

Current and Future Emissions of Urban Chemicals into the Aquatic Environment

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Abstract

Urban environments are hot spots for chemical use and emissions and urban aquatic systems are under constant pressure from exposure to chemical mixtures. Chemical emissions and impacts are expected to change in the future due to socio-economic, climate and technological changes. However, the impact of these changes on chemical use and emissions is uncertain. This study therefore investigated how the emissions of chemicals of concern in European urban aquatic systems might evolve in the future due to global changes.

A systematic review demonstrated that more than 1100 chemicals, belonging to 19 class categories, have been detected in urban environments around the globe. Comparison of the measured concentrations with ecotoxicological data indicated that 168 of these chemicals pose an unacceptable risk for at least one location and should be regarded as priority chemicals.

To determine the current level of risk associated with selected priority chemicals in Europe, two antibiotics and ten metals were monitored in rivers in York (UK), Madrid (Spain) and Oslo (Norway) for one year. Results showed that aluminium, zinc, iron, copper, mercury, chromium and the antibiotic clarithromycin all posed an unacceptable risk.

To investigate how chemicals emissions might change in the future, a framework was developed to extend the Shared Socio-economic Pathway approach, an approach used in climate change forecasting, to forecast changes in chemical emissions in the future. Following, pilot-testing with insecticidal products and antidepressants, the framework was used to forecast antibiotics emission in European freshwater systems in 2050. This resulted in a number of different future emission scenarios characterised by either an increase or decrease in antibiotic emissions depending on the pathway.

Overall, the thesis has demonstrated that chemical pollutants do pose an unacceptable risk to European urban aquatic environment. It illustrates how emissions of chemicals are likely to increase or decrease in the future depending on the pathways that society follows. The findings will be invaluable to decision makers involved in the risk assessment and management of chemical products and the natural environment.

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Abbreviations

AA-EQS	Annual Average Environmental Quality Standard
AF	Assessment Factor
AMAP	Arctic Monitoring and Assessment Programme
AMR	Antimicrobial Resistance
BBP	Benzyl butyl phthalate
DEET	N,N-Diethyl-meta-toluamide
DEHP	Di(2-ethylhexyl)phthalate
EC	European Commission
EC50	Half-Maximal Effective Concentration
ECHA	European Chemicals Agency
ECOSAR	Ecological Structure Activity Relationships
EPA	United States Environmental Protection Agency
EQS	Environmental Quality Standard
GMO	Genetically Modified Organisms
GNI	Gross National Income
HIV	Human Immunodeficiency Virus
HPLC-MS	High Performance Liquid Chromatography Mass Spectrometry
ICO	International Coffee Organisation
ICP-MS	Inductively Coupled Plasma Mass Spectrometry
IPCC	Intergovernmental Panel on Climate Change
IVIVE	<i>in-vitro-to-in-vivo</i> Extrapolation
LC	Liquid chromatography
LC50	Concentration required to kill 50% of the population
LC-MS/MS	Liquid chromatography-tandem mass spectrometry
LOD	Limit of Detection
LOQ	Limit of Quantification
MAC-EQS	Maximum Average Concentration Environmental Quality Standard
MEC	Measured Environmental Concentration
MS	Mass Spectrometry
ND	Not Detected
NOEC	No Observable Effect Concentration
OECD	Organization for Economic Cooperation and Development
OSPAR	Convention for the Protection of the Marine Environment of the North-East Atlantic
PAHs	Polycyclic Aromatic Hydrocarbons
PBT	Persistent Bioaccumulative Toxic
PCBs	Polychlorinated Biphenyls
PEC	Predicted Environmental Concentration
PFBA	Perfluorobutanoic acid
PFCA	Perfluoroalkyl carboxylic acids
PFCs	Perfluorochemicals
PFOA	Perfluorooctanoic acid
PFOS	Perfluorooctane sulfonic acid
PNEC	Predicted No Effect Concentrations

QC	Quality control
QSAR	Quantitative Structure–Activity Relationships
RCP	Representative Concentration Pathways
REACH	Registration, Evaluation and Authorization of Chemicals
RQ	Risk Quotient
SSP	Shared Socio-Economic Pathways
STP	Sewage Treatment Plant
TKTD	Toxicokinetic Toxicodynamic
UE	European Union
UN	United Nations
UNEP	United Nations Environment Programme
USGCRP	United States Global Climate Research Program
UV	Ultraviolet
WBD	World Bank Data
WFD	Water Framework Directive
WHO	World Health Organization
WWTP	Wastewater Treatment Plant

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Declaration

All the chapters of this thesis have been written as papers for international per-reviewed journals. All the papers have been reworked to fit style and format of thesis of the University of York. Current publications status of papers are presented in Table 1.

The papers from chapter 1 to chapter 6 were written by the PhD candidate as a lead author. PhD candidate works with co-authors who advised, edited and corrected papers, which significantly increase the quality of papers. Chapter 5, which is published in the journal *Futures*, is available in annexe 0.1.

For chapter 3, sampled in Madrid were collected and shipped by Francesco Polazzo and sampled in Norway by Samuel Welch and Anne Luise Ribeiro. ICP-MS for metals analysis were conducted by John Angus in the Biorenewables Development Centre in York, UK.

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Table 1 - Status of the papers presented in this thesis with respect to the publication process

Chapter	Authors	Title	Status	Journal
1	Desrousseaux, A.O.S, Sallach, J.B, Boxall, A.B.A	Review of Chemical Pollution in Urban Freshwater System of the World	In prep	<i>Environmental Toxicology and Chemistry</i>
2	Desrousseaux, A.O.S, Sallach, J.B, Boxall, A.B.A	Identifying priority chemical contaminants in urban riverine systems in world	In prep	<i>Environmental Toxicology and Chemistry</i>
3	Desrousseaux, A.O.S, Polazzo F, Ribeiro A.L, Welch S, Angus J, Bergstrom E, Sallach, J.B, Boxall, A.B.A	Temporal and spatial risks of 15 priority chemicals in urban river systems of York, Madrid and Oslo	In prep	<i>Water Research</i>
4	Desrousseaux, A.O.S; Nagesh, P; Gajraj, R; Dekker, S.C; Eitzinger, J; Sallach, J.B; Boxall, A.B.A; Kok, K.	A Shared Socio-Economic Pathway Based Framework for Characterising Future Emissions of Chemicals to the Natural Environment	Published	<i>Futures</i>
5	Desrousseaux, A.O.S, Sallach, J.B, Boxall, A.B.A	Antibiotics emissions scenarios under 3 European SSPs: Eur-SSP1, Eur-SSP4 and Eur-SSP5	In prep	<i>Futures</i>
6	Cains, M; Desrousseaux, A; Boxall, A.B.A; Molande, S; Molina-Navarro, E; Sussams, J; Critto, A; Stahl Jr, R.G; Rother H-A	Environmental Management Cycles for Chemicals and Climate Change, EMC4: A new conceptual framework contextualizing climate and chemical risk assessment and management	In prep	<i>Integrated Environmental Assessment and Management</i>

Chapter 1 - Introduction

1.1 Urban Freshwater Chemical Pollution

From pharmaceuticals used for health to metals for the development of sustainable decarbonised energy systems, natural and synthetic chemicals are used in all aspects of modern life. However, the high use of chemicals by society has led to freshwater bodies being constantly contaminated from chemical emissions (Carpenter *et al.*, 2011; Inostroza *et al.*, 2017; Mushtaq *et al.*, 2020)

Urban environments are hotspots of chemical pollution because of numerous human activities associated with our towns and cities. Construction, industry, hospitals, leisure activities and parks, public transport, traffic all emit chemicals that are then transported into urban natural environments. For example, hospitals and geriatric homes are locations with high consumption of pharmaceuticals colouring (Ortiz de García, García-Encina and Irusta-Mata, 2017). Textile industries utilise metals, dyeing, fixing agents, and whitening agents and surfactants for textile production (Khan and Malik, 2014; Malik, Akhtar and Grohmann, 2014; Pattnaik, Dangayach and Bhardwaj, 2018). Traffic generates dioxins and polycyclic aromatic carbons due to incomplete burning of oil (Chauhan *et al.*, 2010; Joshi, Navalgund and Shet, 2022; Wang *et al.*, 2023).

Chemicals are emitted in urban environment via two main pathways: either via wastewater treatment plants (WWTPs) or by runoff. WWTPs treat collected wastewater to remove organics and then release the treated water to rivers, streams or lakes (Domercq, Praetorius and Boxall, 2018). The efficiency of WWTP depends on technology in place and chemicals are removed to different degrees depending on their physico-chemical properties and persistence (Kasprzyk-Hordern, Dinsdale and Guwy, 2009; Verlicchi, Al Aukidy and Zambello, 2012; Yaman *et al.*, 2017). WWTP effluent has been shown in multiple studies to be a major contributor of most to chemical emissions in urban environments (Roberts & Thomas, 2006; Waiser *et al.*, 2011; Muir *et al.*, 2017). Chemicals can also be emitted by runoff. Chemical runoff and leakage occur when rain falls onto urban hard surfaces which is then transferred to a drainage system (Masoner *et al.*, 2019). Runoff contaminated water is usually not captured and therefore does not go through any treatment plants.

A diversity of chemicals has been detected in urban freshwater bodies including pharmaceuticals, pesticides, cosmetics and personal care products, sterols, Polycyclic aromatic hydrocarbons (PAHs), Polychlorinated biphenyls (PCBs), metals, biocides, additives, flame retardants, perfluorinated compound (PFCs) are many others (Schreder and Guardia, 2014; Chau *et al.*, 2018; GURSOY-HAKSEVENLER *et al.*, 2020; Wilkinson *et al.*, 2022). The pattern of chemical pollution reflects anthropogenic activities of a local environment or the socio-economic status of a city. For example: high concentrations of nitrogen, phosphorus and chromium were detected in Fez (Morocco) reflecting the important leather manufacturing activity of the city (Perrin *et al.*, 2014); high concentrations of sterols and faecal bacteria were seen in Hanoi or Ho Chi Ming (Vietnam) reflecting the absence of or ineffective wastewater management (Chau *et al.*, 2018); high concentrations of PAHs were seen in Thulamela municipaly (South Africa) reflecting local tyres burning activities (Edokpayi *et al.*, 2016); very high concentrations of PCFs detected in Zibo (China) reflecting the presence of the largest fluorine factory of the country (Li *et al.*, 2018)

The emissions of chemicals to urban environments can adversely affect ecological communities. A range of effects of chemicals in freshwater bodies on aquatic living organisms have been reported. For example: endocrine-disrupting chemicals (e.g. bisphenol A; 17 β -estradiol) lead to feminisation of clams in the UK, carps in Spain and tilapia fish in Zimbabwe (Solé *et al.*, 2000; Langston, Burt and Chesman, 2007; Teta *et al.*, 2018); PFOA and other perfluorinated compounds bioaccumulate in animals' tissue and biomagnify throughout the food chain (Stahl, Mattern and Brunn, 2011; Lau, 2015); metals can be lethal at low concentrations for fishes (e.g. mercury, lead) or can alter development, reproduction and survival of fishes, molluscs, daphnids and algae at relevant environmental concentrations (Géret *et al.*, 2002; Levesque *et al.*, 2002; De Schamphelaere, Lofts and Janssen, 2005; Öner, Atli and Canli, 2008; Donnachie *et al.*, 2014); antibiotics emissions lead to the development of antimicrobials resistance genes threatening global health and countries' stability with a pandemic (WHO, 2014; Zhang *et al.*, 2022). Freshwater pollution also affect human health. Recreational activities (e.g. bathing, swimming) can be restricted when pollution is too high. Bathing has been forbidden in different areas in France or the UK because of bacterial-contaminated overflowing wastewater from treatment plant (Penna *et al.*, 2021; BBC News, 2022; France 3, 2022). Polluted freshwater is also used for drinking water and for irrigations

of agricultural field leading to potential serious public health issues (Chen *et al.*, 2013; Wang, Li and Li, 2017).

Urban freshwater chemical pollution is a worldwide threat: in a recent study, antibiotics and pharmaceuticals were monitored in rivers in 104 countries in all continents. Out of 258 rivers monitored, only two rivers that no antibiotics or pharmaceuticals detected (Wilkinson *et al.*, 2022).

1.2 A rapidly changing world

Chemical consumption worldwide is currently operating “outside the safe operating space of the planetary boundary” according to Persson *et al.*, 2022. This means that humanity is currently producing and releasing chemicals that pose risks that are greater than societies can assess and monitor: current chemical consumption could threaten the integrity of Earth System processes (Persson *et al.*, 2022). This risk is expected to increasingly intensify by a variety of global megatrends (Retief *et al.*, 2016).

First megatrend to be considered is demographic change. The world population will level off between 9 and 11 billion in habitants in 2050. While population size is expected to decrease in Europe, the population in Africa is expected to double.

Second, 80% of the world population is expected to live in cities in 2050 (UN-Habitat, 2022). Forty millions of rural acres are expected to change to urban areas to welcome the increasing urban population (UNEP, 2019). Cities will also have to adapt to provide good services (e.g. wastewater treatments, roads infrastructures, hospitals) for urban population.

Despite the fact that water demand could increase up to 80% compared to 2010, climate change will intensify resource scarcity, including water scarcity (UN Water, 2018; Boretti and Rosa, 2019). While terrestrial water storage is diminishing, some regions of the world will suffer from intensive rainfalls and floods events while other regions will suffer from drought. (UN Water, 2023) Last, accelerating technology innovation could change society dynamics. Technology innovation will continue to accelerate, especially in energy technology. The main challenge of technology innovation will not only be the development but the accessibility of these technology to countries that would benefit the most of it (Retief *et al.*, 2016).

Global megatrends are intensifying environmental challenges like water safety and brings new risks and uncertainties (European Environment Agency, 2020). Despite the fact that chemicals are used in all aspects of our lives and are causing harmful effects on human and environmental health, the future outlook of chemicals in societies resulting from socio-economic change, climate change and technological development is unknown.

1.3 Megatrends and chemicals emissions

Urban environments are rapidly changing due to socio-economic, climate change and technological development. These changes will impact the risk of chemicals emissions.

Materials consumption for urban expansion will increase from 10 billion tonnes in 2010 to 90 billion tonnes in 2050 (UN-Habitat, 2022). Increasing materials consumption and water demand for urban expansion will be a challenge, especially in climate change. Climate change events impacts on chemical efficiency, chemical emissions and chemical demand. Increasing temperature decrease the efficiency of pesticides, leading to a higher usage of pesticides. Precipitations can compromise WWTP capacity and increase the amount of untreated wastewater release into the environment (Shrestha *et al.*, 2015; Zouboulis and Tolkou, 2015). Changing climate change diseases patterns and pharmaceuticals demands. For example allergies and other respiratory diseases are expected to increase with temperature change, leading to increasing demand for antihistamines, decongestants or cortisones (Redshaw *et al.*, 2013). While some climate events could lead to a decrease of chemicals emissions (e.g. a decrease in precipitations could decrease traffic-related chemicals runoff), majority of effects studies in the literature are expecting to increase chemicals emissions and worsen current urban chemical emissions.

Socio-economics changing like education, technology development, policies, and regulations can also impact chemicals emissions. Chemical emissions can be limited with strict regulations. The pesticide atrazine is detected at high concentrations in the US but not in Europe. Atrazine was banned in the EU since 2004 while it is still allowed in the US (Deb, 2006; Sass and Colangelo, 2014). Strict regulations can also change chemical demand. The EU bisphenol A banned in 2018 lead plastic industries to subsidised it by other bisphenols with similar toxicity (Rochester and Bolden, 2015; Qiu *et al.*, 2019). Education can also play a role

in individuals and professional behaviours. Antibiotics usage and prescriptions was showed to decrease in hospitals were practitioners followed trainings on antibiotics misuses and antimicrobials resistance genes (Tan *et al.*, 2018; Muloi *et al.*, 2019). Advances in WWTP technology can decrease the load of chemicals emission from WWTP effluent. Ozone and activated carbon are advanced technology significantly increase toxic chemical removal compared to traditional WWTP technology (Pistocchi *et al.*, 2022). These technology is however not easy to expand throughout countries and usually rely on governance politics or financials benefits from private compaignies (Renwick, Brogan and Mossialos, 2015). Adaptation to climate change will also change chemicals demand and emissions. Shift towards electric cars or sustainable decarbonised energy systems requires chemicals like lithium, aluminium or hydrogen to cite a few (Addison, 2018; Hodgkinson and Smith, 2021). Advances in medicines and pharmaceuticals designed could also reduce toxicity and/or quantity of antibiotics needed for a treatment (Yang *et al.*, 2015; Genilloud, 2019).

