

2035 that scientific research is fundamental to decision-making in pollution control,

2036 sustained efforts are needed to enhance technological input. This effort involves

2037 understanding potential emerging pollutants' origins, trends, hazards, and control

2038 technologies. Scientific decision-making facilitates precise and effective pollution

2039 control measures.

2040 Actively engaging in international cooperation is crucial, especially in cases where

2041 comprehensive research information is lacking. Utilizing global expertise and

2042 experiences in scientific research and management accelerates the screening and

2043 environmental risk control of emerging pollutants. Simultaneously, mechanisms for

2044 fund allocation are established, drawing insights from international conventions to

2045 support pollution control initiatives at international, national, regional, and corporate

2046 levels.

2047 Rigorous adherence to national and local requirements for the governance and
2048 sustainable control of ECs is required. Administrative departments should strengthen
2049 the supervision of the production, processing, use, import, and export of prohibited or
2050 restricted toxic and harmful chemical substances and their related products and
2051 scientifically and sustainably manage new pollutants from the source. Those
2052 comprehensive sustainable management strategies encompassing technological
2053 innovation, ecological understanding, and corporate responsibility aim to address the
2054 multifaceted challenges posed by ECs in a sustainable manner.

2055

2056 **MANAGEMENT AND EDUCATION**

2057 **Regulatory measures and policies**

2058 The increasing global production and use of chemicals in a widening range of
2059 applications and products requires a strict hazard assessment and management to
2060 protect public health and the environment. Regulatory measures and policies, therefore,
2061 play a key role in managing the production, use, and disposal of chemicals to minimize
2062 potential harm. These measures aim to strike a balance between industrial innovation
2063 and the search for environmentally safe chemicals to protect the health of organisms at
2064 all biological scales (Wang et al., 2021a; Wang and Yu, 2024).

2065 A cornerstone of chemicals management is national regulation like the European
2066 Registration, Evaluation, Authorisation and Restriction of CHemicals (REACH) and
2067 the assessment schemes of, for instance, the US Environmental Protection Agency (US

2068 EPA) or the Chinese Ministry of Ecology and Environment that require manufacturers
2069 of chemicals to carry out comprehensive safety studies before placing their products on
2070 the market. However, regulatory efforts are not effective or equitable without effective
2071 implementation and enforcement of such policies. On an international scale,
2072 corresponding frameworks, in which scientific experts assess data on chemicals for
2073 potential hazards, exposure levels, bioaccumulation, and toxicity, include the Basel (on
2074 hazardous waste), Rotterdam (on information on exported hazardous substances),
2075 Stockholm on POPs and Minamata (on mercury) Conventions. The Globally
2076 Harmonized System of Classification and Labelling of Chemicals is a prime example
2077 of an international effort at the UN level to standardize management and assessment
2078 practices. Internationally accepted tools for testing, evaluating, and managing
2079 chemicals have been developed by the OECD and its members. Outside the OECD, the
2080 Inter-Organization Programme for the Sound Management of Chemicals provides
2081 comprehensive support to emerging economies and developing countries, where new
2082 chemical industries and consumer markets rapidly develop, but often with limited
2083 infrastructure and capacity for proper management of chemicals and waste.

2084 One of the 17 Sustainable Development Goals (SDGs), launched by the UN General
2085 Assembly in 2015, addresses the sound management of chemicals and all wastes
2086 throughout their life cycles and decreasing their release into air, water, and land.
2087 However, more effort is needed to achieve the goal of preventing significant adverse
2088 effects of chemical pollution on human health and the environment, as stated in the

2089 United Nations Environment Programme's Global Chemicals Outlook II (Anonymous,
2090 2019). It is well-documented that chemical pollution causes a wide range of damages
2091 to human and ecosystem health at local, regional, and global scales (Naidu et al., 2021).
2092 Among other factors, pollution is responsible for global biodiversity loss (Mueller et
2093 al., 2023; Sigmund et al., 2023), human diseases (Fuller et al., 2022; Landrigan et al.,
2094 2018a), soil and water degradation (Backhaus et al., 2012; Beaumelle et al., 2021;
2095 Oginah et al., 2023), stratospheric ozone depletion (Tang et al., 2011) and climate
2096 change (Isaksen et al., 2009).

2097 Policymakers need to balance economic, social, and environmental arguments when
2098 deciding on measures for the sound management of chemicals. Where there is evidence
2099 of environmental impact and harm from exposure to, e.g., endocrine-disrupting
2100 chemicals, PFAS, and many other chemicals, regulators may impose restrictions, bans,
2101 or set limits on emissions and discharges into the environment. These measures are
2102 often based on scientific evidence and aim to protect vulnerable populations and
2103 ecosystems. Here, the precautionary principle is an important strategy that requires
2104 taking preventive action in the face of uncertainty about potential harm. Where
2105 scientific evidence is inconclusive, regulators should opt for a cautious approach and
2106 impose restrictions until further research clarifies potential risks.

