HCWH Europe Recommendations on pharmaceuticals in the environment - September 2016

Health Care Without Harm (HCWH) Europe[1] is the European arm of a global not for profit NGO whose mission is to transform healthcare worldwide so that it reduces its environmental footprint, becomes a community anchor for sustainability, and a leader in the global movement for environmental health and justice. HCWH's vision is that healthcare mobilises its ethical, economic, and political influence to create an ecologically sustainable, equitable, and healthy world.

HCWH Europe works towards promoting a reduction of pharmaceuticals in the environment by collaborating with the health sector, the pharmaceutical industry, and other NGOs, and has recently launched a Safer Pharma campaign that aims to raise awareness, educate the general public and healthcare professionals, and to promote policies that reduce pharmaceutical emissions throughout their entire life cycle (in their production, use, and disposal). Therefore, HCWH Europe calls on the European Commission to develop a strategic approach that protects both the environment and human health. HCWH Europe invites governments, the pharmaceutical industry, and other relevant stakeholders to play an active role in the global effort to reduce pharmaceutical pollution - to protect both public health and the environment in the long-term.

What is the scale of the issue?

In the right place, pharmaceuticals save lives and prevent disease, but it is well known that pharmaceuticals in the environment represent a global pollution problem - over 631 different pharmaceutical agents or their metabolites have been detected in 71 countries on all continents.[2] They are already damaging the environment[3] and in the long-term, they could cause widespread damage to human health.

Worldwide revenue from the sales of pharmaceuticals has almost doubled over the last 10 years, from $559.9 billion in 2004 to $1,057 trillion in 2014, and is expected to grow more over the coming years, with aging populations and improved access to healthcare.[4] The European Union (EU), is the second largest consumer of human medicinal products in the world (24% of the global production), after the United States.[5]

[1] Health Care Without Harm (HCWH) Europe. https://noharm-europe.org
[2] Aus der Beek T, Weber FA, Bergmann A, Hickmann S, Ebert I, Hein A and Küster A, (2016). Pharmaceuticals in the environment-Global occurrences and perspectives. *Environ Toxicol Chem*, 35(4), pp.823-35. http://www.ncbi.nlm.nih.gov/pubmed/26666847
[3] Kümmerer K, (2010). Pharmaceuticals in the environment: sources, fate, effects and risks. *Environmental Science and Pollution Research*, 17(2), pp.519-521.
[4] Statista (The Statistics Portal) (accessed 2016). http://www.statista.com

According to a recent German Environment Agency report,[6] about 4,000 Active Pharmaceutical Ingredients (APIs, the part of the medicine that is biologically active in order to have an effect on the body), are being used in prescription drugs, over the counter therapeutic drugs, and veterinary drugs.

APIs are designed to be highly biologically active in humans and can have unintended effects on other species.[6] Even low amounts of APIs in the environment can have far-reaching effects on ecosystems.[7]

Pathways into the environment

Various categories of pharmaceutical residues have been detected in surface water, sewage effluents, groundwater, drinking water, manure, soil, and other environmental matrices. [2,8,9,10,11,12,13,14,15,16]

Pharmaceutical residues can enter the environment during the production, consumption, and disposal of pharmaceuticals.[17] Pharmaceutical manufacturing is a source of pharmaceutical