How societal changes will affect chemicals demand, usage and emissions in freshwater has not been studied yet. The future risks of chemicals emissions in freshwater systems is currently unknown.

1.4 Scenarios to study future risks of chemicals emissions in urban environments

To be able to study the future chemical emissions in changing societies, scenarios provide a good tool to study multiples alternatives futures (Alcamo and Henrichs, 2008). The shared socio-economics pathways scenarios (SSPs) and representative concentration pathways (RCPs) were developed by the Intergovernmental Climate Change Panels (IPCC) to allow scientists to future different potentials futures under the same storylines (O'Neill *et al.*, 2017). They are used as baseline for climate change and sustainable development research. The SSPs describe five future societies based on their abilities to adapt and mitigate to climate change challenges (O'Neill *et al.*, 2017): SSP1 is a sustainable society based on global cooperation, high investment in human development and a desire for less resources-intensive life-style; SSP3 is a society with high competition between and among regions. Countries are closing on themselves because of high concerns for competitiveness and security. Technology development, human development and environmental concerns are low; SSP4 is a society

Chapter 4 describes a framework developed specifically to adapt existing global and European SSP scenarios to chemical emissions scenarios. The framework involves four steps and allows chemical emissions in the future to be forecast using the SSPs. The framework is then tested for antidepressants and insecticide emissions in European urban freshwater systems in 2050.

Chapter 5 then employs the framework developed in *Chapter 4* to explore how antibiotic emissions to European urban freshwater systems could alter by 2050. Experts from academia, industries and medical practitioners were involved in the scenario development process. Storylines and overall trends for antibiotics emissions in 2050 were developed.

Finally, the conclusions of the work and recommendations for future research in provided in the last part of this thesis.

The sterols detected at the highest concentrations were cholesterol, coprosterol, beta-sitosterol, stigmasterol and stimastanol. Concentrations of cholesterol, coprosterol, beta-sitosterol and stigmasterol above 1 µg/L and up to 68 µg/L were systematically detected in Hanoi and Da Nang (Vietnam). Sterols emissions are associated with faecal pollution and ineffective WWTP. In cities in Vietnam, high faecal pollution was demonstrated in multiple studies because of rapid urbanisation without development of adequate and effective wastewater management (Pham and Kasuga, 2020; Nguyen *et al.*, 2021).

Which chemicals are the most researched in the world? (Table 2)

1. Caffeine n=478

Caffeine was the most researched chemical with 478 data points collected across 44 cities. Caffeine can be found in beverages like coffee, tea or sodas but is also used as a pharmaceutical or a stimulant. Caffeine is the most consumed stimulant in the world with an estimated consumption of 186 mg/L per day per capita in the US (Giovanini de Oliveira Sartori and Vieira da Silva, 2016; Korekar, Kumar and Ugale, 2019). Caffeine was monitored in three cities in South America, one in Africa, 16 in Asia, ten in Europe and 14 in North America. The maximum concentration was 129 µg/L in Sao Paulo (Brazil). Average concentrations were 10 698 ng/L in South America, 2 750 ng/L in Africa, 1 475 ng/L in Europe, 1 104ng/L in Asia and 319 ng/L in North America. The removal efficiency of caffeine by WWTP varies with technology: it can reach 100% with reverse osmosis (Egea-Corbacho Lopera, Gutiérrez Ruiz and Quiroga Alonso, 2019). In a few studies, caffeine concentrations were higher in rivers than in WWTP effluent, possibly indicating illegally untreated wastewater discharge as an important source of caffeine emissions. In Sao Paulo (Brazil), the specific high concentrations of caffeine could result from multiples factors: high population density, high culture of consumption of caffeine (4% of the adult Brazilian population consumed 400 mg/L per day per capita), samplings during a dry season, and a low efficiency water system to cite a few (López-Doval *et al.*, 2017).

2. Carbamazepine n=373

The pharmaceutical carbamazepine was the second most studied molecule researched in 41 urban environments. Carbamazepine is an anticonvulsant and mood stabilizing drug primary used for treatment of epilepsy, bipolar disorder, and trigeminal neuralgia (Ayano, 2016). In this systematic review, average concentrations of carbamazepine were 170 ng/L in Africa, 26 ng/L Asia, 41ng/L in North America, 164 ng/L in South America and 516 ng/L in Europe. The maximum concentration was 67 715 ng/L seen in Madrid (Spain). This high concentration was measured in a wastewater-dominated stream with pharmaceutical plants and a geriatric hospital located near to the sampling point. High concentrations were measured repeatedly at this location, indicating a potential malfunction of the WWTP in question to remove

carbamazepine (González Alonso *et al.*, 2010; Valcárcel *et al.*, 2011). Carbamazepine is a chemical that is not easily removed by WWTPs (usually less than 10%). Removal efficiency can be negligible and can reach 68% with near-anoxic treatment in lab-scale conditions (Zhang, Geißen and Gal, 2008; Hai *et al.*, 2011, 2018).

3. Sulfamethoxazole n= 295

Sulfamethoxazole is a well-known antibiotic that has been used worldwide in combination with trimethoprim since the 1960s (Ho and Juurlink, 2011). The average concentrations of this molecule by continent were 3 044 ng/L in Africa, 194 ng/L in North America, 463 ng/L in Asia, 94 ng/L in Europe and 62 ng/L in South America. The highest concentration (13 800 ng/L) was observed in Nairobi, the capital of Kenya. One important socio-economic factor influencing sulfamethoxazole in Kenya is the HIV and malaria epidemic. Sulfamethoxazole is the recommended treatment for children with HIV-infected mothers with treatments recommended to occur daily up to the age of 4 based on WHO guidelines (WHO, 2015; Kasule *et al.*, 2018). Sulfamethoxazole is also used against malaria in Sub-Saharan Africa and Asia (Homsy *et al.*, 2014). Nairobi River is also contaminated with untreated domestic wastewater, which contributes to sulfamethoxazole emissions. Concentrations of 6 010 ng/L and 5 730 ng/L were also detected in Durban city (South Africa) and Hanoi (Vietnam) respectively. Removal rates for sulfamethoxazole by WWTPs in the literature varies greatly with technologies. It can reach 97.6% in Fenton/photo-Fenton process in lab-scale conditions (Prasannamedha and Kumar, 2020).

4. DEET n= 198

N,N-diethyl-m-toluamide (DEET) is an insect repellent primarily used in domestic products in spray or in skin lotion (Degennaro, 2015). Average concentrations of DEET were close 100 ng/L in Europe, South America and North America and 1297 ng/L in Asia. The maximum concentration 35 000 ng/L was detected in Jakarta, Indonesia. In Europe and North America, detected concentration were lower than in Asia. The impacts of a "local diseases profile" have an impact on DEET emissions. DEET is massively used to prevent malaria and therefore detected in high concentrations in sub-tropical cities (Hanoi and Jakarta). DEET regulations could also have an impact. Regulations in the US allow products with a concentration of 100% DEET while in Europe, maximum concentration allowed is 50%.

5. Ibuprofen n=173

Ibuprofen is a non-steroidal anti-inflammatory drug sold over-the-counter (Bushra and Aslam, 2010). The average concentration of ibuprofen was 1 076 ng/L in Europe, 573 ng/L in North America, 367 ng/L in south America and 249 ng/L in Asia. The highest concentration of 20.7 µg/L was observed in a river channel of Granada, Spain. However, the same location was sampled again the next day and the concentration of ibuprofen had dropped to 5.3 µg/L. The authors explained high concentration by sampling in the dry season in a wastewater dominated stream with low water transport (Luque-Espinar *et al.*, 2015).

6. Diclofenac n=173

Diclofenac, a human and veterinary anti-inflammatory that is used worldwide, was the 7th most researched chemical across all studies. Diclofenac was detected at average concentration of 7 419 ng/L in Asia, 2 021 ng/L in Africa, 315 ng/L in North America, 160 ng/L in South America, and 106 ng/L in Europe. The highest concentration was 116 000 ng/L in Islamabad, Pakistan. In other cities, diclofenac concentrations were below 5 µg/L. High concentrations of diclofenac in India and Pakistan could be explained by the use of diclofenac for veterinary usage in Asia, while it is restricted and only permitted in 5 countries in Europe: Spain, Italy, Estonia, Czech Republic and Latvia (Margalida & Oliva-Vidal, 2017).

Chapter 3: Identifying priority chemical contaminants in urban riverine systems in world

3.1 Introduction

In the last chapter, more than 1100 chemicals were identified that have been monitored in urban aquatic environments worldwide. In this chapter, the risks posed by these chemicals to aquatic organisms are described and a list of priority chemicals for each continent was developed.

Multiple prioritisation methods exist to identify toxic chemicals in the environment. These include exposure-based, hazard-based and risk based- methods. Exposure-based methods usually rely on the use of predicted environmental concentrations (PECs). PECs are calculated on sales, prescription data, per capita consumption, the proportion of the chemical excreted unchanged (for ingested chemicals like pharmaceuticals and diets supplements), and wastewater treatment plant removal rates (Guo *et al.*, 2016; Bu *et al.*, 2020). The advantage of exposure-based methods that employ PEC predictions is that chemicals can be considered that have not previously been measured in the environment. The disadvantage is that the collection of data cited above can be difficult and, for many substances these data do not exist. Exposure-based prioritisation is therefore more applicable to substances like pharmaceuticals because prescription data, sales and metabolism data are more accessible.

Hazard based- methods prioritise chemicals based on factors such as the persistence, bioaccumulation and toxicity (PBT) of a chemical (Howard and Muir, 2010; Berninger *et al.*, 2016; EPA, 2018). As laboratory-PBT based data are very limited, hazard based methods often rely on use of in-silico models, such as EU QSAR Toolbox, EPIsuite, ECOSAR or Vega Hub software, which estimate the PBT properties of a chemical based on its chemical structure. While data on the PBT properties of chemicals can be easily obtained (e.g octanol/water partitioning, half-lives in water), the difficulty with hazard-based method is that the criteria for the identification of PBT chemicals varies greatly between methodologies and a consensus on defined PBT criteria has yet to be reached (Arnot *et al.*, 2012). PBT criteria are for example very different between EU REACH, UNEP or OSPAR frameworks (Moermond *et al.*, 2012).

driven by a high concentration of 7.150 mg/L, detected in Thulamela municipality (South Africa). The pesticides pentachlorophenol also posed a great risk (RQ=23565), especially in Cape Town (South Africa) where it was detected at 9.210 $\mu\text{g/L}$.

In South America 124 chemicals were initially identified of which 84 were detected at least once above the LOQ. RQs were calculated for 81 chemicals. In total, 18 chemicals from 7 class categories had an RQ>1. Pesticides and pharmaceuticals were the largest categories with 6 and 4 priority chemicals respectively. Highest continental RQ was 418 for 17 β -estradiol (pharmaceuticals) and 204 for metolachlor (pesticides). The chemicals metolachlor, caffeine, atrazine, miconazole and 17 β -estradiol had the highest continental RQs in South America compared to the other continents. The number of data collected for South America was less compared to the other continents.

cities were found to be related to multiple socio-economic factors: population size, population density, road density, traffic, wastewater management facilities, regulations and surrounding industries. These correlations between chemical emissions and socio-economic factors should be further studied. Results could allow cities that cannot perform water chemical analysis to determine a full profile of their chemical pollution based on socio-economic information only.

In the future, the risks posed by priority chemicals should be further analysed within cities with temporal and spatial analysis of risks. Understanding if risks are posed in certain areas within a city (e.g. downstream WWTP) or in a specific season or specific event will be key to develop relevant mitigation and adaptation strategies for chemical emissions today and in the future.

In the next chapter, priority chemicals identified here are monitored in three European cities: York (UK), Oslo (Norway) and Madrid (Spain) throughout one year. The aim was to further analyse risks of these priority chemicals across cities (upstream, downstream WWTP and city centre) and across seasons with seasonal samplings.

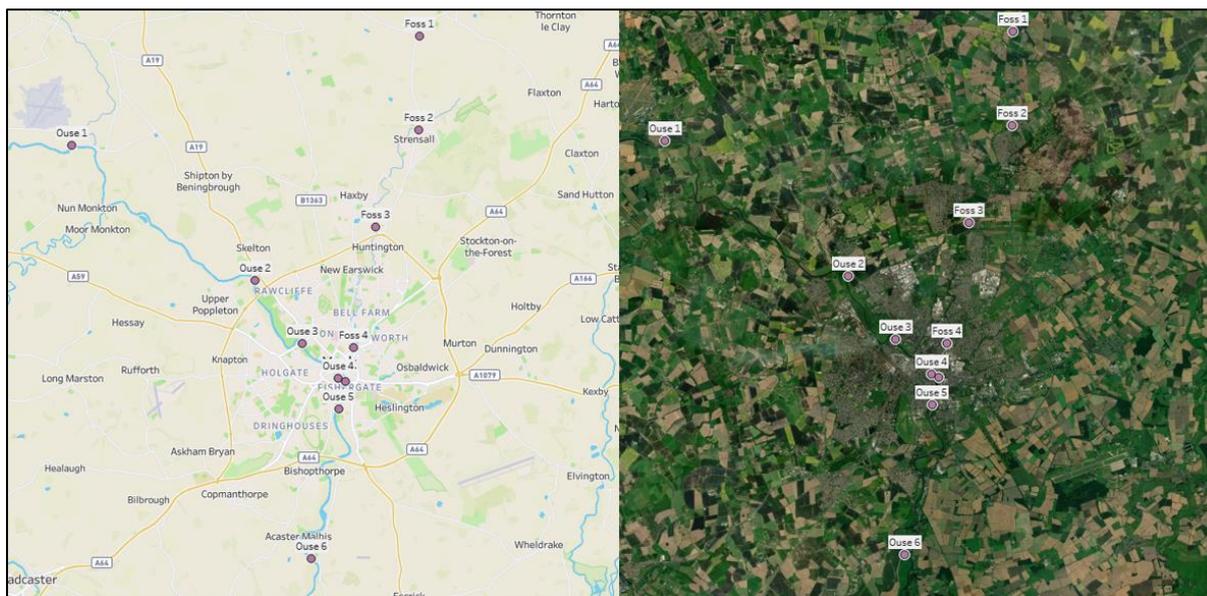


Figure 9 - Locations of the 11 samplings sites on river Ouse and river Foss around the city of York. Panel A shows locations on a streets map and panel B on a satellite map.

Table 5 - Descriptions of samplings sites in York

Site Name	Site description	River
F1	Upstream city perimeter Upstream of WWTP 2	River Foss
F2	Inside city perimeter Downstream of WWTP 2	River Foss
F3	Inside city perimeter Further downstream of WWTP 2	River Foss
F4	Inside city center	River Foss
F5	Inside city center Upstream of the River Foss and the River Ouse confluence	River Foss
O1	Upstream city perimeter	River Ouse
O2	Inside city perimeter Upstream of WWTP 1	River Ouse
O3	Inside city perimeter Downstream of WWTP 1	River Ouse
O4	Inside city center	River Ouse
O5	Outside city center	River Ouse
O6	Downstream city perimeter	River Ouse

Wilkinson et al., (2019). Briefly, samples were placed in a 4D temperature-controlled autosampler. An aliquot of 100 μ L was injected into a ZORBAX Eclipse Plus C18 chromatography column (3.0 \times 100 mm, 1.8 μ m, 600 bar) at a constant flow of 450 μ L/min. Each target compound and internal standards had two transitions monitored by positive electrospray ionization: one transition for quantification and one transition for confirmation. Mass to charge (m/z) ratio, collision energy and retention time of transition 1 and transition 2 of target compounds and internal standards are available in Wilkinson et al., 2019. Mobile phase A consisted of HPLC-grade water with 0.01 M formic acid and 0.01M ammonium formate. Mobile phase B was methanol. Analysis started at 10% mobile phase B. Mobile phase B reached 40% after 5 min, 60% after 10 min and 100 % after 15min where it remains until the end of the analysis. After the analysis of each sample, re-equilibrium to 10% mobile phase B lasted 10 min.

Quantification was obtained with a 15-point calibration curve ranging from 1 to 8 000 ng/L using Thermo Fisher Xcalibur™ Software. The standard method developed by Furlong et al., (2014) was used for all calibrants to obtain same proportion of methanol in final calibrants solutions.

For method quality control, all internal standards were spiked at 80 ng/L in samples, calibrations solutions and blanks. For environmental samples, samples were prepared by spiking 995 μ L of sample with 5 μ L of internal standards solutions at 80 ng/L. Similarly, calibrations solutions were prepared by spiking 975 μ L HPLC-grade water with 5 μ L of internal standards solutions at 80 ng/L and 20 μ L of relevant calibration solution.