2107 Efforts to improve the handling of chemicals go beyond their production and
2108 application stages to include properly disposing of waste and recycling products
2109 containing dangerous substances. While progress has been made in many areas, there

2110 is an urgent need for a more consistent alignment of all actors on this common goal of
2111 chemical safety. International cooperation is therefore essential to address the global
2112 nature of pollution by chemicals and waste. Recently, scientists asked for the
2113 establishment of an overarching international body to facilitate and foster broad
2114 bidirectional science-policy interactions on chemicals and waste (Wang et al., 2021f).
2115 Such a Science Policy Panel (SPP) must address chemical pollution's multifaceted and
2116 heterogeneous impacts that often show dynamic development. The scope of this new
2117 SPP goes beyond the remit of the above-mentioned existing bodies because their scopes
2118 and mandates are limited to certain chemicals, geographical areas, or jurisdictions.
2119 Rather, the SPP needs to work on the large array of “chemicals of emerging concern”
2120 and novel waste streams, besides the well-described legacy pollutants, trying to avoid
2121 “analysis paralysis” (the inability of decision making by overanalysis or overthinking)
2122 (Ågerstrand et al., 2023). The SPP must establish and enforce a strict conflict-of-interest
2123 policy (Schäffer et al., 2023). In particular, experts with a conflict of interest connected
2124 to a financial or material gain would pose a high risk of conflicting and/or incompatible
2125 outcomes or delayed implementation of solutions in the decision-making process and
2126 should not be allowed to participate in the core work of the SPP, but may still participate
2127 and contribute as observers. Independent audits should be established to verify
2128 compliance with conflict-of-interest provisions to recommend corrective action if
2129 necessary and ensure that the outputs of SPPs are transparent, impartial, credible, and
2130 scientifically robust.

2131 The new SPP, currently prepared by the UNEP Open-ended Working Group, is expected
2132 to strengthen these efforts by recognizing the interconnectedness of global chemical
2133 trade and pollution. Through regulatory measures, society can harness the benefits of
2134 chemicals while minimizing the adverse effects of hazardous chemicals.

2135

2136 **Public awareness and education**

2137 Public awareness and education initiatives are instrumental in engaging individuals and
2138 communities in the efforts to address emerging pollutants. By increasing public
2139 knowledge and understanding of emerging pollutants, their sources, and potential
2140 impacts, we can promote responsible behaviour and encourage individuals to make
2141 informed choices that contribute to pollution prevention. There is a need to conduct
2142 public education through educational campaigns, workshops, and outreach programs
2143 on the scientific aspects of ECs, guiding the public in developing a scientific awareness
2144 of the environmental risks associated with ECs and fostering a commitment to green
2145 consumption principles. Those can empower individuals to adopt environmentally
2146 friendly practices and support sustainable behaviours. Meanwhile, drawing inspiration
2147 from existing international conventions, the control of emerging pollutants is executed
2148 in accordance with international law. Besides, leveraging international conventions
2149 becomes pivotal as it refines its regulatory framework and establishes a robust
2150 governance system for emerging pollutants. Collaboratively with the global
2151 community, environmental risk identification, assessment, and control of chemicals are

2152 conducted. This not only realizes commitment to controlling emerging pollutants but
2153 also fosters global initiatives for pollution control, propelling the green development of
2154 the global chemical industry and contributing to worldwide environmental governance.
2155 To actively engage in international environmental agreements concerning ECs and
2156 participate in global initiatives for managing these contaminants is essential. By
2157 actively contributing to international conventions and actions related to ECs, a positive
2158 impact can be made on global environmental governance.

2159

2160 **SOME LESSONS LEARNED**

2161 The systematic discovery of new contaminants has traditionally been a grand goal of
2162 Environmental Sciences. Compound classes that were initially considered safe and inert
2163 (e.g., chlorinated hydrocarbons in the old times, PFAS, at present) turned out to be
2164 prominent contaminants as more comprehensive evidence emerged (Budtz-Jorgensen
2165 and Grandjean, 2018). At the same time, the number of chemicals registered by the
2166 Chemical Abstract Service is increasing exponentially (see Figure 1), augmenting the
2167 likelihood of adverse effects and reinforcing efforts to recognize potential pollutants of
2168 tomorrow early on (Muir et al., 2023b). As illustrated in Figure 1, over the years, many
2169 relevant chemicals, pathogens, and (nano)particles have been discovered. They
2170 subsequently became the subject of in-depth fate and remediation studies before being
2171 the equivalent of “usual suspects” and making their way into regulation and routine

2172 monitoring efforts. While the term “Emerging Contaminants” is an ephemeral
2173 classification, a review of the last decades can highlight the drivers that make chemicals
2174 emerge, and illustrate the timespan between emergence and further action.