[5] Académie Nationale de Pharmacie (2008). Médicaments et environnement. http://www.acadpharm.org/dos_public/1_Rapport_Med_Env_version_JMH_def_JPC.pdf
[6] German Environment Agency (2016). *Pharmaceuticals in the environment - the global perspective*. p.3. https://www.umweltbundesamt.de/sites/default/files/medien/378/publikationen/pharmaceuticals_in_the_environment_0.pdf
[7] Kidd KA, Blanchfield PJ, Mills KH, Palace VP, Evans RE, Lazorchak JM and Flick RW, (2007). Collapse of a fish population after exposure to a synthetic estrogen. *Proc. Nat. Acad. Sci*, 104(21), pp.8897–8901.
[8] Kümmerer K, (2009). The presence of pharmaceuticals in the environment due to human use – present knowledge and future challenges. *Journal of Environmental Management*, 90(8), pp.2354–2366.
[9] Touraud E, Roig B, Sumpter JP and Coetsier C, (2011). Drug residues and endocrine disruptors in drinking water: risk for humans? *International Journal of Hygiene and Environmental Health*, 214(6), pp.437-441.
[10] Kümmerer K (ed.), (2008). *Pharmaceuticals in the Environment: Sources, Fate, Effects and Risks* (third edition). Berlin Heidelberg, Springer-Verlag.
[11] Buerge IJ, Buser H-R, Poiger T and Müller MD, (2006). Occurrence and Fate of the Cytostatic Drugs Cyclophosphamide and Ifosfamide in Wastewater and Surface Waters. *Environ. Sci. Technol.*, 40 (23), pp.7242–7250.
[12] Daughton CG, (2016). Pharmaceuticals and the Environment (PiE): Evolution and impact of the published literature revealed by bibliometric analysis. *Science of the Total Environment*, 562, pp.391-426.
[13] Klatte S, Schaefer H-C and Hempel M, (2016). Pharmaceuticals in the environment – A short review on options to minimize the exposure of humans, animals and ecosystems. *Sustainable Chemistry and Pharmacy*. In press.
[14] Küster A and Adler N, (2014). Pharmaceuticals in the environment: scientific evidence of risks and its regulation. *Philos Trans R Soc Lond B Biol Sci*. 369(1656). http://www.ncbi.nlm.nih.gov/pubmed/25405974
[15] Kümmerer K, (2010). Pharmaceuticals in the Environment - Annual Review of Environment and Resources. *Environment and Resources*, 35(1) pp.57-75. http://www.annualreviews.org/doi/full/10.1146/annurev-environ-052809-161223
[16] BioIntelligence Service (2013). *Study on the environmental risks of medicinal products – Final report.* http://ec.europa.eu/health/files/environment/study_environment.pdf

pollution that can be exacerbated by weak environmental legislation in countries that produce many of the APIs for pharmaceutical products globally.[18]

Pharmaceuticals also enter into the environment during the use phase of their life cycle - by human excretion via wastewater, and animal excretion via runoff from agricultural areas and discharges from aquaculture.[15]

Another route is through incorrect disposal - the most common forms of incorrect disposal are when unused medicines are flushed down the toilet or sink, or when they are disposed of in waste bins destined for landfill sites.[19]

According to Directive 2004/27/EC[20] (relating to medicinal products for human use), EU Member States have an obligation to implement appropriate collection schemes for unused pharmaceutical products. However, no guidelines have been provided on the implementation of these schemes.[19] As a consequence, a number of studies[21, 22] have highlighted significant differences between Member States in terms of collection schemes. Currently, there is deficient and scattered data regarding the implementation and efficiency of collection schemes for unused pharmaceuticals throughout Europe, which makes it unclear whether all EU countries have fulfilled their obligations.[19] Current wastewater treatment plants are unable to completely destroy or remove pharmaceuticals. The amount of these pharmaceuticals remaining after treatment depends on the substance(s) in question, their initial concentration, and the treatment methods employed.[16, 23] Consequently, pharmaceutical residues can re-enter terrestrial systems, spread to surface waters and agricultural lands, and can ultimately end up in drinking water,[24,25] and accumulate in vegetables and fish.[26,27,28,31]

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[17] Thomas KV and Langford KH, (2010). Point sources of human pharmaceuticals into the aquatic environment. In: Kümmerer K and Hempel M (eds), (2010). *Green and Sustainable Pharmacy*, pp.211–223. Berlin Heidelberg, Springer-Verlag.

[18] SumOfUs (2015). *Bad Medicine: How the pharmaceutical industry is contributing to the global rise of antibiotic-resistant superbugs.* https://s3.amazonaws.com/s3.sumofus.org/images/BAD_MEDICINE_final_report.pdf

[19] HCWH Europe (2013). *Unused pharmaceuticals, where do they end up? A snapshot report of European collection schemes.* https://noharm-europe.org/sites/default/files/documents-files/2616/Pharm%20Report_WEB.pdf

[20] Directive 2004/27/EC amending Directive 2001/83/EC on the Community code relating to medicinal products for human use. OJ L 136/34, 30.4.2004. http://ec.europa.eu/health/files/eudralex/vol-1/dir_2004_27/dir_2004_27_en.pdf

[21] Volmer G, (2010). Disposal of pharmaceutical waste in households – A European Survey. In: Kümmerer K and Hempel M (eds), (2010). *Green and Sustainable Pharmacy,* pp.165–178.

[22] Taylor D and Poulmaire M, (2008). *An initial survey of unused and expired medicine take-back schemes in the European Union.* Poster Presentation. KNAPPE International Conference. Nimes, France.