For instrumental quality control, blanks and an instrumental QCs were run every 10 injections during samples analysis. Blanks were HPLC water with internal standards spiked at 80 ng/L. Instrumental QCs were solutions with target compounds at 400 ng/L and internal standards at 80ng/L. Moreover the column and entire system was flushed prior to all analysis and at least 10 blanks were run before and after processing of all analytical batches. Detection limit (LOQ) and quantification limit (LOQ) were determined following Wilkinson et al., 2019. LOD and LOQ are presented in Table 7.

Table 7 - Detection limit (LOD) and quantification limit (LOQ) in ng/L for caffeine, clarithromycin and sulfamethoxazole

	LOD	LOQ
Caffeine	21.03	40.39
Clarithromycin	13	26
Sulfamethoxazole	1.76	3.52

ICP-MS for metals quantification

Quantification of metals was performed by the Biorenewables Development Centre at Dunnington (UK) using an Agilent 7700 series ICP-MS. Briefly, samples were thawed and spiked with 0.1 mL of hydrochloric acid to stabilize silver priori to analysis.

Quantification was obtained with a 5-point calibration curve ranging from 50 to 100 000 µg/L. All acid used was trace metal grade. Blanks and calibrations solutions were run first. Results for each element were fitted onto the calibration curve. The result recorded was then multiplied by the dilution factor, to produce the concentration for each element in the sample. Detection and quantification limit are presented in Table 8.

Table 8 - Detection and quantification limit in µg/L for metals for each analytical run performed

	Spring	Summer	Autumn	Winter
Aluminium	3.5	3.5	2.807	4.905
Phosphorus	172.1	172.1	22.349	52.934
Chromium	0.1	0.1	0.073	0.035
Manganese	0.1	0.1	0.039	0.036
Iron	1.2	1.2	0.937	1.857
Cobalt	0.01	0.01	0.013	0.01
Nickel	0.01	0.01	0.203	0.107
Copper	0.2	0.2	0.173	0.355
Zinc	0.9	0.9	0.767	2.166
Silver	1.6	1.6	1.574	0.056
Tin	0.1	0.1	0.127	0.091
Cadmium	Not measured	Not measured	0.13	0.09
Mercury	Not measured	Not measured	0.35	0.01
Lead	Not measured	Not measured	0.02	0.03

Prioritisation of chemicals

Risk quotient (RQ) of chemicals was measured similarly as in chapter 2. Risk quotients (RQ) were calculated for each chemical, each season and each location using the equation:

$$RQ = \text{AVG} / \text{PNECmin} \quad \text{Equation}$$

Where: AVR= Average measured environmental concentration of a chemical and PNECmin= lowest PNEC or EQS or equivalent-PNEC for each chemical. Because the number of chemicals was more manageable than in chapter 2, PNEC and environmental quality standard (EQS) from government agencies and industries were collected. Database of INERIS (<https://substances.ineris.fr/fr/>), EU WFD (<https://eur-lex.europa.eu/>), US EPA (<https://comptox.epa.gov/>), Canada WQS (<https://ccme.ca/en/current-activities/canadian-environmental-quality-guideline>) and China WGC (Wang *et al.*, 2021) for metals and the AMR industry alliance (AMR Industry Alliance, no date) for antibiotics were examined for PNEC and EQS reference. Lowest PNEC or EQS collected was used as PNECmin.

4.3 Results

Measured environmental concentrations

Twelve metals were quantified in the collected samples: aluminium, cadmium, chromium, cobalt copper, iron, lead, mercury, nickel, silver, tin and zinc. Mercury, cadmium and lead were only measured in samples collected in autumn and winter. Measured environmental concentrations are presented in figure 11-13.

Aluminium and iron were the metals detected at the highest concentrations in York, Madrid and Oslo. Aluminium concentrations ranged from 602-1752 µg/L in Madrid (Figure 11), 416-1166 µg/L in Oslo (Figure 13) and 633-1794 µg/L in York (Figure 12). Iron was detected at 294-1098 µg/L in Madrid, 12-2291 µg/L in Oslo and 320-1501 µg/L in York. Concentrations of aluminium and iron were constant across seasons and locations in the three cities.

Zinc was the metal with the third highest concentrations. Zinc concentrations varied greatly between cities, locations and seasons. In Madrid, concentrations of zinc were below 30 µg/L in summer and autumn with the exception of 288 µg/L detected in SP3 in summer. In Spring

Madrid, 1 µg/L in Oslo and 1.3 µg/L in York. Mercury, cadmium and lead were only analysed in autumn and winter. Mercury concentrations ranged from 0.2 to 3.3 µg/L in York, 0.1 to 6.7 µg/L in Oslo and 0.3 to 1.3 µg/L in Madrid. Cadmium and lead were measured in winter and at concentrations below 6 µg/L. Silver was not detected in this study.

and winter though, RQ of copper was systematically above 10 and up to 485 in Madrid, 7 889 in Oslo and 2 538 in York.

Mercury was not measured in spring and summer samples. In autumn and winter, the RQ of mercury was systematically above 1 and up to 43 in York, 60 in Oslo and 19 in Madrid. In York, RQs ranged from 10-43 in the river Ouse and from 2-28 in the river Foss. In Oslo, RQs ranged from 2-7 in all locations except for location 6 in winter (RQ=60). In Madrid, RQs ranged from 5 to 19. The maximum RQ of 19 was detected in SP5 in winter.

RQs of chromium ranged from 1-9 in Madrid, Oslo and York. Tin had RQs ranging from 1-2 in Madrid. In York and Oslo, tin RQs were systematically below 1 except for O1 (RQ=10) in the summer. Cobalt had an RQ of 1-2 in one location in summer and 3 locations in winter in Oslo. Similarly in York, cobalt RQs ranged from 1 to 3 at 3 locations in spring and 9 locations out of 11 in winter. All other samplings events had RQs below 1. In Madrid, RQs systematically ranged from 1-3 from locations SP7 to SP10 across all seasons. Cadmium had RQs below 1 in autumn and between below 1-3 in the winter in the three cities. Nickel had RQs above 1 at 2 occasions in York and in Oslo across seasons: F4 in summer (RQ = 2.93); O5 in winter (RQ= 3.56) for York and in location 3 (RQ= 1.4) and 5 (RQ = 1.55) in summer for Oslo. In Madrid, nickel RQs ranged from 1-4 for a few sampling events in spring, summer and autumn. In winter, the RQs were between 1-2 in 7 locations out of 9. RQs could not be calculated for silver as this was not detected in any samples. Lead, measured in autumn and spring, had an RQ above 1 in one sampling event only: in O5 in winter in York (RQ= 3.58).

Looking at antibiotics and caffeine, RQs were above 1 on a few sampling events in the three cities and across seasons. Clarithromycin had RQs ranging from 1-2 at 2 locations in summer, 4 in autumn and 2 in winter in Madrid. Similarly in York, clarithromycin posed a risk in the river Foss only at 3 locations in spring, 2 in summer and 4 in autumn. Clarithromycin did not pose a risk in Oslo. For sulfamethoxazole, the RQ was systematically below 1 in all cities and across all seasons. Caffeine had an RQ between 1-3 in SP9 and SP10 in Madrid and between 2-4 in F3 and F4 in York in autumn only. In Oslo, RQ was between 1-3 in one location in spring (location 2), 4 locations in summer (location 3-6), one location in autumn (location 6)

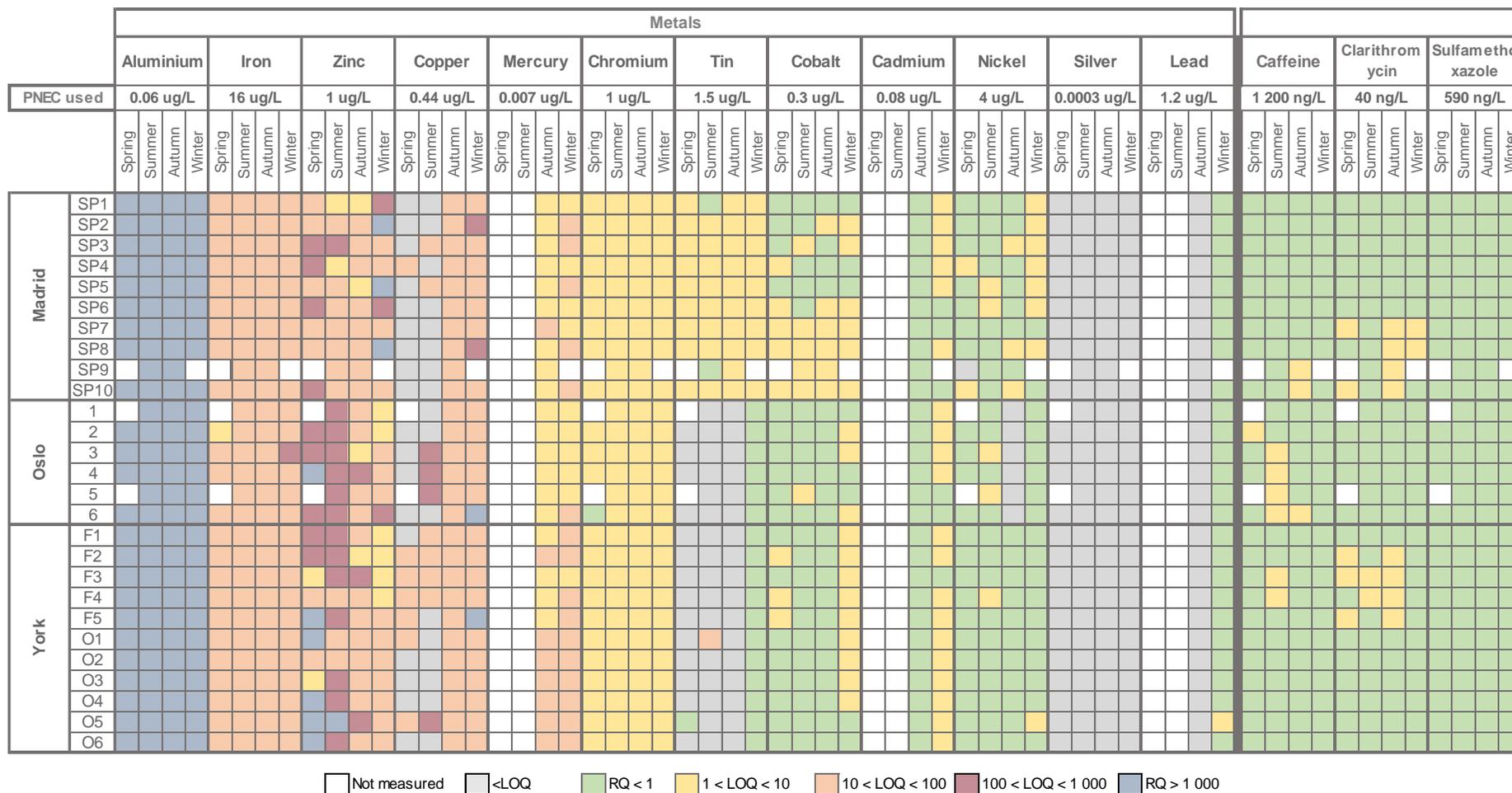


Figure 17 - Heatmap of metals' and pharmaceuticals' RQ across spring, summer, autumn and winter at all samplings locations in Madrid, York and Oslo. Green cells indicated RQ < 1; yellow 1 < RQ < 10; red 100 < RQ < 1 000; blue RQ > 1 000.

4.4 Discussion

The aim of this study was to study and compare the risks of metals, antibiotics, and caffeine for aquatic living organisms in three urban environments. Results showed that metals posed constant and greater risks than pharmaceuticals.

Aluminium posed the greatest risk with RQ systematically above 1 000 in the three cities. Aluminium was the metal detected at the highest concentrations in this study (416 µg/L to 1794 µg/L). These concentrations are not unusual. Similar concentrations are regularly reported in the EU WaterBase River database in Italy, Austria, the United Kingdom and Finland (EEA, 2014). These concentrations cannot be explained by natural background concentrations which are estimated between 6 µg/L and 8.58 µg/L (Cheeseman *et al.*, 1989; Dixon and Gardner, 2015). Anthropogenic sources of aluminium include construction sites, architecture, road infrastructures, outdoor paints, drinking water, personal care products, diet, vaccines, as coagulants in wastewater treatment plants (Eurometaux, 2021). In a similar study conducted in the UK, aluminium was the 2nd most toxic heavy metal in a study conducted in the UK behind copper (Donnachie *et al.*, 2014).

Zinc, iron and copper were the next most toxic chemicals with potential impacts on fishes, daphnids and algae. Zinc concentrations ranged from 3 µg/L to 6 959 µg/L, iron from 12 µg/L to 2 291 µg/L and copper from 1 µg/L to 461 µg/L. Negative effects on aquatic living organisms were reported in the literature at lower concentrations: zinc had a LC50 of 68 µg/L for *daphnia magna* after 48 hours exposure and an LC50 of 116 µg/L for mosquito fish after 48 hours exposure (Taylor, 1978; Mount and Norberg, 1984). Iron, which was the second metal detected at the highest concentrations, had an LC50 of 1220 µg/L reported for *Cyprinus carpio* (carp) (Alam and Maughan, 2008). Similarly, for copper the lowest reported harmful concentrations (EC50) are 0.2–1.3 µg/L for *daphnia magna* and 8.6 µg/L for fathead minnow after 48 hours exposure (De Schampelaere, Heijerick and Janssen, 2002; Markich *et al.*, 2005; Van Genderen and Klaine, 2008). Copper, iron and zinc were the top three priority metals identified in similar study conducted in the very industrialized region in China. In another study in the UK, copper ranked 1st, zinc 3rd and iron 6th. Copper is known to be emitted by the degradation of plumbing and urban architecture. Similarly zinc and iron degrade from construction sites, transportation services and household appliances (Eurometaux, 2021; Panagos & Katsoyiannis, 2019). These metals are also found in domestic waters as they are

used in health supplements and in personal care products for example (Eurometaux, 2021; USGS, n.d.).

Mercury and chromium also posed a systematic but a lower risk compared to iron, zinc and copper. RQs of mercury ranged from 2 to 60 and from 1 to 9 for chromium. Chromium and mercury were ranked 12th and 14th in a study ranking heavy metal risks in the UK and 5th and 10th in a similar study in China. Mercury can degrade from non-ferrous metals production, coal-fired power plants, appliances (batteries, electrical and measuring devices, lighting lamps, etc) and leak out of landfills (AMAP & UNEP, 2019). Mercury is well-known to bioaccumulate and biomagnified throughout the food web. This affects aquatic organisms' survival and health of humans via consumption of contaminated animals (Liu, Cai and O'Driscoll, 2012; Lavoie *et al.*, 2018). Chromium is used in pipes, fittings and surface finishings (including kitchen sinks and domestic appliances) and constitutes 11% of steel (Rule *et al.*, 2006). Chromium was found to have an LC50 of 22 µg/L for *Daphnia magna* after 48 hours exposure (Mount and Norberg, 1984).

For cobalt, nickel and caffeine, the RQ was mainly below 1 and occasionally between 1 and 10. Similarly, for the antibiotics, clarithromycin had an RQ above 1 in York and Madrid on a few occasions, but not in Oslo. Antibiotics were not expected to be measured or pose a risk in Oslo as the river Alna in Oslo does not receive wastewater treatment plant effluent. However, caffeine was detected in the highest concentrations in Oslo (106 – 5 328 ng/L) compared to York and Madrid.

The primary source of caffeine in urban environments is usually WWTP (Li *et al.*, 2020). High concentrations of caffeine in Oslo could be because of a higher consumption by Norwegians, higher urban runoff and/or climatic conditions in comparison with York and Madrid. Norway is the second biggest consumer of caffeine with 21.82 kg/capita consumed in 2016. In comparison, Spain had an estimated consumption of 9.92 kg/capita in 2016 (ICO, 2019; WPR, 2021). Rainfall is also more important in Oslo: 1010 mm/year compared to 755mm/year in York and 415mm/year in Madrid (Climate Data, 2015). Last, climatic conditions of Oslo with lower temperature and less UV radiation could decrease caffeine degradation and therefore contribute to high concentrations in Oslo despite the absence of wastewater treatment plant effluent (Li *et al.*, 2020).