2175 One important driver of discoveries is analytical innovation, as illustrated in Figure 1.
2176 Biannual reviews on Water Analysis and Emerging Contaminants in the journal
2177 Analytical Chemistry are a telling record of how access to new methodologies has been
2178 instrumental in bringing new contaminants to the radar. As exemplified in (Fishman
2179 and Erdmann, 1973), water analysis in the early 1970s was dominated by spectroscopy,
2180 electrochemistry, MS, thin layer, and GC and focused on inorganic species, petroleum
2181 hydrocarbons, and persistent organochlorides. Twenty years later, a broader suite of
2182 organic compounds had become accessible by dedicated sample extraction, HPLC),
2183 GC-MS, and the advent of biochemical methods (Clement et al., 1993; MacCarthy et
2184 al., 1993). In the early 2000s, the introduction of matrix-assisted laser desorption-
2185 ionization (MALDI)-MS made fingerprinting of bacteria possible, and the introduction
2186 of LC-MS revolutionized routine monitoring of organic compounds like
2187 pharmaceuticals and personal care products. At that time, the term “Emerging
2188 Contaminants” came up (Koester et al., 2003). Today, twenty years later, high-
2189 resolution mass spectrometers and advanced data processing have catalyzed non-target
2190 screening for organic compounds, bringing to our attention a broad contaminant range,
2191 including PAFS and inadvertent transformation products (Richardson and Ternes,
2192 2020).

2193 Another driver of emerging concern is situations in which chemicals are not necessarily
2194 new but occur in such quantities that they can no longer be overlooked. Hence, the
2195 general public feels urged to address them according to the precautionary principle,
2196 even though analytical methods are yet to be established for some of them. Examples
2197 are engineered micro- and nanoparticles, microplastics (Ivleva, 2021), or hydraulic
2198 fracturing chemicals in unconventional gas exploration (Hoelzer et al., 2016). Well-
2199 known chemicals may also become of emerging concern at the moment that they are
2200 subject to stricter drinking water standards, such as perchlorate (Kucharzyk et al., 2009)
2201 or PFAS (Braun, 2023). The emergence of new diseases, such as during the SARS-
2202 CoV-2 pandemic, can finally drive the installation of entirely new monitoring efforts,
2203 such as screening wastewater for COVID variants (Maryam et al., 2023).

2204 Environmental science can make particularly important contributions if it succeeds in
2205 discovering problematic transformation products as ECs that would otherwise remain
2206 overlooked. Examples are disinfection by-products such as bromate during water
2207 treatment (von Gunten, 2018). A particularly visible case is 6PPD-quinone, a highly
2208 toxic ozonation product of the tire additive 6PPD (N-(1,3-dimethylbutyl)-N'-phenyl-p-
2209 phenylenediamine), which has led to an enigmatic acute mortality of coho salmon in
2210 the U.S. Pacific Northwest.

2211 In particularly notorious cases, chemicals emerge as contaminants after they were
2212 introduced to replace other, regulated ones. Examples are methyl, *tert*-butyl ether
2213 (MTBE), or 1,4-dioxane, which were introduced in lieu of tetraethyl lead to boost

2214 octane numbers in gasoline (Grisham, 1999), or the second generation of PFAS, which
2215 have replaced the first one of PFAS or PFOA – only to be recognized to be equally
2216 problematic (Sedlak, 2016).

2217

2218 **FUTURE DIRECTIONS AND CHALLENGES**

2219 Achieving sustainable development remains a lofty goal rather than a concrete reality
2220 without unified global endeavors to mitigate and prevent environmental pollution.

2221 While regulations have been implemented to address legacy contaminants, many

2222 unregulated chemicals and biological entities continue to be released into the

2223 environment. Moreover, enforcement and implementation of regulations for existing

2224 pollutants are inconsistent or lacking in many regions globally, posing significant

2225 threats to public health, biodiversity, and ecosystem services. The escalating presence

2226 of ECs in the environment raises apprehensions regarding their enduring and

2227 unforeseen impacts on ecosystems, water quality, and human welfare. This

2228 comprehensive review thoroughly examined the sources, behavior, pathways, and fate

2229 of ECs in the environment from various perspectives. Additionally, we explored the

2230 impacts of these contaminants on planetary health, encompassing humans, animals, and

2231 their interconnected environments, all within the framework of One Health.

