



CHEM Trust's comments to the proposal by Peru, Uruguay and the International Society of Doctors for the Environment (ISDE) to nominate Environmentally Persistent Pharmaceutical Pollutants (EPPPs) as an emerging policy issue under the Strategic Approach to International Chemicals Management (SAICM).

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CHEM Trust is highly supportive of the proposal to consider pollution by pharmaceuticals as an emerging issue under SAICM. This is a growing global problem that needs greater coordination worldwide in order to ensure that best practices for mitigating the effects of such pollution are shared and effectively implemented.

The revised proposal is to be presented at the second meeting of the Open-ended Working Group (OEWG) to be held in Geneva on 14-17 December 2014. CHEM Trust sincerely hopes that the OEWG will decide to add this issue to the agenda of the fourth session of the International Conference on Chemicals Management, and that the proposal will then be adopted by the Conference.

More information can be found on the following SAICM web page:

http://www.saicm.org/index.php?option=com_content&view=article&id=458:epi-eppp&catid=222:saicm-emerging-policy-issues&Itemid=687

CHEM Trust considers that the proposal to consider Environmentally Persistent Pharmaceutical Pollutants as an emerging issue has much merit and is very timely. We therefore whole heartedly support this proposal, which if accepted, will do much to help the global community effectively deal with this growing threat. We congratulate Peru, Uruguay and the ISDE for bringing this issue to the fore.

In this document CHEM Trust is suggesting a number of relatively minor edits, which we hope will be considered by the proponents for their revised text. Firstly, CHEM Trust suggests that the name of the proposal should be changed from EPPP (Environmentally Persistent Pharmaceutical Pollutants) to Widespread or Environmentally Persistent Pharmaceutical Pollutants (WEPPPs). An alternative title could be just Pharmaceuticals in the Environment (PIEs).

In the '**State the problem**' section, we also suggest a few minor changes to the introductory sentences, "Many Pharmaceutical chemicals... and disseminate in the environment." This could be re-phrased to read, "Pharmaceutical chemicals include substances used to treat humans and/or animals, and thus also embrace veterinary medicines. Many such substances are designed to persist in the body long enough to exert their desired effects. They therefore tend to resist degradation

during passage through the body and may present a risk when they or their active metabolites or degradation products enter the environment. Some of these substances may persist in the environment for a very long time and meet the definition for persistent chemicals as laid down in the Stockholm Convention on Persistent Organic Pollutants. However, even substances with somewhat lower persistency would be of high concern, if their usage was such that they were widespread in the environment and continuously found, due to their ubiquitous and frequent usage. These pharmaceutical substances which are either persistent or widespread in the environment need an international response to reduce the risks posed by such substances.

In this proposal we use the term 'Widespread or Environmentally Persistent Pharmaceutical Pollutants (WEPPP)' to denote these chemicals."

In addition, we suggest that the following paragraph is amended slightly to read as follows. "Although pharmaceutical residues entering the environment are included in legislation in some countries, they are insufficiently addressed as a pollution problem in most countries."

In the following text, the minor amendments suggested by CHEM Trust are shown in track changes.

A project commissioned by the German Federal Environment Agency (UBA) has provided a new global data-base on pharmaceuticals in the world environment. This is to be finalised in 2015, but interim distribution maps are now available. This project has collated measured environmental concentrations and with more than 120,000 entries, ~~this data-base shows~~ ~~has shown~~ that WEPPPs have become a global problem. In all UN regions, levels of some pharmaceuticals in the environment are potentially high enough to be harmful to aquatic organisms. ~~with potentially harmful concentrations for aquatic organisms found in all UN regions.~~

~~Chemicals of P~~pharmaceutical chemicals are ~~origin a~~, widely used globally for therapeutic purposes, including the treatment of disease ~~in by~~ humans, as well as in ~~and~~ domesticated companion animals and in livestock used ~~for~~ food production. Residues from pharmaceuticals can ~~for an intended purpose they can~~ persist in the environment and ~~residues can now be~~ ~~are presently~~ found in drinking water. They are ~~also~~ found in fish and other ~~organisms in the wild,~~ ~~animals~~ where they may accumulate.

Pharmaceuticals reach the environment mainly in three ways:

- Manufacturing plants producing the active substances may release pharmaceuticals into the aquatic environment.
- Humans and animals treated with pharmaceuticals excrete residues, intact or metabolized, into their urine and faeces, from ~~wher~~ ~~er~~ ~~ich~~ they pass into sewage treatment plants or directly into the environment. Sewage treatment plants often have no specific procedures ~~or techniques~~ to eliminate WEPPPs.
- Unused or expired pharmaceuticals may be disposed from households or hospitals and reach the environment, either via sewage water or via urban solid waste handling.

With the exception of ~~downstream~~ ~~treatment~~ plants receiving water from pharmaceutical industries (where large amount of pharmaceutical chemicals have been monitored ~~in some countries~~) (17), the

concentrations of active residues of chemicals of pharmaceutical origin detected in surface waters and sediments may be low but they may be continuously present or persist for long periods of time, contributing to chronic and persistent exposure (2-5).