Except for copper and cadmium, there was no difference in risk posed by chemicals across seasons. Chemicals chosen in this study are not known to be used seasonally, therefore concentrations detected in the environment were also stable across seasons. Other chemicals known for seasonal consumptions (urban pesticides like insect repellants) would have however been expected to pose different risk throughout the season in the environment. For copper, RQ was constantly above 10 in autumn and winter. In spring and summer, copper was mostly below the detection limit and on a few occasions had an RQ above 10. One explanation for these high RQ variations would be COVID-19. Copper is highly associated to vehicle brake lining and tire wear in urban environments (Eurometaux, 2021; Panagos & Katsoyiannis, 2019). Samplings in Spring and summer were taken in March and August 2021 after lockdown periods in the three cities and during summer holidays. Previous studies have demonstrated low traffic during lockdown periods (Rossi, Ceccato and Gastaldi, 2020; Brown, Barnes and Hayes, 2021; Haghazad *et al.*, 2022). Low numbers of car journeys and transportation traffic at these time could explain copper been <LQO on multiple occasions. RQ of copper would then depends on local activities/transportation.

Zinc RQ varied greatly between locations. RQ ranged from 4 to 3 510. Risk was particularly high in spring and summer in Oslo and in York. This could be because of high recreational activities happening in the water during these months. As mentioned previously zinc is used for multiples purposes in urban environments included in boat and cars' fuels. Boat rental companies and cruises ships activities are high during these months in Oslo and in York. There are multiples boat companies based at locations O4 in York which might explain the high zinc RQ in O4 and downstream sampling locations. These companies do not operate in autumn and winter, which would explain lower risk in these months.

Impacts of locations can also be seen for clarithromycin and caffeine. Clarithromycin and caffeine's RQ were higher after location SP7 in Madrid possibly because of release of effluent of "Butarque" WWTP near the sampling location. Clarithromycin also posed a constant risk in river Foss in York but not in river Ouse. This is probably because of the lower river flow (compared to river Ouse) and proximity of the sampling locations to the point of WWTP effluent discharge.

Except for tin, there was no difference between chemical profile pollution between the three cities. Metals were detected at similar levels and in the same order from highest to lowest

concentrations across the three cities: aluminium, iron, zinc, copper, chromium, nickel, tin, mercury, lead, cobalt, cadmium, and silver. Except for tin, the levels of risks were the same in the 3 cities. Tin posed a systematic risk in Madrid but not in Oslo or York. Tin concentrations in Madrid ranged from 1 µg/L to 4 µg/L.

This study showed that metals present a much greater risk to aquatic organisms compared to antibiotics. The average risk quotient for aluminium was 15 000 times higher compared to the average risk quotient for clarithromycin. Similarly, Johnson et al., 2017 found that zinc posed a relative risk a million time greater compared to beta-blocker metoprolol. This can be explained by multiples reasons. First metals are detected in greater concentrations than pharmaceuticals. This is because metals are used for many purposes (in plumbing, in architecture, in construction, in transportation, in paints and household appliances to cite a few) and in higher quantities compared to pharmaceuticals (Eurometaux, 2021). In Europe 8 kilotons of copper is estimated to enter freshwater bodies per year (S. Comber et al., 2022). In comparison, 4264 tonnes of antibiotics were consumed by human in Europe in 2018 (OECD, 2022).

Second, the PNEC used for metals were more conservative in this study compared to others. While the authors chose to use the lowest PNEC value or EQS found in the literature and in regulatory report, others studies used median ecotoxicity values as the PNEC (Johnson *et al.*, 2017; Su *et al.*, 2017). This is because ecotoxicity of metals is difficult to determine and varies with water chemistry, organic contents, hardness of water and specification of metals (Gardner *et al.*, 2008). There is no general agreement between scientists and regulators on metals' ecotoxicity yet. For example the PNEC of nickel is 4 µg/L for EU WFD AA-EQS, 52 µg/L and 420 µg/L for chronic and acute exposure limits proposed by the US EPA (European Commission, 2019). Other metals like cobalt or tin have no EQS. Another example is aluminum. Aluminium is considered as a relatively low metals of concern for living organisms in water pH above 6. At pH below 6.5, aluminium occurs mainly in $\text{Al}(\text{OH})_2^+$, $\text{Al}(\text{OH})^{2+}$, and Al^{3+} forms. Aluminium tends then to be reactive and unstable, leading to the precipitation of aluminium on gill's surface, killing living organisms (Comber et al., 2005; Gardner et al., 2008). Because environment freshwater pH is mainly between 6.8 to 9, aluminum is therefore not always included in studied looking at toxicity of metals (Rule et al., 2005; Su et al., 2017). In this study, pH water was not measured below 7.02. Aluminium

had however a LC50 of 89 µg/L for young crustacean *Hyalella Azteca* in pH water of 7 (Borgmann *et al.*, 2005). In comparison, PNEC of clarithromycin and sulfamethoxazole came from the AMR industry alliance based on industrial consensus agreement.

As the methodology used in this paper was mainly to be able to analyse and compare the risk of metals with antibiotics, more research would be needed to have a final and definite analysis of the risks of these chemicals. Potential additives or synergetic effects of metals and antibiotics mixtures would need to be taken into account: previous studies have showed that antibiotics resistant genes are promoted in presence of metals (Stepanauskas *et al.*, 2006; Zhang *et al.*, 2012; Ye *et al.*, 2017). The natural background concentrations should be analysed for each location and water chemistry should be included metal toxicity assessments. Moreover pH depressions in urban environments because of snow melts and acid rains was previously demonstrated (Jeffries, Cox and Dillon, 1979; Johnson, Turner and Kelly, 1982). Effects of pH variations and potential impacts of future acidification of water because of climate changes should be included in risk analysis.

Next research step

In this chapter, out of fifteen priority chemicals identified in chapter 2 and measured in this chapter in three European cities, 13 had RQ above 1 and therefore posed a risk at least at one sampling event: the metals aluminium, iron, zinc, copper, mercury, chromium, tin, cobalt, cadmium, nickel, lead as well as caffeine and the antibiotic clarithromycin. Only silver and sulfamethoxazole did not pose a risk in this study. The risks of 13 priority urban chemicals are suspected to change and potentially increase in the future because global change and megatrends such as increasing and migrating population, urban expansion, resources scarcity, climate change and technology innovation (Retief *et al.*, 2016; Van den Brink *et al.*, 2018). These megatrends will affect chemical production, usage and degradation in the environment, which will in turn change their risks.

To study how global change will affect the risk of priority chemicals in the unknown future, multiples future societies should be considered. The Shared Socio-Economics Pathways (SSPs) scenarios were developed by the IPCC to allow scientists to study environmental problematic under the same future storylines. SSPs are a set of 5 qualitative scenarios of future changes

in demographics, human development, economy and lifestyle, policies and institutions, technology, and environment and natural resources (O'Neill *et al.*, 2017). SSPs have not been adapted to chemicals emissions yet.

In the next chapter (Chapter 4), a framework was developed to adapt global-SSPs and extended-SSPs (e.g. European SSPs; Agricultural European SSPs) to chemical emissions. The framework is first illustrated for antidepressants and insecticides emissions in European freshwater bodies in 2050. In chapter 5, the framework is pushed forward and developed with stakeholders from academia, industries and regulators for antibiotics. Antibiotics were chosen to be extended in chapter 5 rather than metals for multiple reasons: 1) the literature on sources and pathways of antibiotics in urban environment is extensive. This allows a better understanding and therefore better scenario development for the future; 2) stakeholders available to contribute to scenario development process were antibiotics experts and last; 3) antibiotics resistance gene is listed in the top 10 global health threats by UNEP (UNEP, no date).

Chapter 5 - A Shared Socio-Economic Pathway Based Framework for Characterising Future Emissions of Chemicals to the Natural Environment

5.1 Introduction

In the last chapter, chemicals that currently pose a risk in European urban aquatic environments were identified through a monitoring study of three contrasting European cities. In the future, the emissions and effects of these priority chemicals could alter as a result of societal changes in response to global megatrends such as climate change and urbanisation (Balbus *et al.*, 2013; Redshaw *et al.*, 2013; Hader *et al.*, 2022). However, the extent of changes in emissions, which will drive the effects, is currently unclear.

Societal changes happen rapidly and affect the consumption and emissions of chemicals (Bunke *et al.*, 2019) so in the future the use of chemicals will likely increase further. For example, despite increased human development, the prescriptions and consumption of antidepressants are continuously increasing in developed countries and are expected to be exacerbated by natural disasters in the future (Olié *et al.*, 2002; Exeter, Robinson and Wheeler, 2009; Redshaw *et al.*, 2013; Gualano *et al.*, 2014; To, Eboime and Agyapong, 2021). Pesticides have experienced a rapid shift in usage in the last 60 years. Pesticides use has increased by 15-20-fold since the 60s to increase food production and respond to global food demand (Oldenkamp, Beusen and Huijbregts, 2019). Because they are very toxic chemicals which may affect human health and the environment, pesticides frequently receive negative media coverage in some public debate (Rani *et al.*, 2021; Le Monde, 2022; Newsbeat, 2022). However the pressure to meet food demands for the 9 billion inhabitants predicted by 2050 (Popp, Petó and Nagy, 2013; Finger, 2021) will mean that pesticide use could continue to increase. Changes in consumption will lead to changes in emissions, exposure and risks to the natural environment. For instance, the risk posed by antibiotic ciprofloxacin to aquatic species has increased by 10-20 fold worldwide in twenty years because of increasing exposure (Oldenkamp, Beusen and Huijbregts, 2019). Future societal changes will therefore affect the

number, the quantity and the diversity of chemicals and subsequently chemical risks in different ways.

Few societal changes have been studied to determine their impact on chemical emissions. Advanced technologies for wastewater treatment can decrease the load of chemicals released in water bodies (Yaman *et al.*, 2017; Fairbairn *et al.*, 2018); legislation and regulation can limit the number of compounds available on the market (van Dijk *et al.*, 2020); chemical engineering can create genetically modified crops (GMO) that reduce the number and volume of fertilisers and pesticides used by farmers (Klümper *et al.*, 2014). At the same time, new chemicals, designed to satisfy specific needs, can also be more persistent and more dangerous for the environment (e.g. perfluorooctanoic acid); GMO crops can promote resistant pests that will require stronger and potentially more toxic pesticides (Van Acker, Rahman and Cici, 2017). The societal changes (including socio-economic factors such as human development, urbanization, demographics change, inequalities, international agreements, economic growth, diets, etc) have not been studied together to estimate their potentials effects on chemical emissions for the future. Potentially important trends in future environmental emissions may be missed if all aspects of societal changes are not considered. This also means that mitigation and adaptation strategies to deal with future chemical pollution are based on incomplete evidence.

One approach to inform the research and management of chemical emissions in the future under global change is to use scenarios. Scenarios explore multiple alternative futures with the aim of evaluating strategies to respond to any potential adverse changes (Jones *et al.*, 2015). A very influential set of recent scenarios are the representative concentration pathways -RCPs- (van Vuuren *et al.*, 2011) and the shared socio-economic pathways -SSPs- (O'Neill *et al.*, 2017), developed by the global climate change research community. The SSPs describe five contrasting socio-economics pathways with their abilities to adapt and mitigate to global change challenges. They are based on six categories: demographics, human development, economy and lifestyle, policies and institutions, technology and environment and natural resources. Each category is further detailed with SSP elements like, among others, population growth, fertility and urbanisation for demographics or education, health investment and equity for human development. For each SSP storyline, a socio-economic situation is described with variation of SSP elements (e.g. health investment is high under

SSP1 and low under SSP3). They are meant to be used as baselines for climate change and sustainable development research. SSPs are made to serve the global climate change community, but they are also designed to be extended to multiple sectors and scales and improve consistency with all global change-related research. Different sectors and geographic scales, including land-use management in central Asia, European agriculture or more recently the United Kingdom, have downscaled scenarios based on the SSPs to explore the impacts of future climate conditions (Mitter *et al.*, 2020; Nunez *et al.*, 2020; Pedde *et al.*, 2021). Scenario development and scenario extensions are a relatively recent area of research, but the number of scenario studies has increased rapidly in recent years. An article looking at achievements of the climate change scenario framework reported 1,400 articles that used and/or developed scenarios based on SSPs since 2010 (O'Neill *et al.*, 2020). Nevertheless, such scenarios have not yet been developed for emissions to the environment from the chemical sector.

Ideally, global SSP scenarios would be extended to all the chemicals within the chemical sector. The research community focusing on chemical emissions in the future could then work under the same storylines and extend those scenarios to more specific research questions if needed. To do so, key drivers and relevant scale for all chemicals must be defined. This is not possible as key drivers and relevant scale vary between and among groups of chemicals. A single set of narratives cannot adequately cover all chemicals because of the diversity of chemicals' physical and chemical properties, environmental behaviour, human usage and future needs for society.

To be able to study chemicals in the future, here, we present a framework, based on the socio-economic and climate scenarios (combined SSP-RCPs), for the development of scenarios for emissions of single chemicals or groups of similar chemicals to the natural environment in the future. 'Chemicals', being a heterogeneous group, do not have the same drivers of emissions and relevant study scales for all classes. A 'simple' extension of SSPs cannot, therefore be made, the thematic focus of scenarios developed must be for single chemicals or groups of similar chemicals. We therefore illustrate the approach for antidepressant and insecticide emissions in Europe in the 2050s.

Antidepressants and insecticides were chosen for multiple reasons. Their usage is reported to come from different drivers in the literature. On one hand, antidepressant usage is driven by sociodemographic drivers like education, social cohesion, inequalities and/or culture

(Henriksson and Isacson, 2006; Hiilamo, 2014; Lewer *et al.*, 2015; Park, Jang and Chiriboga, 2018; Gomez-Lumbreras *et al.*, 2019). On the other hand, usage of insecticides can be driven by cultural practices (e.g. type of crops, crops rotation, conventional vs. non-conventional practices), regulations, technology development but also by consequences of climate change like increase temperature or increase rainfall (Bloomfield *et al.*, 2006; Meissle *et al.*, 2010; Brookes and Barfoot, 2018; Wan *et al.*, 2018; Rhodes and McCarl, 2020). Consumption has consistently increased in the last 50 years and is expected to continue. However, looking at SSP storylines, the changes in antidepressants and insecticides' emissions in the future are uncertain. Global changes that are projected to occur over the next 30 years could have an effect on antidepressant and insecticide consumption and, therefore, on emissions into the environment. These future emissions must be understood in order to assess future risk and mitigate their impacts.

Here we propose a four-step framework, inspired by the approach developed by Mitter *et al.*, 2019 for the European agricultural sector, and apply it to antidepressants and pesticides to demonstrate the framework's utility as a tool to gain a better understanding of future chemical emissions and the way that societal change influences this future.

5.2 Methods

A groups of eight scientists with expertise in scenario developments, in environmental sciences, in chemistry and in toxicology gathered to develop the following four-step framework to characterise chemical emissions in the future under the SSPs. The framework, presented in Figure 18, is inspired by the methodology developed by Mitter *et al.*, 2019 to European SSPs to Agricultural European SSPs and follow standards methodologies for scenario development (O'Brien, 2004; Rounsevell and Metzger, 2010; Rose and Star, 2013; Priess and Hauck, 2014).

Step 1: Define key characteristics of scenarios

The first step focuses on the determination of key characteristics of the scenarios required. This is an essential step to have a clear understanding of the specifications and boundaries of

the scenarios, as well as to answer “why”, “for whom” and “how” are those scenarios being developed. The following questions should be addressed:

- **What is the goal and purpose of the scenario?** the goal and purpose of the scenarios must be determined: Why are the scenarios needed? What are the questions we want to answer with the output from the scenarios?
- **Which chemical or group of chemicals is being investigated?** The chemical or group of chemicals for which the scenarios are to be applied should be defined. Multiple chemicals/molecules could be considered as one group of chemicals for scenario development if molecules have the same dynamics in the society, environmental behaviours and fates within the temporal and spatial scale chosen further in step 1. If a group of chemicals is to be considered, similarities in production, usage, consumption and environmental behaviours are mandatory. Here, we want to avoid selecting multiple chemicals that would be impacted by socio-economic drivers in different ways, making the development of a scenario storyline for all chemicals included impossible.
- **Which environmental matrices are being considered?** Do the scenarios focus on air, water, or soil compartments? We recommend to only select one matrix as chemicals can behave differently in different environmental compartments.
- **What temporal scale is required?** Are the scenarios focusing on future of chemicals in 2030, 2050, 2100 etc?
- **What geographical scale is required?** Are the scenarios focusing on a city, a country or a continent? Urban environments? Urban environments in developed countries? A small geographical scale involves an easier understanding of the dynamics of the system, but literature can be limited on the system in question. Moreover large scale SSPs might be more difficult to extend because they are not specific enough for smaller scale systems. A large geographic scale has more chances to have available SSPs (e.g. Europe, United Kingdom), but the system might be more difficult to understand and to apply to a chemical or group of chemicals. Determination of temporal and spatial scale are necessary to define the system boundary in which scenario will be developed and should be primarily determined by the goal and purposes of the scenarios.
- **How many and which SSPs need to be explored?** There are multiple SSPs that are available in the literature: global SSPs, European SSPs, water-sector SSPs, drought

characteristics in China SSPs to cite a few (Riahi *et al.*, 2017; Graham *et al.*, 2018; Kok *et al.*, 2019; Su *et al.*, 2021). Depending on the characteristics of the scenarios wanted, the most relevant and logical SSPs should be selected for use. The number of scenarios can range from a minimum of two scenarios to five (all SSP scenarios). A single scenario should not be developed by itself, as it should be comparable to another.