2232 Notwithstanding the extensive insights into ECs presented in this review, substantial

- 2233 challenges persist within the current global development systems, hindering effective
- 2234 efforts to mitigate the impact of environmental pollution on planetary health.
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- 2237 a b s b i l n j b k q » » o j b t l o h » T e b k » ^ » » o b d r i ^ q a » » e b j f ^ i » f p » m e ^ p b a » l r q » » f q » f p » l a p k »
- 2238 o b m i ^ ` b a » t f e » » k l q e b o » m l p k q f ^ i i v » ^ r p f k d » k b t » l o a f a b o b k q » » m b p l o b k s f o l k j b k q i »
- 2239 l o e r j ^ k » e b ^ i q e » f j m ^ ` q » » Q e f p » m o l ` b p p » » o b n r f o b p » » ^ i ^ k ` b » b q b b k » » e b » b k b q f q l o »
- 2240 p v k q e b q f » » ` e b j f ^ i p » ^ k a » » q e b » m l p k q f ^ i » » o f p h p » T f e » » q e l r p ^ k a p » l o » k b t » » p v k q e b q f » »
- 2241 ` e b j f ^ i p » b k p o f k d » » e b » b k s f o l k j b k q j ^ k v » k l q » e l o l r d e i v » » p p q a » » e b o b » f p » » k b b a » d »
- 2242 f k p k p f e » » o b p b ^ o ` e » l k » B @ » » k a » » o b ^ q » » » l j m o b e b k p f s b » n r _ i f » » a ^ q _ ^ p b » a b q f i f k d »
- 2243 q e b f o » p l r o ` b p » » k a » » b k s f o l k j b k q i » _ b e ^ s f l r o » T b j r p q » ^ a s ^ k ` b » ^ a s b o p b » l r q l j b »
- 2244 m ^ q e t ^ v p » » % d k h i b v » b q » ^ i » » / - . - & ^ k a » » o l p p * p n b ` f b p » b u q ^ m l i ^ q l k » ^ m o l ^ ` e b p »
- 2245 % ^ I l k b » b q » ^ i » » / - / 0 8 » J ^ a d f l q f * @ » p ^ i r ` f » b q » ^ i » » / - / l & q » » r k a b o p q ^ k a » » e b j f ^ i »
- 2246 ^ a p f _ r p p » e ^ q e f » o d b q m ^ o f ` r i ^ o i v » p r p ` b m q _ i b » p n b ` f b p » » k a » » a s ^ k ` b » » e b » m o b ` f p f l k l o »
- 2247 b k s f o l k j b k q i » » p p b p p j b k q » d o » B @ » » % o l l h p » b q » ^ i » » / - / l & » A l f k d » p l » m o l j f p b p » d »
- 2248 f k d o j » » ` e b j f ^ i » » p r _ p q q q l k p » » f k » » l j j b o ` b » t f q e l r q » o b d o b q » » % f j j b o j ^ k » ^ k a »
- 2249 > k ^ p q p » » / - . 2 & ^ k a » » e b » p r p q f k ^ _ i b j l i b ` r i ^ o » a b p f d k l o i b p p e ^ v ^ o a l r p p r _ p q k ` b p »
- 2250 % @ l f p e » b q » ^ i » » / - . 3 & »
- 2251 ? + B ^ ` e » » b ^ o » » e l r p b e l i a p » » k a » » t l o h m i ^ ` b p » » l k q f _ r q » p f d k f q ^ ^ k q v » d » » b k s f o l k j b k q i »
- 2252 ` l k q j f k ^ q l k » _ v » o b i b ^ p f k d » e ^ o j a r i » » e b j f ^ i p » » e o l r d e » s ^ o f l r p b s b o v a ^ v » m o l a r ` q » »
- 2253 f k ` i r a f k d » d l q e m ^ p b » » p e ^ j m l l » » _ l a v » » o b ^ j p » » » i b ^ k f k d » » ^ d b k q » » ^ k a » » m i ^ p q f » » ^ d p » »