[23] Köhler C, S Venditti S, Igos E, Klepiszewski K, Benetto E and Cornelissen A, (2012). Elimination of pharmaceutical residues in biologically pre-treated hospital wastewater using advanced UV irradiation technology: A comparative assessment. *Journal of Hazardous Materials*, 249-240:70-77.

[24] World Health Organization (2012). *Pharmaceuticals in drinking-water.* http://www.who.int/water_sanitation_health/publications/2012/pharmaceuticals/en/

[25] Huerta-Fontela M, Galceran MT and Ventura F, (2011). Occurrence and removal of pharmaceuticals and hormones through drinking water treatment. *Water Research*, 45(3): 1432–1442.

Causes for concern

At present, there is little published information, and a lack of transparency regarding the quantities of APIs produced per year, or the amounts that are being discharged into the environment.

Designed to be biologically active, APIs are also developed to remain unchanged and stable during their passage through the body, which means they often persist outside the body and as a consequence, can accumulate in the environment. Therefore, these substances have the potential to significantly impact both the environment and non-target organisms.[12,19]

Recent scientific literature has provided various examples of animals and other organisms exposed to pharmaceuticals in water or soil.[2, 6, 14] Animals are also exposed when they feed on other animals which have been medicated, and behavioural, physiological, and histological effects have been observed in animals exposed in this way.[7, 27, 31] The most dramatic environmental effect witnessed in relation to pharmaceuticals was the near extinction of vultures feeding on animals that have been treated with diclofenac in Pakistan.[29,30]

Through water and food consumption, humans can be unintentionally exposed to pharmaceutical residues.[31] Although it has already been proven that low concentrations of pharmaceuticals in the environment can affect animals and other organisms, little is understood about their effects on humans.[13, 31]

There are 3 groups of pharmaceuticals that are particularly active in low concentrations and therefore have attracted the attention of researchers and policy-makers: endocrine-disrupting pharmaceuticals (i.e. hormones), anti-cancer treatment drugs (which are toxic to living cells by design), and antibiotics (because of the threat of the development of antibiotic resistant bacteria).[15]

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[26] Jelic A, Gros M, Ginebreda A, Cespedes-Sánchezd R, Ventura F, Petrovica M and Barcelo D, (2011). Occurrence, partition and removal of pharmaceuticals in sewage water and sludge during wastewater treatment. *Water Research*, 45(3), pp.1165-1176.
[27] Arnold KE, Ross Brown A, Gerald T, Ankley GT and Sumpter JP, (2014). Medicating the environment: assessing risks of pharmaceuticals to wildlife and ecosystems. *Phil. Trans. R. Soc. B* 369: 20130569.
[28] Sarmah AK, Meyer MT and Boxall ABA, (2006). A global perspective on the use, sales, exposure pathways, occurrence, fate and effects of veterinary antibiotics (VAs) in the environment. *Chemosphere*, 65(5), pp.725-759
[29] Oaks JL, Gilbert M, Virani MZ, Watson RT, Meteyer CU *et al*., (2004). Diclofenac residues as the cause of vulture population decline in Pakistan. *Nature*, 427, pp.630-633.
[30] Green RE ,Taggart MA, Senacha KR, Raghavan B, Pain DJ, Jhala Y and Cuthbert R, (2007). Rate of Decline of the Oriental White-Backed Vulture Population in India Estimated from a Survey of Diclofenac Residues in Carcasses of Ungulates. *PloS One*, 2(8).
[31] HCWH Europe (2014). *How doctors can help reduce pharmaceutical pollution.* https://noharm-europe.org/documents/how-doctors-can-help-reduce-pharmaceutical-pollution

However, there are also problems surrounding other categories of drug substances, as was recently highlighted by Stockholm County Council in their categorisation of immunosuppressants (drugs that lower the body's ability to reject a transplanted organ), heart medications, and anti-acne medications among the pharmaceuticals of moderate concern.[32]

Policy context

In recognition of the growing problem of pharmaceuticals in the environment, the UN Strategic Approach to International Chemicals Management (SAICM), adopted 'Environmentally Persistent Pharmaceutical Pollutants' as an emerging policy issue in their process in autumn 2015.[33] In their 2012 report, the World Health Organization (WHO), stressed the importance of prioritising the emerging issue of pharmaceuticals in drinking water in the overall context of water safety management, including microbial and other chemical risks that may threaten the safety of drinking water.[24]

In Europe, according to Article 8c of Directive 2013/39/EU[34] (a directive regarding priority substances in the field of water policy), the European Commission has been asked to develop a strategic approach to address water pollution by pharmaceuticals by September 2015. This deadline has come and gone, and a lack of action by the Commission means that there is a continued risk to public health, health systems, and the environment from pharmaceutical pollution.