They may pose a threat of important magnitude for public health with potentially significant adverse effects on the environment and on human health, particularly as exposure may start prior to ~~since~~ conception and continue throughout pregnancy and during all the phases of development, with possible important consequences for adult life. There may be increased impacts on ~~→e.g. special impacts on~~ vulnerable populations (including the elderly, sick, and children) (6-8).

As described above, WEPPPs are already found in water all over the world. This ~~is a~~ diffuse exposure in the environment might contribute to endocrine disruption, the development of microbes resistant to antibiotics (1), and reproductive effects that may lead to the ~~derive on~~ extinction of species and imbalance of ~~sensible~~ ecosystems (9-10). Furthermore, such contamination may contribute to, genetic, developmental, and immune system health effects in humans and other species.

As the world's population is growing and ageing, more people in the developing world can afford medical treatment, and as new treatments are developed, the degree of environmental pollution from chemicals of pharmaceutical origin can be expected to increase. This highlights the need for ~~without further~~ developing adequate risk management measures. Thus, to mitigate current and to prevent future problems, there is an urgent need for global recognition and global management actions ~~have to be established~~.

Information that can be used to assess the nominated issue

a) Magnitude of the problem and its impact on human health or the environment taking into account vulnerable populations and any toxicological and exposure data gaps

The new global data-base on WEPPPs has shown that more than 630 different pharmaceutical compounds have been found to occurring in the aquatic environment. Among WEPPPs found in drinking water are atenolol and metoprolol (beta blockers), citalopram (antidepressant), diclofenac, ibuprofen and naproxen (anti-inflammatories), tetracyclin and trimetoprim (antibiotics) (6).

According to the data-base, the occurrence of diclofenac in the aquatic environment has been documented in 50 countries globally, followed by carbamazepine (anti-epileptics), ibuprofen, sulfamethoxazole (antibiotics), and naproxen (45 countries). Also, the data-base has shown that often even average concentrations measured are above PNEC (Predicted-No-Effect-Concentration) levels, implicating adverse effects on organisms.

State of the knowledge:

i) Pharmaceuticals are a special kind of chemicals. They are manufactured to be biologically active in living organisms and to have relatively long half-lives. This makes them more risky when released into the environment, where they can impact nature.

ii) The levels of pharmaceuticals in surface or drinking water are generally below 1 mg (milligram) per litre, often measured in ng (nanogram) per litre (2, 8). This low concentration might appear to guarantee that they hardly pose any problem to public health. Assuming a concentration of 100 ng/l of a pharmaceutical that in humans has a DDD (defined daily dose) of 10 mg implies that a volume of

100,000 litres would be required to make up one single DDD. Such a calculation, however, is an oversimplification that does not take into account several important dynamic aspects of the low chronic exposure to concentrations of pharmaceuticals in the water or the vulnerable population exposure, for example ~~during~~ since conception and including other ~~during~~ susceptible periods of development.

iii) Aquatic organisms may bio-concentrate and bio-accumulate lipid soluble chemicals, including pharmaceuticals. It is well known that certain fish species, like herring, may contain very high concentrations of the persistent and lipophilic chemicals DDT (dichlorodiphenyl-trichloroethane, an insecticide) and PCB (polychlorinated biphenyls, a group of industrial chemicals earlier used in, for example, electrical capacitors and building materials). The same mechanisms may also be operated when applied for chemicals synthesized for pharmaceutical uses reach the environment. For example, bioaccumulation of citalopram (SSRI, antidepressant) and propoxyfen (painkiller) has been found in perch in the Baltic Sea, and therapeutic levels of levonorgestrel (a sex hormone) have been found in rainbow trout downstream from a sewage plant (9).

iv) Pharmaceutical chemicals are not conceived or designed to enter in the environment and persist there, but rather are developed for a clear pharmaceutical purpose. Pharmaceuticals are synthetic chemicals. They belong to a wide group of different chemical families and may also react differently in the environment. When a new medicine is developed, its pharmacological and toxicological effects are tested in acute trials before it is approved being accepted for marketing. However, clinical test procedures are not entirely sufficient to completely guarantee that a new pharmaceutical is devoid of unacceptable side effects when used in large cohorts of patients for a long time. Furthermore, there are currently no comprehensive test methods to assess whether delayed effects such effects may occur in humans after long-term exposure to pharmaceutical residues use in humans (including effects from exposure to mixtures) during periods of development. Neither do existing test methods assess the potential full range of effects that might occur in aquatic microorganisms and or how they may affect other animals. Based on this, the effects of persistent and diffuse long-term exposure to low doses of pharmaceutical synthetic chemicals, for long periods of time, are not well known or studied.

v) The diffuse dissemination of the WEPPS in the environment may indiscriminately expose vulnerable populations: embryos/foetuses, children and adolescents, men and women of reproductive age, and the elderly elderly persons. Some of the pharmaceuticals found in surface waters are prescribed to patients under special controlled conditions for short periods of time, due to the risk of side effects. Others are prohibited from being prescribed to pregnant women or children. These chemicals were not synthesized to expose the general population in a diffuse manner. This presents a new and emerging issue with regard to chemical safety and global pollution.