- 2254 Qebxi`hl oap`kpm`obk`vxlj »lj m`kfbp`abd`oafkd`æbfkdobafbkq»ka`nr`kqfqb»
- 2255 rpbaxfk`æbfomol ar`q»lj mif`^fpp`æbfabkqf`^ql k»l oæb»`lkqj fk`kq»mbl nib»
- 2256 j`^v»bbuml pba»l »ka`æbml`fbkq`i`eb`i`æ`æfph»ppl`f`fa`æ`æbj`MC>P`pbosbp»
- 2257 `p»»mfj`bbu`j`nibxl`opr`e»`ebj`f`^ip`A`bpmf`_`bfkd`fk»lj`j`bo`f`i`rpb`p`k`b`æb»
- 2258 .61-p»»æbfomol`uf`fq»t`^p»kl`qt`fabiv»ob`l`dkfvba»rkfi»æb»i`^q».66-p»Plj`b»
- 2259 `lj`m`kfbp»t`bob»^t`^ob»l`o`æb»ml`fbkq`i»`uf`fq»l`o`MC>P»`r`q»`l`kqkr`ba»d`»
- 2260 fk`l`oml`o`^`æbj`fk`æbfomol`ar`q»Qefp`p`bk`ofl`æfdeifdeq`æbfj`ml`oq`k`b`xl`o`
- 2261 q`kpm`obk`v`fk»`ebj`f`^ij`^kr`c`q`ofkd`mol`b`ppbp»ka`r`kabop`l`obp`æb`kb`b`ppfq»
- 2262 d`o»lj`m`ebk`pfs`b`p`p`kd`xl`o`ebj`f`^ip`_`bd`ob`æbfomol`l`oml`o`ql`k`fk`d`»l`kprj`bo»
- 2263 dl`lap»
- 2264 @+ Bcd`oap`l`»lj`_`^`q`bks`fol`kj`bk`q`i`ml`iir`ql`k`æ`b`m`bop`p`p`k`q`e`^`iib`k`dbp`p`fk`ir`afkd`æb»
- 2265 `lj`nibufq»l`o`ml`iir`q`k`q»»fk`^`abnr`^`q`»`ekl`il`df`^`i`»pl`ir`ql`kp»»ka`»af`æ`r`iq`fbp`fk»
- 2266 fj`mibj`bk`q`d»`lj`m`ebk`pfs`b»`bks`fol`kj`bk`q`i»`ml`if`fbp»`@`æbj`f`^`i»`obj`baf`^`ql`k»
- 2267 q`ekfnr`bp`l`ap`k`m`ob`booba»m`o`al`uf`^`iiv`obpr`iq`fk`l`ob`^`q`o`bks`fol`kj`bk`q`i`fj`m`^`q»
- 2268 æ`k»`æb»`ml`iir`ql`k»`æbv»`^`fj`»`d`»`obj`baf`^`q`»`T`efib»`_`fl`il`df`^`i`»`j`b`æ`l`ap»`ifhb»
- 2269 _`fl`obj`baf`^`ql`k»»ka`m`evd`obj`baf`^`ql`k`l`cbo`b`l`*`æfb`kaiv»`i`q`ok`^`q`sbp`p`æbv»`ob`ibpp»
- 2270 bæf`fbk`q`ka`j`l`ob`xj`b`*`l`kprj`fk`d`»Qeb`fk`ql`ar`ql`k`l`oi`_`*`dol`t`k`l`o`bk`dfk`bboba»
- 2271 j`f`ol`l`od`^`k`f`pj`p`ar`ofkd»_`fl`obj`baf`^`ql`k»`ipl`»`^`o`fbp`æb`æfph`l`o`af`por`m`fk`d`k`^`q`o`i`»
- 2272 b`l`pvp`p`j`p`ka`»`^`r`p`fk`d`r`kd`ob`p`bbk`xj`m`^`q`»`aa`ob`p`p`fk`d`æb`p`b`»e`^`iib`k`dbp`o`b`nr`f`obp»
- 2273 fk`p`k`p`f`q`ba»ob`p`b`o`e»l`k»»fk`kl`s`^`q`sb»obj`baf`^`ql`k»l`m`ql`kp»d`»b`æb`^`q`sbiv»`l`k`q`l`i»
- 2274 ml`iir`ql`k`l`b`ke`^`k`b`bks`fol`kj`bk`q`i`æb`i`æ`»ka`j`^`ufj`fv`b`b`l`il`df`^`i`»pr`p`q`fk`^`_`fifq`»