- **Which climate projections should be explored?** The use of many chemicals will be affected by weather conditions such as temperature, moisture content and flood events. For the system of interest, therefore, projections of future weather patterns associated with the selected SSPs should be obtained to provide a foundation for identifying any climate-driven changes in chemical use during Step 2.
- **Who is the target audience?** The targeted audience can be climate change scientists, social scientists, regulators, industries, public, etc. The format of the scenarios and the level of detail should be relevant to the knowledge and needs of the targeted audience.
- **What will be the form of the scenario?** How will the scenario look: an infographic? a set of storylines? a table with increasing and decreasing chemicals trends? Output scenarios can have any format, but must be relevant to the scenario's goal, purpose and targeted audience.

Step 2: Review and prioritisation of the potential impacts of changes in socio-economic and climate on chemical emissions

In step 2, a combination of literature searching and expert elicitation is used to develop an evidence-base on how chemical emissions could change in the future. This analysis considers: a) the socio-economic changes expected for the selected SSPs from Step 1; and b) the effects of projected changes in weather patterns on chemical use. The findings from the systematic review are then used in an expert consultation exercise to select the most important future changes for chemical emissions which are then used as a basis for the emission scenario development in Step 3.

These drivers can be related to socio-economics elements (similar to SSP elements in O'Neil *et al.*, 2017) or climate change elements (e.g. natural disasters, temperature). The idea here is

to understand how the thematic focus is influenced in a society and to develop a list of drivers by conducting a systematic review.

To do the systematic review, we recommend using the elements of the SSPs initially chosen in step 1 to extend to specific search terms. The driver(s) and findings should be extracted from the articles. We found that the search terms “association”, “impact”, “influence”, “effect” and “connection” might extend search results to a large number of relevant articles when looking for dynamic/interactions between drivers and the thematic focus. Direct (e.g. leakage from production site; release from road runoff) and indirect drivers (e.g. consumption; outbreaks of diseases) should be considered in the systematic review.

For some chemicals, climate change driven effects will need to be considered alongside socio-economic driven effects. For example, use of UV-filter molecules in sunscreens might be expected to increase due to projected increases in hot and dry weather. Increased pest disease pressures resulting from changes in climate could alter the use of insecticides, herbicides and fungicides. As climate change has multiple possible future outlooks, selection of climate change scenario is needed. Representative Concentration Pathways (RCPs) provide estimations of plausible future changes in greenhouse gas emissions, that translate into a different range of temperature and precipitation outputs. We recommend using RCPs for climate change integration as SSPs and RCPs can be combined in a scenario matrix architecture (van Vuuren et al., 2017). These ‘integrated scenarios’ help to understand the combined effect of socio-economic change and climate change. Relevant RCPs and related climate change impacts should be chosen and integrated in the same way as SSPs in the scenarios.

Because not all aspects of a society have been researched with respect to chemicals, relevant literature is limited. To enrich the comprehension of the thematic focus dynamic in a society and the list of drivers of the SSPs to extend and the thematic focus should be analysed one by one. The elicitation of experts’ judgement is encouraged. This allows the inclusion of multiple perspectives and opinions on the thematic focus in a society. Expert judgements can be solicited in multiples ways (e.g. personal interview, group interviews, development of fuzzy cognitive maps, surveys) depending on cost and logistical limitations. If an SSP element is considered relevant to the thematic focus by scenario developers and/or experts, then it should be added to the list of drivers.

When the systematic review is done, prioritisation or determination of key drivers is recommended. Drivers (direct and indirect) do not have the same importance to the thematic focus. Two methodologies are recommended here:

- Scenario developers can conduct a qualitative synthesis based on literature review and, if applicable, experts' input to determine which drivers are key drivers for scenario development. A criterion could be 'a driver that influences the consumption of chemical "x" is more relevant than a driver influencing the production of "x"'.
- Experts' judgements can also be solicited to define key drivers using the same methodology as mentioned before. A survey to experts with specific questions (e.g. Do you consider this driver to have a high, medium or low influence on the thematic focus?) could be used to identify key drivers. Experts' time involvement is then limited, and experts are free to complete the survey on their own time.

Step 3: Develop chemicals emissions scenarios:

This step of the framework is focused on the development of scenarios. We recommend doing it in two parts. The first part is to focus on each key driver and each scenario at a time. The second part is to gather all the effects of drivers, consider the drivers' direct and indirect impacts on the thematic focus and propose an overall effect on the thematic focus.

For the first part, each key driver is studied individually. For each key driver, an impact on the thematic focus must be defined following 3 steps:

- A.** Gather outputs from the literature review and experts' judgements from step 2 for the chosen driver
- B.** Identify how the driver is said to change/be in the SSP to extend in step 1 (e.g. in SSP1, the world population increases until 2100)
- C.** Propose an impact of the driver on the chemical or group of chemicals. The impact could be qualitative (e.g. increase/decrease) or semi-quantitative (e.g. small/medium/high increase). The proposed-impact should be consistent with the findings from literature review and with how the driver is said to change/be in the SSPs. The reasoning should be rational. The following statements should be verified:

- The driver's proposed-impact is consistent with the findings on how the driver impacts the thematic focus in the literature review
- The driver's proposed-impact is consistent with the literature review and with how the driver is said to change in the SSPs to extend
- The proposed-impact can be explicated by rational thinking

For the second part, the driver's direct or indirect impact on the thematic focus must be explained. For example: "Changing population size does not have a direct impact on the emissions of chemical X in the environment, however changing population size impact consumption of chemical of X. Increase consumption of X is found to be positively correlated to emissions of X in the environment. Therefore for the development of our scenario we consider population size to be an indirect driver positively correlated to emissions of chemical X in the environment" When all driver's impacts on the thematic focus are explicit, an overall effect can be proposed and presented in the format chosen on step 1.

Step 4: Consistency checks

This last step aims to check consistency and to assure quality control of the developed scenarios. For this step, the scenario products developed are checked for consistency with the systematic review and with the SSPs. Consistency with the systematic review consists of verifying that a driver's dynamic in the environment and in the society are the same across the literature and scenario developed. For consistency with the SSPs, driver's evolution must be similar across SSPs chosen to extend in step 1 and in scenario developed (e.g. if population side increase in SSP1 chosen to extend, population side must decrease in the scenario developed). Conducting these consistency checks multiple times is essential for quality control of the scenario development process (Priess and Hauck, 2014). When time and financial resources permit, we recommend to conduct consistency checks with experts (Ernst *et al.*, 2018; Mitter *et al.*, 2019). Consistency checks can also be done by scenario developers by repeating and verifying step 3 multiples times.

Uncertainties

There are uncertainties when scenarios are developed. Uncertainties can arise around lack of system understanding of the thematic focus, on the thematic focus within a society and on the study of the future that is fully unknown.

In step 2, uncertainties can arise around lack of understanding on how chemicals behave in the environment or a society. This could be due to lack of data availability or literature on the chemical in question but also on the dynamics of a society. Or general

In step 3 of our framework, the SSPs' storyline and other products must be interpreted for the development of chemical emissions scenarios (e.g. population growth increases strongly). Vagueness and ambiguity of scenario terminologies make interpretations of SSPs different between researchers. Techniques to address these uncertainties can be to increase the number of scenarios to develop, to perform sensitivity analysis or to solicit experts (Gao *et al.*, 2016; Rounsevell *et al.*, 2021). The advantage of involving experts is to build consensus on uncertainties, but also to discuss and obtain diverse expertise on the chemical focus, allowing an improved understanding. Uncertainties should not deter the development of scenarios but should be considered in output scenario interpretations.

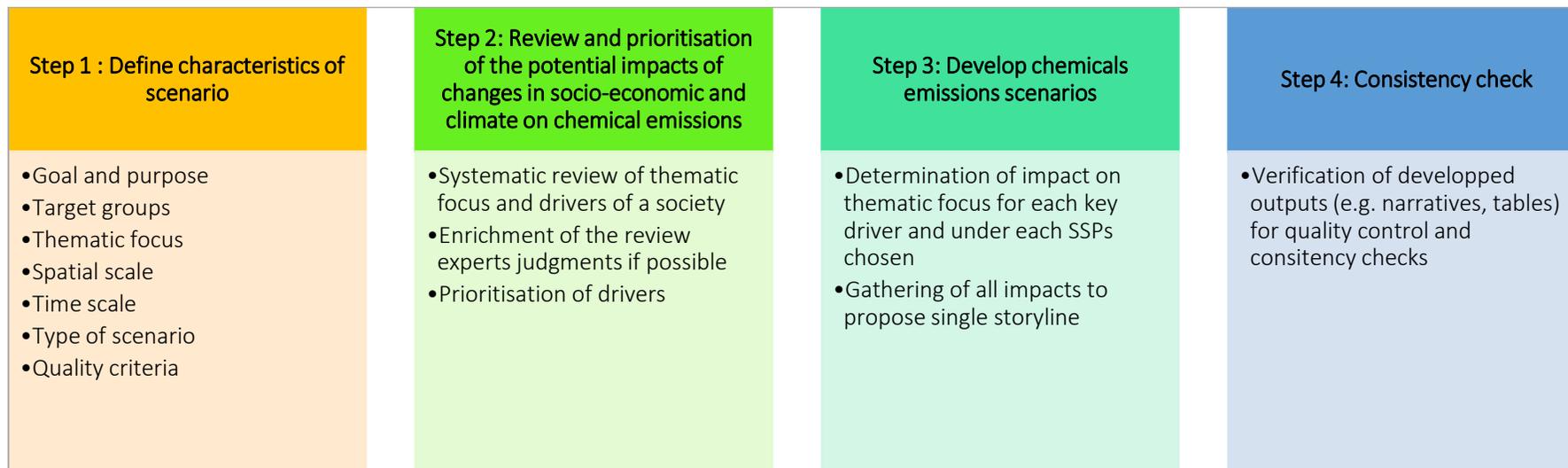


Figure 18 – Framework proposal to extend SSPs storylines to single chemicals emissions or group of chemical sharing similar features

13.2 Results

The framework is illustrated for two case studies: antidepressant and insecticide emissions in European freshwater systems in 2050. The methodology followed is the same as the one presented previously except that exploratory reviews were conducted instead of systematic reviews. Moreover uncertainties on scenario developed were not investigated. The reasons are that fully developed scenarios for antidepressants or insecticides would require individual articles with more extensive reviews and engagement with experts. This does not impact the aim of this section which is to illustrate how the proposed framework can be applied.

Antidepressants emissions at European scale for 2050 (Eur-Ant-SSPs)

Antidepressants are regularly detected in European fresh water monitoring campaigns, mostly in urban environments where consumption is high and waste water treatment does not effectively remove this type of molecule (Metcalf *et al.*, 2016; Wilkinson *et al.*, 2022). Traces of antidepressants in the aquatic environment threaten aquatic ecosystems by altering swimming and cryptic behaviours of invertebrates and behaviour and the development and reproduction of aquatic vertebrates (Sehonova *et al.*, 2018). Global changes that are projected to occur in the next 30 years will likely affect antidepressant consumption and therefore, emissions into the environment. These future emissions must be understood in order to assess future risk and mitigate their impacts. Here, we develop antidepressant emissions scenarios under global change.

Step 1: Define characteristics of scenarios of Eur-Ant-SSPs

The characteristics of the chemical emissions scenario wanted were developed:

- **What is the goal and purpose of the scenario?** Extend European SSPs (Kok *et al.*, 2019) to antidepressant emissions to envision multiple scenarios of antidepressant emissions in 2050
- **Which chemical or group of chemicals is being investigated?** Within the EU market, antidepressants currently available, antidepressants currently developed but not registered yet and future antidepressants molecules developed under the green chemistry framework by Ganesh *et al.*, 2021

- **Which environmental matrices are being considered?** European freshwater aquatic systems
- **What spatial scale is required?** Europe
- **What temporal scale is required?** 2050
- **How many and which SSPs needs to be explored?** European SSP1 (Eur-SSP1), SSP4 and SSP5 (Kok *et al.*, 2019). Eur-SSP1 is selected to study antidepressant emissions in a sustainable society with less resource-intensive lifestyles, high human investment and high social cohesion. Eur-SSP4 and Eur-SSP5 are selected to study antidepressant emissions in nuanced societies with high inequalities in human development and some environmental considerations in Eur-SSP4, and intensive lifestyle with high human investment and high environmental considerations for Eur-SSP5.
- **Which climate projections should be explored?** Climate change impacts human mental health in multiples ways in the literature. Increased temperature could lead to more aggressive behaviour and extreme events to stress-related psychiatric disorders (Padhy *et al.*, 2015). The consumption of antidepressants among practices located within 1 km of a flood areas increased compared to further distance lands (Milojevic, Armstrong and Wilkinson, 2017). Climate change-related declining/changing societies affect mental health with more psychiatric disorders (e.g. ecoanxiety, post-traumatic events stress, depression, survivor guilt) (Hayes *et al.*, 2018; Cianconi *et al.*, 2020; Palinkas and Wong, 2020). The impacts of climate change is therefore considered for antidepressants emissions scenarios. Climate change is considered and integrated with RCP 4.5, 6 and 8.5 combined with Eur-SSP1, Eur-SSP4 and Eur-SSP5 respectively.
- **Who is the targeted audience?** Scientists from the climate change research community like eco-toxicologists, chemists and social scientists working at European scales.
- **What will be the form of the scenario?** Tables with antidepressants trends for each key driver and qualitative storylines assessing the overall effects of the set of drivers for each scenario.

Step 2: Review and prioritisation of the potential impacts of changes in socio-economic and climate on chemical emissions

An exploratory review was conducting using the Scopus search engine. The search terms “antidepressant” in combination with the Eur-SSPs drivers’ elements. Fifty one articles were

identified. Further targeted searching was conducted when cited literature yielded relevant peer-reviewed articles. Articles were kept if they confirmed the following statements: 1) the article focuses on change in trends in antidepressants use/consumption; 2) the change in antidepressants trends is related to a socio-economics, technological or climate change; 3) the article does not focus on people with medical pre-conditions; and 4) the article focused on Europe, a country in Europe or a society similar in socio-economic development as Europe. In total, 23 relevant articles were kept. Articles covered primarily drivers related to demographics and human development change. The driver(s) studied and their impacts on antidepressant were extracted from each article and are presented in Table 9.