Stockholm County Council (SCC), is proactively addressing pharmaceutical pollution as part of its preventative environmental health work at a regional level in Sweden. It has developed an online database with environmental information on approximately 800 pharmaceutical substances. SCC uses this data to develop recommendations for the "Wise List"[35] - a formulary of essential medicines for patient care in the Stockholm region. Although the Wise List primarily focuses on medical benefits and side effects, when multiple pharmaceuticals have the same benefits, the environmental classification can be considered. Use of the Wise List is not mandatory, but more than 80% of the pharmaceuticals prescribed by the SCC health system are in accordance with the recommendations in the Wise List.[31]

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[32] Stockholm County Council (2014). *Environmentally classified pharmaceuticals, 2014-2015*. http://www.janusinfo.se/Global/Miljo_och_lakemedel/Miljobroschyr_2014_engelsk_webb.pdf

[33] Environmentally Persistent Pharmaceutical Pollutants (EPPPs) at International Conference on Chemicals Management (ICCM) 4 autumn 2015 in Geneva http://www.saicm.org/index.php?option=com_content&view=article&id=520&Itemid=714

[34] Directive 2013/39/EU amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy. OJ L 226/1, 24.8.2013. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32013L0039&from=EN

[35] Stockholm County Council Drug and Therapeutics Committee (2015). *The Wise List*. http://www.janusinfo.se/Documents/Kloka_Listan/The-Wise-List-2015.pdf

HCWH Europe's recommendations for the reduction of pharmaceuticals in the environment

1. *Minimise the entry of pharmaceuticals into the environment throughout their life cycle*

We need a multi-sectoral, multi-stakeholder approach that includes pharmaceutical companies, doctors, veterinarians, pharmacists, academics, patients, the general public, hospitals, care homes, water and waste companies, and legislators to minimise and prevent the release of APIs into the environment throughout their life cycle (i.e. in their production, use, and disposal). All policies and forms of engagement to this end should be applied using the precautionary principle (whereby in cases where scientific data do not permit a complete evaluation of the risk, withdrawal from the market should be considered for products that are likely to be hazardous). Member States need to set reduction targets with measurable impacts and annually report publicly on the reduction achieved.

2. *Achieve zero discharge and eliminate the release of pharmaceuticals into the environment from manufacturing plants*

Governments need to strengthen laws to eliminate pollution, monitor rigorously, impose fines, and withdraw licences if needed. The ultimate aim should be a zero discharge policy. National governments and regulators around the world need to expand the regulatory framework for Good Manufacturing Practice (GMP), to include environmental safety. The GMP legislation (i.e. Directive 91/412/EC[36] and Directive 2003/94/EC[37]), should require pharmaceutical production facilities to apply environmental safety standards to achieve a zero discharge goal.

3. *Increase transparency and improve consistency along the supply chain*

Pharmaceutical companies should know their supply chains, insisting on consistently high standards throughout. Companies need to report publicly on their environmental and worker safety standards. This will prevent multinational pharmaceutical corporations operating double standards in low, middle, and high-income countries, whereby they maximise profits by importing APIs from countries with weak regulatory systems. This needs to be equally applied to medicinal products for both human and veterinary use.

[36] Directive 91/412/EC laying down the principles and guidelines of good manufacturing practice for veterinary medicinal products. OJ L228/70, 17.8.91. http://ec.europa.eu/health/files/eudralex/vol-5/dir_1991_412/dir_1991_412_en.pdf

[37] Directive 2003/94/EC laying down the principles and guidelines of good manufacturing practice in respect of medicinal products for human use and investigational medicinal products for human use. OJ L 262/22, 14.10.2003. http://ec.europa.eu/health/files/eudralex/vol-1/dir_2003_94/dir_2003_94_en.pdf

4. *Extended producer responsibility - make the pharmaceutical industry accountable for pharmaceutical waste throughout the life cycle*