2275 Q`fil oba» obj baf`ql k» pp`qdfbp» `l kpfabofkd» pnb`fg` » pfq» `l kafql kp» ^ka»
 2276 `l kqj fk^kq`e^o` qofpq`p»kbb»d » _b»abs bil nba»d »k^sfd`q»q bpb»`lj nibu»
 2277 `e^iibkdbp»Pj` miv»pq`fa»)» b»kbb»d »`as^k`b»dobbk»^ka»pr`pq`fk^_ib»`ebj fpq»
 2278 ^ka»dobbk»bkdfkbbofkd»d »ob`ifwb»j l ob»pr`pq`fk^_ib»nl iir`ql k»mobs bkql k»fk»qeb»
 2279 a`q`ob+
 2280 A+ Qeb»fkqf`^`q`fkqomi^v»_bq`bbk»bksfol kj bkq`i`nl iir`ql k»`ka»`ifj`^q»`e^kdb»^ka»
 2281 l`qbo»e`d`op`l`o`dil`_`i`bksfol kj bkq`i»`e^kdb»mobpbkq»`xl`oj`fa`_ib»`e^iibkdb»q`e`q`
 2282 `^kkl`q`b`q``hiba»fk»fpl`i`ql`k`»Qebpb»bksfol kj bkq`i`fppr`bp»`ob»fkqo`l`kkb`fa»`ka»
 2283 `^k»j`mifc»b`e`q`bo»obpr`iq`kd»fk»mol`d`r`ka»`l`kpbnr`bk`bp`xl`ob`l`pvpqj`p»er`j`^k»
 2284 eb`iqe»)»^ka»qeb»mi`kbq`^q`i`adb»Ob`l`dkf»vfk`d»qeb»fkqoifk`hba»k`q`ob»l`o`q`bpb»
 2285 `e^iibkdbp»fp»fj`mbo`q`sb»d`o»d`oj`ri`q`kd»pr`pq`fk^_ib»pl`ir`ql`kp»q`e`q`p`c`dr`^`oa»
 2286 b`l`pvpqj`p»er`j`^k»`bii`*_`bfkd»)»^ka»qeb»mol`pnb`q»l`o`a`q`ob»dbkbo`ql`kp»E`bk`b»
 2287 q`ebob»fp»`mobppfk`d`kbb»d`ofk`qdo`q`a»`nmol`^`ebp»q`e`q`l`k`r`oobkq`v»q``hib»dil`_`i»
 2288 bksfol kj bkq`i»`e^kdb»)»r`kabonfkkba»_v»p`fbk`b*_`pba»nl`if`fbp»^ka»`l`ii`^`l`o`q`sb»
 2289 bkab`sl`r`op»Qefp»el`if`pq`»pp`q`dv»fj`fj`mbo`q`sb»d`o»q`p`b`ofkd»qeb»`l`oia»d`t`^`oap»`»
 2290 j`l`ob»obpfifbkq`^ka»pr`pq`fk^_ib»er`q`ob»

2291 In summary, the continuous generation and utilization of new products contribute to the
 2292 introduction of ECs into the environment. To confront this challenge effectively,
 2293 comprehensive research is imperative to understand the sources and potential
 2294 repercussions of these pollutants on human health, ecosystems, and animals, embracing
 2295 the One Health approach. Furthermore, evaluating how these contaminants interact

2296 with various environmental factors, both living and non-living, is crucial within our
2297 ever-changing environments. Leveraging advancements in analytical techniques and
2298 artificial intelligence is indispensable for monitoring these emerging environmental
2299 pollutants and predicting their behaviour within intricate environmental systems.
2300 Additionally, careful consideration of the potential risks stemming from advancements
2301 in material production across diverse domains, including biotechnology and
2302 nanotechnology, is vital for fostering the responsible development of materials for
2303 environmental purposes. Addressing environmental pollution demands a paradigm shift
2304 in our lifestyles, advocating for policies geared towards minimizing contaminants and
2305 implementing coordinated efforts to tackle existing pollutants through global
2306 cooperation. This collective endeavor is vital for safeguarding the health and
2307 sustainability of our planet for the benefit of both current and future generations,
2308 aligning with the principles of One Health.

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2346 E. wrote a section about some lessons learned. Y. F. and Y. W. organized and revised
2347 references. All authors discussed and approved the final manuscript.