Table 9 – Drivers studied and their impacts on antidepressant in articles identified in the exploratory review

Category	Driver(s) studied in article	Article's findings	Source
Demographics	Age	Antidepressant use increased for non-elderly adults age 18 to 64 and the elderly age 65 and older but not for children under 17 between 1997 with 2002 for U.S. Civilian Noninstitutionalized Population.	Stagnitti, 2005
Demographics	Gender	Increase in the use of antidepressants by both males and females between 1997 and 2002 for U.S. Civilian Noninstitutionalized Population	Stagnitti, 2005
Demographics	Gender	Association between the use of antidepressants and mental health did not vary substantially between men and women.	Van der Heyden et al., 2009
Demographics	Gender	From 2009–2010 through 2017–2018, the percentage of adults who used antidepressants increased among women, but not men.	Brody & Gu, 2020
Demographics	Migration	Immigrants with depression initiate antidepressants more often than the Finnish-born population, but they also discontinue them earlier.	Kieseppä et al., 2022
Demographics	Urbanisation	Higher rates of antidepressant use among patients living in urban compared with rural communities.	Leventhal Perek et al., 2019
Human development	Social cohesion	Beliefs that mentally ill people are 'dangerous' were associated with higher use. Individual beliefs such as they will 'never recover' or 'have themselves to blame' associated less regular use of antidepressants.	Lewer et al., 2015
Human development	Social cohesion	Belief in the harmfulness of antidepressants is associated with a general lack of exposure to depression, leading to an underestimation of its seriousness and of the necessity for intervention.	Jorm et al., 2005
Human development	Social cohesion	Drug use as a treatment in people with a psychiatric disorder can be interpreted from different points of view according to cultural characteristics that could play a decisive role in people's opinion, physicians and patients, regarding these diseases and in their decision regarding the use of antidepressants.	Gomez-Lumbreras et al., 2019
Human development	Social cohesion	Antidepressant consumption increased drastically between 2000 and 2011, from 8.18 to 36.12 DDD per 1,000 inhabitants per day because of less stigmatized by public opinion of mental health diseases.	Gualano et al., 2014
Human development	Education	No differences in the consumption of antidepressants have been found between the North and South of Europe.	Gomez-Lumbreras et al., 2019
Human development	Education	Antidepressant use was higher among non-Hispanic white (16.6%) adults compared with non-Hispanic black (7.8%), Hispanic (6.5%), and non-Hispanic Asian (2.8%) adults.	Brody & Gu, 2020
Human development	Education	Antidepressant use increased for white non-Hispanics, other non-Hispanic and did not change significantly for black non-Hispanics or Hispanics between 1997 with 2002 for U.S. Civilian Noninstitutionalized Population.	Stagnitti, 2005
Human development	Education	A trend towards a greater prescription of antidepressants and fewer suicides after an educational programme on depression.	Henriksson & Isacson, 2006
Human development	Access to healthcare	Increases for both insured and uninsured persons between 1997 with 2002 for U.S. Civilian Noninstitutionalized Population.	Stagnitti, 2005
Human development	Access to healthcare	Higher healthcare access associated with regular use of antidepressants.	Lewer et al., 2015
Human development	Socio-economic status ; Access to health	Healthcare and educational workers in Denmark are at increased risk of depression and that this risk is partly mediated by the high emotional demands of the work.	Madsen et al., 2010
Exceptional event	Exceptional event	Antidepressant prescribing in general practice substantially increased, whereas the number of people in contact with adult mental health services, and the number of referrals to those services decreased in the UK in 2021 (COVID) compared to 2015.	Armitage, 2021
Exceptional event	Exceptional event	Since March 2020, the number of patients reimbursed weekly for antidepressants has increased compared to the period from January 2015 to February 2020 (COVID).	Levaillant et al., 2021
Economics and lifestyle	Economy	Consumption of antidepressants increases in Greece since the economics crisis.	Madanos et al., 2014
Economics and lifestyle	Economy	The unemployed and the employed with job insecurity not only have worse mental health and, consequently, a higher need for care, but also report a higher use of mental health care and antidepressants.	Buffel et al., 2015

Table 9 – (continued) Drivers studied and their impacts on antidepressant in articles identified in the exploratory review

Climate change	Extreme event - Flooding	There was an increase of 0.59% (95% CI 0.24 to 0.94) prescriptions in the postflood year among practices located within 1 km of a flood over and above the change observed in the furthest distance band. The increase was greater in more deprived areas.	Milojevic et al., 2017
Climate change	Extreme event - Flooding	With a relative risk (RR) of 1.54 (95% CI, 1.39-1.62) corresponding to an estimate of 409 new deliveries of psychotropic drugs during the three weeks following the storm, this study confirms the importance of the psychological impact of Xynthia. This impact is seen on all three classes of psychotropic drugs studied. The impact is greater for tranquilizers (RR of 1.78; 95% CI, 1.59-1.89) than for hypnotics (RR of 1.53; 95% CI, 1.31-1.67) and antidepressants (RR of 1.26; 95% CI, 1.06-1.40). The RR was higher for females than for males.	Motreff et al., 2013
Climate change	Extreme event - Heatwaves	While only incremental increases in morbidity and mortality above previous findings occurred in 2008, health impacts of the 2009 heatwave stand out. These findings send a signal that the intense and long 2009 heatwave may have exceeded the capacity of the population to cope.	Nitschke et al., 2011
Climate change	Extreme event - Wildfires	The results show an increased rate of PTSD, depression, and generalized anxiety at several times of follow-up post-wildfire, from the subacute phase, to years after. An increased rate of mental health disorders post-wildfire has been found in both the adult and pediatric population, with a number of associated risk factors, the most significant being characteristics of the wildfire trauma itself.	To et al., 2021
Climate change	Global change	Mental health impacts represent both direct (i.e. heat stress, exposure to extreme weather events) and indirect (i.e. economic loss, threats to health and well-being, displacement and forced migration, collective violence and civil conflict, and alienation from a degraded and potentially uninhabitable environment) consequences of acute, subacute and long lasting climate-related events.	Palinkas et al., 2020
Multiples	Age ; Gender	Antidepressants use is higher in women than in men, and increases progressively with age in both sexes.	Gomez-Lumbreras et al., 2019
Multiples	Age ; Gender	Antidepressant use increased with age, overall and in both sexes—use was highest among women aged 60 and over (24.3%). During 2015–2018, 13.2% of adults aged 18 and over used antidepressant medications in the past 30 days. Use was higher among women than men.	Brody & Gu, 2020
Multiples	Age ; Education	Disbelief in the medical model of depression and family shame reduced willingness to use mental health counseling and antidepressants in older population in Korea.	Park et al., 2018
Multiples	Urbanisation ; Environment	Antidepressant medication has strong associations with neighborhood conditions including socioeconomic satisfaction and the seasonality of particulate matter under 2.5 µm in the air.	Lee et al., 2022
Multiples	Urbanisation ; Education	Lower rate of antidepressant use was found in urban and rural Arab-majority communities.	Leventhal Perek et al., 2019
Multiples	Urbanisation ; Age	Associations of neighbourhood socioeconomic and physical characteristics with older people's antidepressant use were small and inconsistent.	Tarkiainen et al., 2021
Multiples	Age ; Socio-economics status	Antidepressant medication use was higher for adults with at least some college education compared with those with a high school education or less.	Brody & Gu, 2020
Multiples	Gender ; Education	In men, antidepressant treatment was less common among low educational groups than among high educational groups'. In women, socio-economic position was not associated with antidepressant use.	Kivimäki et al., 2007
Multiples	Gender ; Socio-Economics Status	Use of antidepressants was significantly associated with female gender , higher socioeconomic status , and unemployment in Rio Grande do Sul State in Brazil in 2006.	Garcias et al., 2018
Multiples	Socio-economic status ; access to health	Socioeconomically disadvantaged respondents reported greater antidepressant use than those who were not classified as disadvantaged. These findings suggest Australia's universal health-care system does promote equitable health care across the population.	Buttenworth et al., 2013
Multiples	Age ; Gender ; Inequalities	More young adult females used antidepressants in municipalities where relative poverty had increased. Fewer elderly females used antidepressants in municipalities where the Gini index (calculating distance between the richest and the poorest) increased. More young adults used antidepressants in municipalities where the number of those not being educated or trained had increased.	Hillamo, 2014
Multiples	Age ; Gender ; Social cohesion	An increase in the number of persons over 65 years of age living alone was positively associated with an increase in the use of antidepressants among elderly females.	Hillamo, 2014
Multiples	Age ; Gender ; Education	In this elder sample, taking into account depressive symptom severity and other confounds, antidepressant use is nearly half as likely among men and African Americans.	Grunebaum et al., 2008

To prioritise drivers, nine experts on chemical emissions from academia were solicited. Based on the exploratory review provided and their expertise, experts were asked to assign a priority (high, low or uncertain) for all SSPs elements of Kok et al., 2019 and climate change drivers. If 70% of experts defined a driver as “high” priority, the driver was considered key and selected for scenario development. For antidepressant emissions, 11 key drivers were identified: population growth, inequalities, urbanization, economy, social participation, social cohesion, healthcare access, healthcare investment, education, technology development and extreme droughts and floodings events (see Annexe 4.1). Those drivers were studied exclusively in step 3 to develop emissions scenarios.

Step 3: Develop chemicals emissions scenarios

Prioritised drivers of antidepressants emissions in European aquatic freshwater systems selected in step 2 were studied individually. An emissions trend (increasing, decreasing or both) was proposed for each prioritized driver. Each driver’s individual future trend is presented in section 3.1 and in Table 10, and output scenario storylines are presented in the section 3.2. Note that because of time and financial restrictions and because these scenarios storylines were mostly developed to illustrate the framework, step 3 was developed using desk-based research conducted by the authors.

Step 3.1 Antidepressants emissions trends by priority drivers in Eur-Ant-SSPs

The 11 prioritised drivers were studied one at a time based on results from the exploratory review, historical data and storylines from Eur-SSPs (Kok *et al.*, 2019). If a key driver has no specific indication in Eur-SSPs (e.g. “Inequalities”), storylines provided in global SSPs for Rich-OECD countries (high-income countries – GNI per capita above \$13 205 – according to the World Bank) were used (O’Neill *et al.*, 2017; WBD, 2022). When considered relevant and useful for the general understanding of antidepressant emissions in a society, effects of key drivers were extended to mental health or depression by desk-based research.

- Population growth

The total European population was 738 million in 2010. European population growth is estimated to increase in SSP1 (up to 769 million) and SSP5 (847 million) and to decrease in SSP4 (716 million). Based on historical data, we concluded that antidepressants emissions is

positively correlated to population growth, therefore antidepressants emissions increase in Eur-Ant-SSP1 and Eur-Ant-SSP5 and decreases in Eur-Ant-SSP4.

- Inequalities

In Global SSPs, inequalities were found to be “reduced across and within countries” in SSP1, “high, especially within countries” in SSP4 and “strongly reduced, especially across countries” in SSP5. Correlations between inequalities and antidepressants or mental health can be difficult to interpret as inequalities can cover poverty, unequal career opportunities or unequal access to education among others. The consensus though is that higher inequalities is correlated to low mental health (Murali and Oyebode, 2004; Yu, 2018) and indirectly to antidepressant consumption. We concluded that in Eur-Ant-SSP1 and Eur-Ant-SSP5, because inequalities decrease, antidepressants emissions decrease. In Eur-Ant-SSP4, we concluded that antidepressant use will increase.

- Urbanisation

Urbanisation is high and well-managed in global SSP1, medium with mixed type of urbanisation across and within cities in SSP4 and high and better managed over time in SSP5. The dynamic between urbanisation and antidepressants or/or mental health is unclear from the literature. Some articles showed that antidepressant use was higher in urban environments (Leventhal Perek *et al.*, 2019). Another study found that rural individuals are at increased risk to suffer from depression than people living in urban environments (Wang *et al.*, 2019). The type and quality of urbanisation also influences mental health (Triguero-Mas *et al.*, 2015; Wheeler *et al.*, 2015). For Eur-Ant-SSP1 and Eur-Ant-SSP5, because urbanisation increases with environmental considerations and desire for better management, we concluded that antidepressants emissions decrease. In Eur-Ant-SSP4, because of the infrastructure inequalities and the lack of consideration for the environment, we concluded that antidepressants emissions increase.

- Economy

Economy development in Eur-SSPs increases gradually in SSP1 and is defined as a “high economy” in SSP4 and SSP5. An exploratory review showed that high economy in terms of high employment and job security is correlated with less antidepressant consumption compared to unemployed or employed with no job security (Buffel, Dereuddre and Bracke, 2015). For Eur-Ant-SSP1, we interpreted that gradual economy in a human-based society with

high and security employments result in a decrease in antidepressant emissions. For Eur-Ant-SSP4, economic competition and low consideration for human well-being was translated as employment but with insecurity. We concluded antidepressant increases for Eur-Ant-SSP4, but also in Eur-Ant-SSP5 where we concluded that competition surpasses human consideration.

- Social participation and social cohesion

Social participation is high in SSP1 and SSP5 and low in SSP4. Similar projections were determined for social cohesion in European SSPs. High social cohesion (e.g. playing sport, social encounters) is associated with lower depressive symptoms and better mental health (Almedom, 2005; Wang *et al.*, 2019). An exploratory review also showed that society divergence and malicious regards to the mental health issue discourage individuals to take antidepressants (Jorm, Christensen and Griffiths, 2005; Lewer *et al.*, 2015; Park, Jang and Chiriboga, 2018). While impacts of social participation was not directly studied with respect to antidepressants, we considered that social participation and social cohesion are positively related. We concluded that antidepressants emissions decrease in Eur-Ant-SSP1 and Eur-Ant-SSP5 and increase in Eur-Ant-SSP4 based on social participation and social cohesion.

- Healthcare investment and healthcare access

In Eur-SSPs, human health investment and access is high for SSP1 and SSP5 and high for elites and medium for lower class for SSP4. In the literature, access and investment in healthcare was positively associated with antidepressant use and better mental health outcomes (McGorry *et al.*, 2007; Chisholm, 2015). We therefore concluded that antidepressants emissions increase in all Eur-Ant-SSPs.

- Education

In Eur-SSP1 and Eur-SSP5, education is high. In Eur-SSP4, the number of highly educated people decreases. Articles found in the exploratory review showed that antidepressant consumption was less for highly educated groups. Education in terms of culture was also found to be an influencing factor (Kivimäki *et al.*, 2007; Stierman *et al.*, 2015). "Open-minded" environments with less judgement and more cohesion were found to encourage individuals to seek help and accept antidepressant treatment (Gomez-Lumbreras *et al.*, 2019). High numbers of educated and, indirectly, high support for human development was translated

into antidepressant emissions decreasing in Eur-Ant-SSP1 and Eur-Ant-SSP5 and, inversely, increasing in Eur-Ant-SSP4.

- Technology development

Technology development is “high, but not persuasive” in Eur-SSP1, “High in some areas; low in labour intensive areas” in Eur-SSP4 and “strong and crucial” in Eur-SSP5. For antidepressant emissions, technology development could cover improved wastewater treatment technology or shifts in antidepressant chemistry design (Ganesh *et al.*, 2021). Green chemistry encourages the development of less toxic molecules, for instance molecules that are less persistent or less bio-accumulative (Kümmerer, 2007). We concluded that because of high investments in technology development in Eur-SSP1, Eur-SSP4 and Eur-SSP5, antidepressant emissions decrease for all Eur-Ant-SSPs.

- Extreme droughts and floodings events

Droughts and flooding are increasing in Europe RCP 4.5, RCP6 and RCP 8.5 (Tabari *et al.*, 2021). The exploratory review showed correlations between extreme weather events and mental health (Nitschke *et al.*, 2011; To, Eboreime and Agyapong, 2021). Number of antidepressant prescriptions increases after floodings events (Motreff *et al.*, 2013; Milojevic, Armstrong and Wilkinson, 2017). We therefore concluded that antidepressant emissions increase under all RCPs considered.

Table 10 – Eur-Ant-SSP1, Eur-Ant-SSP4 and Eur-Ant-SSP5 antidepressant emissions scenarios for Europe for the year 2050 for each key drivers defined

SSPs drivers	SSPs sub-drivers	Eur-SSP1 ¹ and other SSPs	Eur-Ant-SSP1	Eur-SSP4 ¹ and other SSPs	Eur-Ant-SSP4	Eur-SSP5 ¹ and other SSPs	Eur-Ant-SSP5
Demographics	<i>Population Growth</i>	Relatively low growth ²	↔	Low growth ²	↔	Relatively low growth ²	↔
Economy and lifestyle	<i>Inequalities</i>	Reduced across and within countries ²	↘	High, especially within countries ²	↔	Strongly reduced, especially across countries ²	↘
Environment and natural resources	<i>Urbanization</i>	High and well-managed ²	↘	Medium with mixed urbanisation type across and within cities ²	↔	High with a better management over time ²	↔
Human development	<i>Economy</i>	Gradual (with hiccups at the beginning) ¹	↘	High ¹	↔	High ¹	↔
	<i>Social participation</i>	High for rich OECD countries ²	↘	Low for rich OECD countries ²	↔	High for rich OECD countries ¹	↘
	<i>Social cohesion</i>	High ¹	↘	Low ¹	↔	High ²	↘
	<i>Healthcare investment</i>	High ²	↔	High for elites, medium for lower class ²	↔	High ²	↔
	<i>Healthcare access</i>	High ²	↔	Medium ²	↔	High ²	↔
	<i>Education</i>	High ¹	↘	High for elites, medium for lower class ¹	↔	High ¹	↘
Technology	<i>Development</i>	High, but no pervasive ¹	↘	High in some areas; low in labour intensive areas ¹	↘	Strong and crucial ¹	↘
Climate Change	Extreme events	RCP-4.5 to 6 : droughts and floods increase ²	↔	RCP6 : droughts and floods increase ²	↔	RCP-8.5 : droughts and floods increase ²	↔

most crops, increase temperature, rainfall, pest pressure and extreme climatic events lead to increase insecticides emissions. Insecticides emissions increase in all Eur-Ins-SSPs.