The pharmaceutical industry's accountability for the impact of their products should not end at the point of sale. The Extended Producer Responsibility concept, already established in the automotive and electronics sectors,[38] also needs to be applied to the pharmaceutical sector. Pharmaceutical manufactures should contribute to financing collection schemes under the extended producer responsibility clause of the Waste Framework Directive.[39]

5. *Assess the potential environmental risks of all pharmaceuticals*

Most of the pharmaceuticals detected in the environment were authorised prior to 30th October 2005, when the 'Guideline on the environmental risk assessment (ERA), of medicinal products for human use',[40] came into force. Pharmaceuticals authorised before this date currently do not require an ERA. This exemption should be removed and an ERA conducted when renewing the market authorisation of any pharmaceutical. This should be based on the "No data no market" principle that applies to chemical substances regulated under the REACH Regulation.[41]

6. *Use green procurement as a tool to switch to pharmaceuticals with a lower environmental impact*

Public procurers can send a clear signal by setting environmental criteria for tendering in order to drive change in the market, using the Public Procurement Directive[42] to purchase socially responsible and environmentally sound pharmaceuticals. The joint UN Procurement project is an example of procurers working with supply companies to shift towards procuring more sustainable products.[43] Stockholm County Council is also facilitating green procurement by publishing the best available data on the persistence and likelihood of environmental impact from specific APIs.

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[38] Organisation for Economic Co-operation and Development (OECD) (accessed 2016). *Extended Producer Responsibility*. http://www.oecd.org/env/tools-evaluation/extendedproducerresponsibility.htm
[39] Directive 2008/98/EC of the European Parliament and of the Council of 19 November 2008 on waste and repealing certain Directives (Article 8). http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32008L0098&from=EN
[40] European Medicines Agency (2006). *Guideline on the environmental risk assessment of medicinal products for human use*.
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2009/10/WC500003978.pdf
[41] Regulation (EC) No 1907/2006 concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals. OJ L 396, 30.12.2006. http://eur-lex.europa.eu/legal-content/en/TXT/PDF/?uri=CELEX:02006R1907-20160401
[42] Directive 2014/24/EU on the public procurement and repealing Directive 2004/18/EC. OJ L 94/65 28.3.2014. http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014L0024&from=EN
[43] United Nations Informal Interagency Task Team on Sustainable Procurement in the Health Sector (SPHS) (2016). *Saving Lives Sustainably*. http://savinglivesustainably.org

7. Encourage rational use and improve education about pharmaceuticals

Over-prescription and overuse, especially of antibiotics, needs to be reduced. The rational use concept[44] should be reinforced by including environmental criteria in the curricula of medical, pharmacy, and nursing schools. Prescription guidelines for medical professionals need to be tightened and enforced.

8. Improve wastewater treatment

Wastewater treatment technologies are crucial components in the water management process. Wastewater treatment technologies need to be improved at municipal level and not just at a hospital level, as many patients continue treatment at home. Technologies that remove or destroy pharmaceutical contaminants in wastewater should be further developed and emission limits continuously lowered. Implementing advanced wastewater treatment technologies will reduce pharmaceutical pollution and in the longer term could completely eliminate environmental releases.

9. Dispose of unused pharmaceuticals safely

The inappropriate disposal of pharmaceuticals, such as by flushing them down the toilet, results in environmental pollution[16,19] and needs to be eliminated. Take-back schemes should be harmonised and expanded across the EU to prevent unused pharmaceuticals from reaching the environment. Member States should implement non-incineration treatment for all healthcare waste, including pharmaceuticals. Introduce clear labelling on each package on how to dispose of unused medicine that will guide doctors, pharmacists, nurses, and patients. Data on collection and disposal should be gathered and published annually.

10. Develop comprehensive legislation to reduce the impact of pharmaceuticals on the environment

Pharmaceuticals should not be treated differently than other groups of chemicals such as pesticides, biocides, and industrial chemicals. Models from other regulatory approaches that are already in place should be applied when drafting the strategic approach to pollution of water by pharmaceutical substances. In addition to this, the EU must develop comprehensive legislation to address the other means by which the pharmaceutical industry can affect the global environment and human health. Mandatory targets, systematic reporting, enforcement, and stakeholder engagement are all necessary to achieve this goal.

For more information about HCWH Europe, please visit: www.noharm-europe.org or email: europe@hcwh.org

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[44] World Health Organization. *Essential medicines and health products*. http://www.who.int/medicines/areas/rational_use/en/