2348

2349 **DECLARATION OF INTERESTS**

2350 The authors declare no competing interests.

2351

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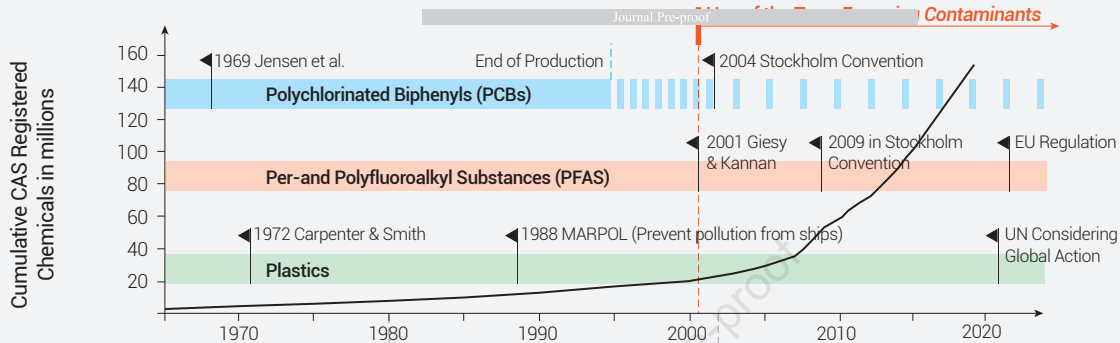
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From Industrial Use to Emergence as Contaminants to Regulation: PCBs, PFAS and Plastics as Examples

Accessible / Upcoming Analytical Methods

Spectroscopy, Electrochemistry, Chromatography (Gas, Gel, Thin Layer), Mass Spectrometry (GC-MS)

High Performance Liquid Chromatography (HPLC), Ion Chromatography (IC)

LC- (Tandem) MS

Toxicity screens

LC- High Resolution Tandem MS

Advanced Data Science Workflows

Bioanalytical methods

MALDI-MS

-> Non-Target Analysis

Prominent / Emerging Contaminant Classes over Time (Examples)

Heavy metals, Nutrients, Pesticides, Chlorinated hydrocarbons, Petroleum constituents

Surfactants

Endocrine-disrupting compounds (EDCs)

Pathogenic bacteria

Cyanotoxins

MTBE, Dioxane

Antibiotic resistant microorganisms

Per- and Polyfluoroalkyl Substances (PFAS) 1st Generation

Perchlorate

Brominated flame retardants

Pharmaceuticals and personal care products (PPCPs)

PFAS 2nd Generation

Antibiotic resistance genes (ARGs)

Nanoparticles

Micro- and nanoplastics

Liquid crystal monomers

Virus

Genetically modified organisms (GMOs)