Comparison of our results with the literature was difficult because, to our knowledges, this represents the first attempt at developing future chemical emission scenarios. Nevertheless, possible change in antidepressants and insecticides emissions in the future have been studied in the literature. Articles usually focus on a single future situation. There is, to be best of our knowledge, no consideration of multiple alternative futures.

Human health or diseases was studied under the influence of climate change (McMichael, Woodruff and Hales, 2006; Epstein, 2009; Mills, Gage and Khan, 2010; Barrett, Charles and Temte, 2015). More specifically to antidepressants, similar dynamics between key drivers and antidepressant consumption or emissions were found in the literature. Antidepressant consumption was found to increase in the future because of climate change, and more specifically because of increase in floods and natural disasters (Redshaw *et al.*, 2013). Projections of population size and gender was found to increase consumption by 61% by 2090 in a study conducted in the Netherlands (Van Der Aa *et al.*, 2011). Schlüsener *et al.*, 2015 found an increase of antidepressant consumption in the future due to climate change but concluded that demographic development and change in lifestyle was probably more important. In our scenarios, demographic change was considered to have a bigger impact on antidepressant emissions in the environment as well, but a lesser impact compared to human developmental drivers.

Regarding insecticides, usage and costs were found to increase under extreme weather events (Rhodes and McCarl, 2020), precipitation and rainfall (Chen and McCarl, 2001), pesticide efficacy (Matzrafi, 2019) and climate change and land-management (Kattwinkel *et al.*, 2011) in the future. The influence of technological change was debated in a study looking at pesticide efficiency: authors found that increased pesticide consumption could be related to pesticide decreases in efficiency. Consistent with our findings, change in molecule design could therefore play an important role in reducing pesticide consumption and, consequently, pesticide emission in the future (Matzrafi, 2019).

These studies are relevant to understand the influence of a single or few key drivers on a thematic focus. They are, however, less informative of future conditions as they do not consider a society as a complex system where socio-economics, technological and climate

change interact and influence each other. They, by default, disregard current societal debates (e.g. economics degrowth), actions (e.g. Fridays for Futures and Extinction Rebellion movements) on global change and their impacts on the society. Despite being uncertain, those societal dynamics should be included in future research. In our framework the society is considered as a whole. Socio-economics, technological and climate change drivers interact with each other and can be weighed against each other. In Eur-Ant-SSPs, human development drivers were considered to have the greatest impact on antidepressants emissions. For Eur-Ins-SSPs, land-use, policy and climate drivers had the greatest impacts on insecticides. This framework adapted from the methodology of Mitter et al., 2019 permits for the first time the study of chemical emissions in the future under the shared socio-economics pathways scenarios and in dynamic complex socio-economics societies. The framework is applicable to single molecules or groups of chemicals sharing similar features with an easily applicable methodology.

The two sets of scenarios developed demonstrates the ability of the framework to fit different chemicals. We studied antidepressants with an exploratory review of 23 relevant articles and insecticides, with 25 articles. Antidepressants and insecticides had 10 and 9 key drivers defined respectively. Population growth, technological development and education were key drivers in common for both examples. Our final scenario showed that antidepressants and insecticide emissions both decreased in SSP1 and increased in SSP4. SSP5 had opposite future trends: antidepressant emissions decreased while insecticide emissions increased. The reason is that human development and wellbeing are highly emphasised in SSP5 (which decrease consumption of antidepressants), but environmental regulations and financial investment in the agricultural sector are low due to a desired-liberal society (which increase insecticide usage). Moreover, the impact of climate change is more relevant to insecticide usage and socio-economic trends do not permit an overall reversal of insecticide emissions trends. For Eur-Ins-SSP1, climate change makes the reduction of insecticide usage difficult but is compensated by socio-economic trends.

Scenario development, whether it is for the development of single future trends for each key driver or for the development of storylines, involves uncertainties. There are more uncertainties when literature is limited and when there are multiple sources of chemicals in the environment. For future chemical scenarios, we recommend involving experts and

off between quality criteria can happen. In our framework, plausibility and consistency are prioritised over creativity.

A key step in the process of scenario development is comprehending the current situation. This requires the understanding of the past and current trends in chemical release and occurrence. However, the data needed to assess chemical emissions (e.g. production, consumption and trade) are limited to select regions of the world and are often only available for select groups of chemicals such as pharmaceuticals and pesticides. Where data does exist, this is often commercially sensitive so is not always freely available. There is a need to generate data on chemical usage in regions where these data do not exist and for increased data transparency so that researchers can more easily access existing datasets. Access to improved emissions data will facilitate the development of chemical emissions scenarios and, subsequently, support the development of mitigation and adaptation strategies to avoid the negative impacts of chemicals in the future.

In the next chapter, the framework is enhanced and used to forecast antibiotics emission in European freshwater systems in 2050.

Despite clear benefits for human and veterinary health, high consumption of antibiotics leads to high antibiotic pollution in freshwater systems which potentially contributes to the selection of antimicrobial resistance genes (AMR) worldwide (WHO, 2014). Antibiotic emissions with the development of antimicrobial resistance genes threaten global health and stability and potentially resulting in a future pandemic where antibiotics will not be efficient anymore (WHO, 2014).

Emissions of antibiotics into freshwater systems are thought to be causing harm to living organisms, on the stability of ecological systems and on the quality of water (Polianciuc *et al.*, 2020). These risks are expected to change in the future under global change. Societies are going through global changes (socio-economics, technological and climate change) that are affecting all aspects of our lives, including how chemicals are consumed (Retief *et al.*, 2016; Van den Brink *et al.*, 2018). For example climate change is affecting diseases patterns which, in turn, affects pharmaceutical demand (Redshaw *et al.*, 2013). At the same time actions are taken worldwide by regulators and industries to limit antimicrobial resistance genes. For example: in April 2023, the European Union adopted actions to combat antimicrobial resistance in a One Health approach; and the AMR Industry Alliance (more than 100 biotech, diagnostics, generics and research-based pharmaceutical companies and associations) is taking a united front to promote sustainable solution to curb antimicrobial resistance genes (AMR Industry Alliance, no date; UE, 2023). However, global societal and climate change will impact emissions and risks of antibiotics to an extent that is currently unknown.

Therefore the aim of this chapter was to extend three European-SSPs scenarios (Eur-SSP1, SSP4 and SSP5) to antibiotics emission scenarios for European urban freshwater systems in 2050 using an enhanced version of framework developed in Chapter 5.

6.2 Methods

Methodology used for scenarios development

To develop antibiotic SSP scenarios for 2050, the framework described in Chapter 4 was used.

Systematic reviews of antibiotics

A systematic review of the impacts of socio-economic drivers on antibiotic use and emissions within a socio-economics societies was conducted. The systematic review was conducted using the Web Of Science database using the following key words: (“surface water” or “freshwater”) AND (“urban” or “city”) AND (“influence” or “impact*” or “effects*” or “source*”) AND (“anthrop*” or “human*”) and (“Antimicrobial*” OR “antibiotics*”). For each article that was identified, the socio-economics drivers studied and its impacts on antibiotics was noted in an excel file. A list of key drivers was then developed for antibiotics.

System diagrams were developed to visualise key socio-economics drivers and pathways of antibiotics towards freshwater systems in urban environments. All drivers identified were placed on a virtual board. Relationship between drivers were determined based on the literature and dynamic of an European democratic society. Relationships were represented with arrows. Final system diagram was copied on diagrams.net.

Experts’ selection and participation

Seventeen experts were solicited to collect their opinions on future impacts of socio-economics drivers on antibiotics . Four experts worked in chemical regulation and legislation, three in production companies, and ten in academia. The experts from academia specialized in antibiotics design development, antibiotics emissions, science behaviours, and/or were practitioners. Experts were identified using online research and via professional networks.

Three experts answered positively to participate to this research: Expert 1 is an advisor to an association of industries fighting AMR, expert 2 is an Associate Professor specialising in behaviour science and a UK Government advisor on antimicrobial resistance and prescription and last, expert 3 is a medical doctor and Research Professor in antibiotic resistance. Further information on expert’s background, past and present positions are available in Table 13.

drivers were identified: medicines regulations, human development and environmental policies. Human development policies had impacts on access to health facilities, water and sanitation, health investment and professional and public education (human development drivers). Human development policies alongside with environmental policies had an impact on technology investment and consequently on technology development. Technology development was connected to the “antibiotics consumers” areas of the diagram by “antibiotics design/availability” and to “sewage and water systems” in the “city organisation” area.

Last, “climate change” considers four climate events: temperature change, extreme-weather events, floods and precipitations. “Climate change” drivers are connected to “population health” and to “antibiotics availabilities” in the diagram.

too broad to specifically address social and economic issues related to antibiotics emissions: policies change would lead to a small increase of antibiotic emissions for expert 1. For Eur-SSP4 however, expert 1 believed that because environmental policies are high in pockets, policy development could specifically target antibiotics emissions reductions and could lead to slightly decreasing emissions. All experts believed low environmental considerations and the business focus of regulations and quality of governance in SSP5 would lead to medium to strong increase of antibiotic emissions.

Lastly for technology development, the experts answers differed. For expert 2, technology development would lead to a small decrease of emissions under Eur-SSP1 and Eur-SSP4 and a medium decrease for Eur-SPP5. Experts 1 and 3 only gave answers for Eur-SS1 and Eur-SSP5. Expert 1 believed that high but not pervasive technology development in Eur-SSP1 would lead to a small increase in emissions but strong and crucial technology development in all domains in Eur-SSP5 would lead to a small decrease in emissions. Expert 2 believed the opposite: emissions would slightly decrease under Eur-SSP1 and slightly increase under Eur-SS5.

Expert 2 and expert 3 provided a level of confidence in their answers. Expert 2 considered that there were high uncertainties concerning the potential effects of drivers on antibiotics emissions and gave a level of confidence of 1 (very low confidence). Expert 3 had levels of confidence ranging from 2 to 4. Expert 3 had the highest level of confidence to propose a potential impact on antibiotics emissions for drivers of precipitation, access to health facilities, water and environmental regulations in Eur-SSP1 and precipitation and regulations and quality of governance in Eur-SSP4. In Eur-SSP5, expert 3 had a level of confidence ranging from 2 to 3.

infections and the consumption of antibiotics. Overall, **antibiotic emissions greatly increase** in European freshwater systems.

European Antibiotics SSP5

In 2050 in Europe, there is a strong faith in the potential for technology to resolve any human or environmental issue like antimicrobial resistance. Technology developments in wastewater technology or new advanced treatments that requires fewer antibiotics are strong and easily implemented within the society. There is high investment to increase human well-being which includes access to good health institutions, clean water and sanitation for all provided by strong institutions. Regulations does not play part as technology development is considered stronger on a free-market without institutional barriers. The environment degrades and the frequency and duration of climatic events increase with constant fossil fuels explanations. Despite strong technology development, the absence in regulations in a world where bacterial infectious diseases increase greatly makes that antibiotics consumption for human and veterinary used increased. Overall, **antibiotics emissions increase** in the European freshwater systems.

Appendix

Annexe 0.1: A shared socio-economic pathway based framework for characterising future emissions of chemicals to the natural environment

Annexe 6 – Manuscript in preparation: Environmental Management Cycles for Chemicals and Climate Change, EMC⁴: A new conceptual framework contextualizing climate and chemical risk assessment and management

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Abstract

The Environmental Management Cycle for Chemicals and Climate Change (EMC⁴) is a suggested conceptual framework for integrating climate change aspects into chemicals risk management. The interaction of climate change and chemical risk brings together complex systems that are imperfectly understood by science. Making management decisions in this context is therefore difficult and often exacerbated by a lack of data. The consequences of poor decision making can be significant for both environmental and human health. This paper reflects on the ways in which existing chemicals management systems consider climate change and proposes a conceptual framework that acts as a tool for decision makers operating at different spatial scales. This tool highlights key questions to help the decision maker identify chemical risks from climate change, management options and, importantly, the different types of actors that are instrumental in managing that risk. Case studies showing decision making at different spatial scales are presented highlighting the conceptual framework's applicability to multiple scales. With the United Nations Environmental Programme's current development of an intergovernmental Science Policy Panel on Chemicals and Waste, the opportunity has been presented to action the inclusion of research highlighting the environmental and health impacts of chemicals and climate change interlinkages,

Key Points

- **The chemicals and climate change nexus need to be mainstreamed into chemical risk management strategies and policies nationally, regionally and internationally.**
- **Explain in one sentence EMC⁴!**
- **A key requirement of chemical management strategies is the conceptualization of differences between actors regarding their capacity, within an actor network, to perform actions both in the chemicals and climate communities.**
- **UNEP's new intergovernmental Science Policy Panel on Chemicals and Waste needs to prioritize research and data gaps on the impact of climate change and chemicals interlinkages.**

				hazardous pesticides, etc.		
	Chemicals Road Map	WHO	Advisory/roadmap guidance	All chemicals and waste	Provides road map of actions where the health sector plays a role in the multi-sector management of chemicals	Global and multi scale
	International Code of Conduct on Pesticide Management	FAO and WHO	Advisory guidelines/voluntary	Pesticides	Provides guidelines (including criteria for identifying highly hazardous pesticides) for governments, industry, and civil society on best practices to reduce health and environmental impacts around a life-cycle approach.	Global scale
	Inter-Organization Programme for the Sound Management of Chemicals (IOMC)	rotating agency lead	Advisory/roadmap guidance	All chemicals and waste	A nine United Nations Agency that provides facilitating, coordinating, and capacity building on the sound management of chemicals.	Global scale
	GAAPL	UNEP	Legislation	Air pollutants	Provides recommendations to strengthen air quality governance as well as guides countries to effectively address air pollution	Global scale

	WHO global air quality guidelines	WHO	Legislation	Air pollutants	To provide guidance to help reduce levels of air pollutants (quantitative health-based recommendations for air quality management, expressed as long- or short-term concentrations for a number of key air pollutants)	Global scale
Management of regional pollution	MAP	UNEP	Advisory and facilitation service	Harmful chemicals and waste	Protect the Mediterranean sea from pollution and obtain a clean and sustainable Mediterranean sea environment.	Mediterranean countries
	REACH	EU member countries competent authorities (and Third countries responsible departments)	Legislation	Industrials chemicals	To protect human health and the environment by the registration, evaluation, authorization, and restriction of chemicals prior to entering the market	EU countries
	TSCA	FDA	Legislation	Multiple types of chemicals	To protect the public from unreasonable risk of injury to health or the environment by the regulation of the manufacture, import, distribution, use, and	USA

					disposal of new and existing chemicals in U.S. commerce	
	FIFRA	USDA	Legislation	Insecticide, Fungicide, and Rodenticide	To ensure that pesticides will not cause unreasonable risk to human health or the environment by the governance of the registration, distribution, sale, and use of pesticides	USA
	CERCLA/RCRA	EPA	Legislation	Solid waste and hazardous waste, and remediation of contaminated sites	For the proper management of hazardous and non-hazardous solid waste by law and by waste management program, and remediation of contaminated sites	USA
	ECHA	EU commission	Regulatory	Multiple types of chemicals	For the safe use of chemicals to benefit human health, the environment and innovation and competitiveness in Europe by legislation	EU countries
	OSPAR	OSPAR commission	Legislation	Hazardous substances	To protect the marine environment of the North-East Atlantic by the adoption of decisions, which are legally binding on the Contracting	Marine Environment of the North-East Atlantic

Management of water quality in a catchment	Domestic and regional regulations (e.g. EU Water Framework Directive)	EU commission	Legislation	Currently 45 chemicals (metals, pesticides, pharmaceuticals)	To ensure good ecological status of aquatic systems by regulatory controls and the development of divers programs for river restoration for the removal of barriers to fish migration or for the reduction of diffuse pollution.	EU countries
Environmental impact assessment / Strategic Environmental Assessment of new developments	EU EIA and SEA Directives	EU commission	Legislation	Certain public and private projects (airports, nuclear installations, railways, roads, waste disposal installations, wastewater treatment plants, etc.)	To ensure that projects that are likely to have a significant impact on the environment are identified and assessed, within an appraisal process, before these projects proceed to development.	EU countries
Management strategies by Industry (Industry-dependent)	AMR industry alliance safe manufacturing framework	AMR industry alliance	Advisory	Antibiotics, pesticides, industrial chemicals	To promote responsible antibiotic manufacturing.	industry
Management of Agricultural pollution	Nitrate directive	EU commission	Legislation	Nitrate	To reduce nitrate used in agriculture by establishing codes of good agricultural practices and developing	EU countries

					measures to prevent and reduce water pollution	
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Table 16. The implications of climate change for global through to highly localized environmental management scenarios from a chemical impacts perspective.