Protein contaminants

Inoculations with novel strains

Radionuclides and nuclear waste

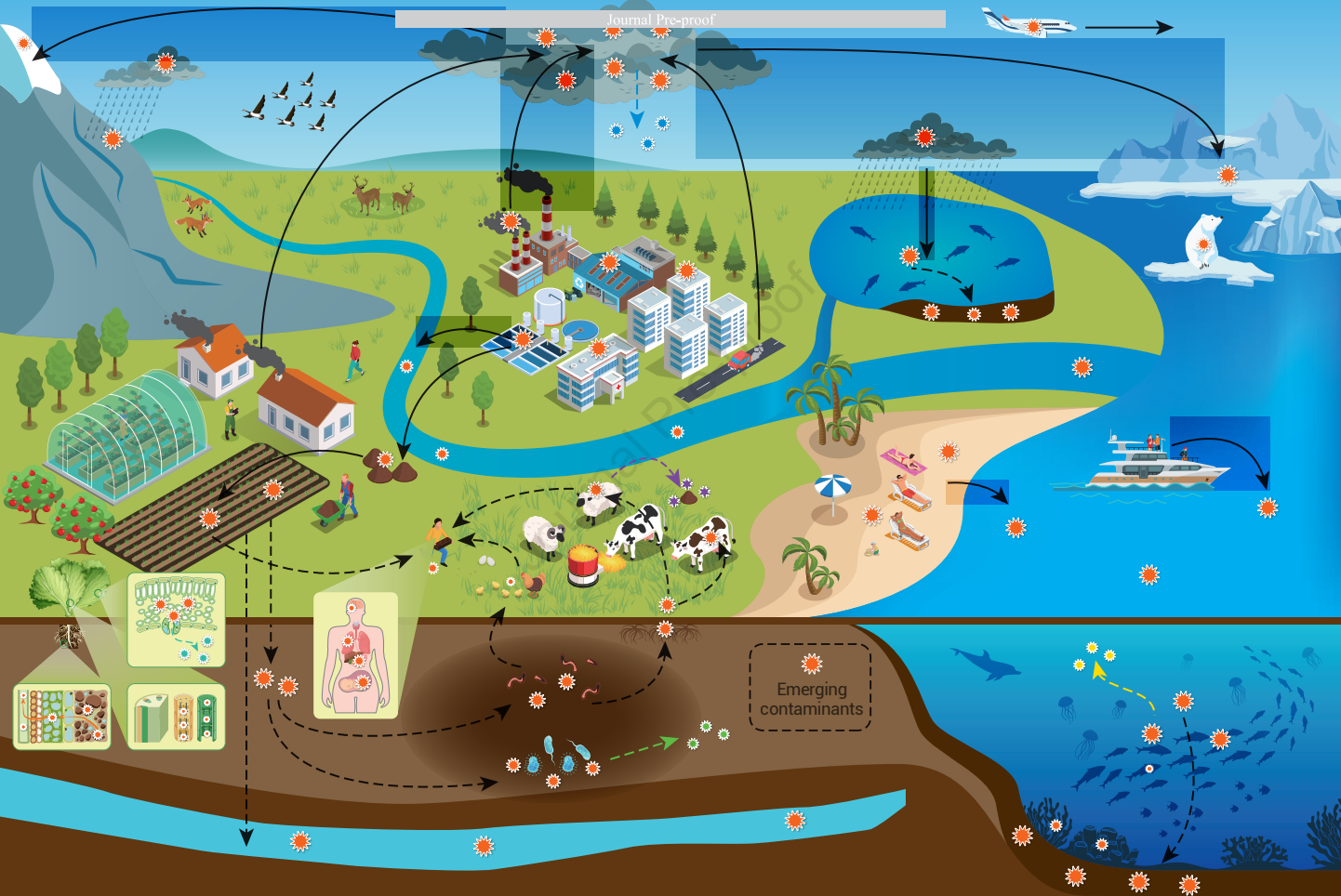
Different-RNA types

Environmentally persistent free radicals

UVCBs

Certain peptide complexes





- Respiratory and dermal toxicity
- Inducing diseases
- Cellular injury
- Long-range transmission risk



Suspended particulates

Air

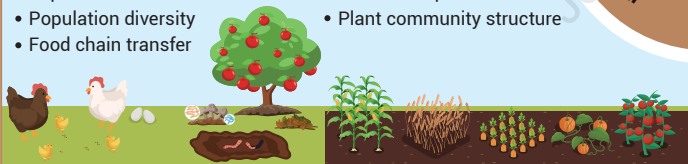
Human

Emerging
contaminants

Soil

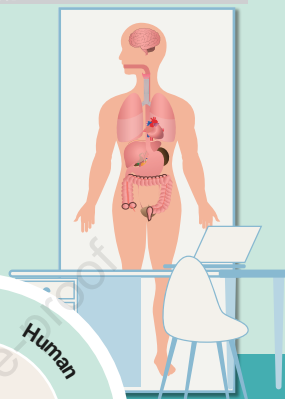
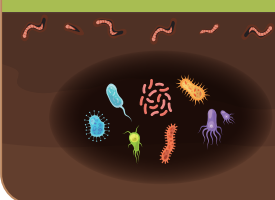
Water

- Bioaccumulation
- Growth and development
- Reproductive functions
- Population diversity
- Food chain transfer



- Plant growth, plant health
- Nutrient absorption
- Water transport
- Plant community structure

- Microbial community structure
- Nutrient cycling
- Organic matter decomposition
- Metabolic activities
- Soil fertility



Nervous system

Arsenic, mercury, and perfluoroalkyl substances

Respiratory system

Heavy metals, persistent organic pollutants, nanoparticles, viruses

Immune system

Antibiotics, antibiotic resistance genes, persistent organic pollutants, disinfectant by-products

Endocrine system

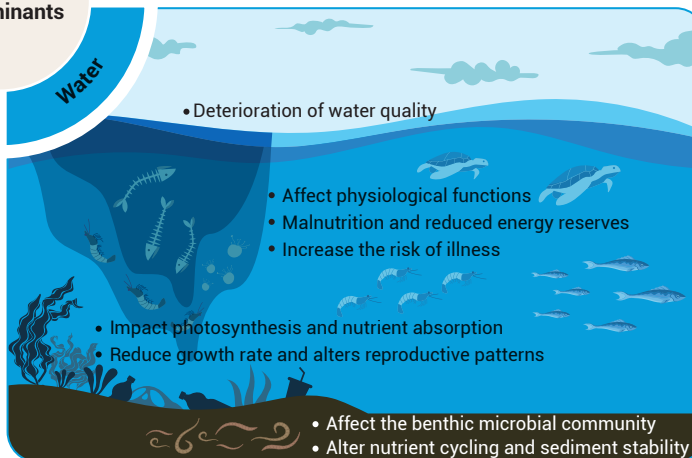
Endocrine-disrupting compounds

- Deterioration of water quality

- Affect physiological functions
- Malnutrition and reduced energy reserves
- Increase the risk of illness

- Impact photosynthesis and nutrient absorption
- Reduce growth rate and alters reproductive patterns

- Affect the benthic microbial community
- Alter nutrient cycling and sediment stability



AI