Management scenarios	Scale	Approach used	Implications of CC from a chemical impact perspective	References
Minamata Convention	Global	<ul style="list-style-type: none"> ● Ban on new mercury mines, the phase-out of existing ones, the phase out and phase down of mercury use in a number of products and processes ● Emissions to air, land and water are controlled ● Regulations of artisanal and small-scale gold mining. ● Considers interim storage and disposal of mercury and sites contaminated by mercury 	<ul style="list-style-type: none"> ● The speciation of mercury at a site will be altered due to increases in the incidence of flood events and sea level rise ● The connectivity of key ecological and human receptors to sources of mercury will alter due to extreme events 	WHO, 2021.
Development of a contaminated land register for a country	National	<ul style="list-style-type: none"> ● Data on previous site use, used to identify whether a site is potentially contaminated ● Monitoring of sites performed to determine level of contamination and these data compared to threshold values or to assess risks to controlled waters 	<ul style="list-style-type: none"> ● Increase in frequency and magnitude of flood events or sea level rise, resulting from climate change, could create new pathways to aquatic systems and require classification of sites to be reconsidered 	

elimination, substitution or changes regarding fuel production and feedstocks will have repercussions in the chemical industries and likewise application of various engineering solutions, new greener and sustainable chemistry insights will lead to changes of material flows and emissions. Various dependencies and possible co-benefits from changes need consideration, will most likely, influence what management options are seen as acceptable. The role of governance, and perceived opportunities for chemicals management, may also need a more holistic approach in order to make possible the larger changes in material flows that are needed in order to meet climate challenges.

Furthermore, a scientific understanding of various steps, and information needs, in designing effective chemicals management is crucial, and so is also the interplay between science and management. The further development of the panel is therefore of specific interest.

3. Case Study Application of EMC⁴

We developed eight guiding assessment and management questions that risk assessors and risk managers should ask themselves to better understand how climate change will affect the assessment and management of environmental chemical risks (see Table 17). The three case studies of varying scale (e.g., global, regional, and local) are used to answer the eight questions and illustrate how the Environmental Management Cycle for Chemicals and Climate Change (EMC⁴; in Figure 20) can be used by risk assessors and risk managers to frame the integration of climate change into environmental risk assessments. These case studies provide contrasting scenarios to show how there is no one answer or management solution that fits all.

For the “changes in externalities” and “risk assessment” component of EMC⁴, the following questions should be addressed:

- 1. Driving Forces: What are the current chemical risks associated with your case study or context?**
- 2. Pressures: How is the climate changing within the area/region of concern?**
- 3. State: How will the physical stressors (e.g., precipitation extremes) induced by climate change affect the fate, transportation, and toxicity of the chemical, or the susceptibility of the exposed ecosystem/humans?**
- 4. Exposure: How will climate change affect the use/release/toxicity of the chemicals of interest?**
- 5. Effects and Impacts: Is there evidence and data available to understand the relationship between the chemical risks and climate change impacts?**

For the “risk management and implementation” component of the EMC⁴, the following questions should be addressed:

- 6. What actors need to be involved in the assessment and management of these risks?**
- 7. How can change of actors’ behavior be motivated and how can it occur in ways to mitigate greenhouse gas emissions, chemical emissions, and climate change impacts at the same time?**

8. What policy options (e.g., “carrots or sticks”) are available to affect change while taking into consideration the pros and cons of each option?

Global case study: Integrating climate change into SAICM

The Strategic Approach to International Chemicals Management (SAICM) is a global chemicals management framework adopted by the United Nations in 2006. One of SAICM’s stated functions is to identify and call for action on global Emerging Policy Issues, such as the product lifecycle of textiles. More than 1900 chemicals are used in the production of clothing; the EU classifies 165 as hazardous to health or the environment (EPRS, 2019). To understand how the externalities driving chemical risks in this system may change in the face of climate change it is necessary to characterize the risks as they currently stand. The UNEP Chemicals Branch (2011) identified several risks, including:

- **pesticides used in the growing of natural fibers, and any dyes used in their formulation;**
- **effluent from the manufacture of dyes and colorants (e.g., dye baths); and**
- **effluent from the tanning and treatment of leather products.**

China represents over 35% of global textile exports ([Leal Filho et al., 2020](#)) and its future climate has been modelled using the IPCC’s SRES B2 Scenario ([Xu et al., 2006](#)). If by the 2080s air temperatures significantly increase and there is an overall increase in precipitation and flooding, there would then be significant precipitation decreases in specific regions in winter and summer. Increased temperatures and drought are associated with increased pests in cotton crops in China (Huang and Hao, 2018) and therefore increased pesticide use. Organophosphate pesticides have been found in flood sediments across China (Qian, *et al.*, 2020. Linxi Yuan, *et al.*, 2013) and transportation of chemicals applied to soils or deposited in freshwater through this route is likely to increase. Further examples of how climate change can impact the risks from chemicals due to the textile industry in China are provided below in Table 3.

In terms of the risk management and implementation component of EMC⁴, a chemical pressure such as that resulting from textile manufacture, use and disposal is global in nature due to the nature of the supply chains involved. Without a global response the impacts of chemical pollution may simply be transferred to a weaker, and therefore cheaper, regulatory regime. Since 2006, SAICM has been one of the primary actors in coordinating global action on chemical management. The question is whether the new framework emanating from the SAICM Beyond 2020 process can incentivize governments to ask the questions listed above. Particularly for a better understanding of the changes in externalities climate change presents and the impact it will likely have on chemicals risk management and implementation within countries. Secondly, UNEP is currently developing a Science Policy Panel which is intended to bridge the information gap between governments and current scientific research on chemical and waste risks. The Science Policy Panel is ideally placed to collate and communicate existing knowledge of the likely impact of climate change on chemicals risk assessment, in addition to taking steps to understand, prioritize, and close evidence gaps. A remaining gap is a process to identify the different actors necessary for the designing of stringent management mechanisms to tackle the issue and the follow up actions to ensure the risk is managed.

Regional case study: Nutrient pollution in European catchments

The European Union (EU) water policy, highlighted by the European Water Framework Directive (WFD; OJEC, 2000), aims at achieving a good ecological status in all surface waterbodies by 2027. This ecological status is determined with several indicators, including the nutrients concentrations. In fact, nutrients pollution, mainly in the form of diffuse pollution from agriculture, has been a concern in Europe for several decades now, and particularly since the proclamation of the Nitrates Directive in 1991 (OJEC, 1991). However, despite all the efforts done, nutrients pollution is still one of the main environmental problems in Europe, and one of the most important threats for aquatic ecosystems (EEA, 2018; Grizzetti *et al.*, 2017). The impact of global change on the fate and transport on nutrients in Europe is uncertain and a deep analysis of current findings is needed to plan adequate management strategies to cope with this problem, and particularly to reduce the risk of eutrophication. Also, the ongoing war, and potential food security issues in its wake, influence the European handling of the issues.

Table 17 provides a brief overview of how global change (climate change and their associated changes in the society) might affect nutrient pollution in European catchments, which tools are available to investigate this problem and who is playing a role in the matter (e.g. actors, policy options). Nutrients pollution management will not be an easy task in the next few decades in Europe since the impacts might be different depending on the region: climate will change differently (e.g., increasing precipitation in the north, decreasing in the south) and the social changes will take different directions too (e.g. Mack *et al.*, 2019; Molina-Navarro *et al.*, 2020). However, actions are being taken to address this problem, including coping with the WFD and the Nutrients Directive requirements, a sustainable food system pursued in the implementation of the Green Deal or the imminent Integrated Nutrient Management Action Plan (https://agriculture.ec.europa.eu/farming/organic-farming/organic-action-plan_en; https://ec.europa.eu/info/law/better-regulation/have-your-say/initiatives/12899-Nutrients-action-plan-for-better-management_en).

Local case study: Legacy and active contamination of the South River, VA, USA

We describe the South River, Virginia site as an example of considering climate change in ecological risk and remedial decision-making at a local / site scale Table 17. The explicit inclusion of climate change as a compounding stressor produced a suite of prospective risk assessments that facilitated a risk management and implementation process producing management actions tailored to both the exposure and impact of chemical and climate change-induced stressors. More than 20 years of investigation culminated in a plan for remediating legacy mercury at this site (Stahl, Kain *et al.* 2014, Stahl Jr 2022). This included specific evaluation of ecological risks coupled with climate change (Johns, Graham *et al.* 2017, Landis, Ayre *et al.* 2017). Results of the ecological risk assessments were incorporated into an adaptive management (AM) framework (Foran, Baker *et al.* 2015), designed to evaluate the effectiveness of remedial actions. Restoration actions were also coupled with the remedial actions and were driven by considerations described elsewhere (Kapustka, Bowers *et al.* 2015, Hooper, Glomb *et al.* 2016). All work was conducted under the Resource Conservation and Recovery Act, Corrective Action program (RCRA-CA), overseen by the Commonwealth of Virginia, and the U.S.

Environmental Protection Agency. Additional information can be found at www.southernriverwatershed.org

Table 17. Guiding assessment and management questions for integrating climate change into environmental risk assessment. Three case studies (e.g., global, regional, local) provide example applications of these questions.

Guiding assessment and management questions:	Global: Integrating climate change into SAICM regarding textiles	Regional: Nutrients pollution in a European catchment	Local: Mercury contamination in South River, WV, USA
1. What are the current chemical risks associated with your case study?	Pesticide usage, effluent of dyes, treatments, coatings & detergents, microplastic release	Nutrients diffuse pollution from agriculture, point sources pollution, eutrophication.	Methyl mercury (MeHg), PAHs, organochlorine pesticides
2. How is the climate changing within the area/region of concern?	Textiles a global industry, however increased flooding, weakening of the monsoon, increased air temp and reduced precipitation expected in textile growing/manufacturing areas	Changes will be different across Europe: Temperature will increase, while precipitation might increase in the north but decrease in the south.	Increased river temperature; Increased inland flooding
3. How will the physical stressors induced by climate change affect the fate, transportation, or the susceptibility of the exposed system?	Lower dilution capacity for pollutants, increased run-off into fresh and marine water, increased deposition and into new areas, change in transformation of metabolites	Lower dilution capacity for nutrients, increased erosion and thus nutrients transport, higher risk of eutrophication (increased nutrients availability and temperature)	Habitat alteration for aquatic species; Release/resuspension of contaminated soil into river; Increased suspended solids
4. How will climate change affect the use/release/toxicity of the chemicals of interest in the exposed system?	Increased and changed pesticide & fertilizer usage, increased and changed use of textile treatments (e.g. anti-mold),	Uncertainty about fertilizer use: changing crop distribution, population growing, green	Legacy MeHg contamination; Increasing population and land development, increases PAHs;

	likely change in the way society uses & washes textiles,	policies, etc. Changes in the water demand for multiple uses.	Increasing population and agricultural production increases organochlorine pesticides, suspended solids
5. Is there evidence and data available to understand the relationship between the chemical risks and climate change?	The impact of climate change on the types of chemical pollution caused by textiles is increasingly well evidenced. The impact of climate change on textiles as a source of chemical risk is not well understood.	EU member states have a strong monitoring network to cope with the WFD requirements, registering nutrient concentrations (among other parameters) in every continental and transitional waterbody. Availability of hydrological and ecological models incorporating climate change scenarios provided by downscaled regional climate models.	Historical record of assessed stressors and monitored assessment endpoints; Multi-year feasibility study of each management options; Downscaled regional climate change projects specific to South River
6. What actors need to be involved in the assessment and management of these risks?	International Governments, UNEP, IOMC, industry bodies, new global science/policy panel	EU administration, Ministries of Environment, River Basin Authorities, farmers and/or regional administrations.	South River Science team (consortium of academics, consultants, government personnel, NGOs)
7. How can human behavior be modified in a way to mitigate greenhouse gas emissions, chemical emissions, and climate change impacts at the same time?	Consume less clothing and fabric-based products, preferentially buy sustainable fabrics, wash clothes less often, avoid fabrics with applied treatments, improve	Decreasing fertilizer use, working towards a sustainable and high-tech agriculture; implementing nature-based solutions to improve water quality through nutrient uptake,	Adaptive management to monitor and assess efficacy of: riverbank stabilization;

		carbon sequestration and biodiversity conservation.	adding riparian vegetation and trees; agricultural best management practices
8. What actions or policy options (e.g., carrot or stick) are available to affect change while taking into consideration the pros and cons of each option?	Harsher regulation of emissions, incentivize integrated pest management, incentivize improvement in manufacturing and detergent technology, improved collection for re-use, repair & recycling, improved transparency/labelling, consumer awareness campaigns	Water Framework Directive, Nitrates Directive, European Green Deal, EU's Common Agricultural Policy. Definition and implementation of specific catchment adaptation plans, nested in the national and regional adaptation strategies.	Collaborative assessment and management process driven by diverse knowledge and experience needed to ensure successful long-term bank stabilization by working with the existing old-growth trees along the bank.

4. Implications and Path Forward

In contrast to the other papers in this series, our task was to determine if and how any new approaches for incorporating climate change projections into ecological risk assessment could become a standard practice in chemical management programs and policies. While the case studies provided by the other work groups in this workshop (cite the Yakima River, GBR, and pesticides manuscripts) focused on spatial and temporal scales suitable for ecological risk assessment, our focus was on chemical management at multiple geographic scales. Particularly as management occurs across scales. This was the backdrop for developing the EMC4 conceptual framework.

In the Introduction and Section 2 we touched on how climate change can influence the fate and effects of chemicals, and potential barriers to address this in chemical management programs. Nations first cooperated to address climate change in 1992 (Rio Convention), and the first specific climate change convention was celebrated in 1995 (COP1, Berlin), yet in 2022 when the most recent convention was held (Paris), measurable progress to achieve the goals nations set for themselves remains elusive. It appears also to be the case with SAICM that nations desire to participate and make progress, but that progress has been slow (SAICM, Independent Evaluation of the Strategic Approach, 2019). Yet this presents the risk management and policy community with an opportunity since SAICM is under review and changes are likely. Thus, with the acknowledgment of a need, consideration of climate change could be incorporated into the SAICM Beyond 2020 framework/approach. Given that many frameworks rely on pre-existing knowledge and research for evidence based chemical decision making (e.g., Stockholm), there is a need for a coordinated effort to understand and explain the relationship between chemicals and climate change on a global scale to stimulate an evaluation of the data that exist (e.g., SPI, IOMC).

In this series of papers, case studies have been provided for chinook salmon (Landis et al. This series) in the U.S. Pacific Northwest, the Great Barrier Reef in Australia (Jenny / Sophie et al., this series), pesticides in Norway (Jannicke / Rik / Sophie, this series), and have shown the methodology for incorporating climate change projections into a wide variety of ecological risk assessments, at various spatial scales, and for differing environmental situations. These methods could be operationalized in the near future as there appear to be little, if any, technical barriers to preclude their use for ecological risk assessments. The next logical step would be to incorporate them into chemical management programs worldwide and to require that they are used in future industry data submissions for new chemicals, and for new uses of existing chemicals. The consequences of not incorporating climate change considerations into chemical management programs range from increased pesticide susceptibility of nontarget species, to approving widespread use of a new chemical that will, perhaps, exhibit the same harmful, environmental profile as ozone-depleting chemicals of the 1950s-1970s. The latter is something we should endeavor to avoid.

Since many chemical management programs and frameworks rely on pre-existing knowledge and additional research on chemical management decision making (e.g Stockholm) the use of the EMC4 Framework would enhance incorporating climate change. Thus, it makes sense to develop a scientific expert process to evaluate chemical fate and effects data that exist, and the implications that may result due to climate change (e.g. SPI, IOMC). With the development of the UNEPs new Chemical and Waste Science Policy Panel, the opportunity is there, key is that those setting up the

IPCC, IPBES and IRC type of panel include this focus during the horizon scanning and other prioritization mechanisms put in place. Key would be for the new Science Policy Panel to interact with the IPCC to discuss uncertainties in the analyses, and whether there is a need to fill data gaps. While the new panel's focus is "policy relevant, not policy prescriptive", it could also suggest approaches and tools that might be useful to decision makers in the governmental and business communities involved with chemical manufacture and management.

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