vi) a large proportion of excreted or disposed medicines reach the public sewage treatment plants. Today, most sewage plants do not have the capacity to ensure that the treated water does not contain pharmaceutical chemicals. This is sometimes also the case for the industries' own sewage plants. In many parts of the world, effluent sewage plant water is reused as drinking water or as irrigation water for food crops, which raises concerns about the safety of such water whereas it may, not always be usable after sewage treatment. Detection and monitoring on a global scale of WEPPS

in drinking and surface water, as well as in animals and plants, is necessary to understand the magnitude of the problem. ~~Concerns are raised by the as shown by the~~ UBA commissioned global data- base ~~which shows that many countries have found low levels of some pharmaceuticals in drinking water.~~ On a precautionary basis, the aim should be to reduce as much as possible, the levels of pharmaceuticals in drinking waters and groundwaters. The first step is to recognize WEPPPs as an emerging issue, in order to be able to invest the necessary human and financial resources ~~to and~~ develop effective environmental detection methods and monitoring strategies.

b) Extent to which the issue is being addressed by other bodies, particularly at the international level, and how it is related to, complements or does not duplicate such work.

WEPPPs are insufficiently addressed ~~or not covered~~ by other international or regional agreements or arrangements. However, in

~~in~~ 2013, UN agencies and the EU Commission started activities regarding this issue. Below are noted some of the noteworthy global activities, followed by regional and then country specific initiatives.

~~and Sweden have been introducing regulations 10 years ago.~~

i) **Global activity:** Greening procurement – joint UN project on sustainable procurement of pharmaceuticals

Five UN Agencies (UNDP, UNEP, UNFPA, UNOPS, and WHO) have jointly started a project to improve the sustainability of their respective health care projects, and thereby to diminish possible future negative environmental effects of pharmaceuticals used in these respective projects.

Two different approaches ~~to reach the target~~ are planned:

(a) to develop and introduce technical guidelines on sustainable procurement of health care products including pharmaceuticals, thereby creating an incentive for manufacturers to strive towards production of ~~more~~ “greener” products, and

(b) to include protection against emissions of environmentally hazardous pharmaceuticals or their by-products in the GMP (Good Manufacturing Practice) mandatory to all the pharmaceutical industry in their production of pharmaceuticals.

The project is planned to last for 4-5 years, including fund raising, development of a working plan and technical guidelines, contacts with producers, analysis of possible methods to stimulate “green” production of drugs, and training of procurement staff to handle the guidelines efficiently. The project started with a consolidating workshop in Bonn, August 28-30, 2013.

ii) **Global activity:** The German Environment Agency (UBA) sponsored Workshop on Pharmaceuticals in the Environment which was held in Geneva in April 2014 (<http://pharmaceuticals-in-the-environment.org/en>). This initiative clearly complemented this proposal to consider pharmaceuticals in the environment as an emerging issue under SAICM.

iii) **Regional activity:** In the EU, a noteworthy project is the “Study on the environmental risks of medicinal products” (http://ec.europa.eu/health/human-use/environment-medicines/index_en.htm). This study for the European Commission, by BIO Intelligence Service, is to

provide the basis to develop a strategic approach to pollution of water by pharmaceutical substances.

The rationale for this EU strategic approach is outlined in Directive 2013/39/EU of the European Parliament and of the Council of 12 August 2013, amending Directives 2000/60/EC and 2008/105/EC as regards priority substances in the field of water policy.

In this directive, the European Parliament and the Council instructs the Commission to look further into the problem of pharmaceuticals in the environment, and asks for proposals on how to handle the problem.

The text of the directive in the appropriate sections is as follows:

“Article 8c: Specific provisions for pharmaceutical substances

Pursuant to Article 16(9) of Directive 2000/60/EC, and where appropriate on the basis of the outcome of its 2013 study on the risks posed by medicinal products in the environment and of other relevant studies and reports, the Commission shall, as far as possible within two years from 13 September 2013 develop a strategic approach to pollution of water by pharmaceutical substances. That strategic approach shall, where appropriate, include proposals enabling, to the extent necessary, the environmental impacts of medicines to be taken into account more effectively in the procedure for placing medicinal products on the market. In the framework of that strategic approach, the Commission shall, where appropriate, by 14 September 2017 propose measures to be taken at Union and/or Member State level, as appropriate, to address the possible environmental impacts of pharmaceutical substances, particularly those referred to in Article 8b(1), with a view to reducing discharges, emissions and losses of such substances into the aquatic environment, taking into account public health needs and the cost-effectiveness of the measures proposed.”

The proposal to include WEPPPs as an emerging issue under SAICM can be seen to effectively compliment this EU initiative.

iv) Regional activity: In 2009, European Environment Agency hosted a workshop on this issue, and their report on “Pharmaceuticals in the Environment: Results of an EEA workshop” is freely available (EEA Technical report No 1/2010 ISSN 1725-2237).

v) Regional activity: The Baltic Sea Region Project on Sustainable Management of Pharmaceuticals.

vi) National activity: Sweden has been investigating and introducing various control measures for over a decade. For example, the ‘Stockholm project’ is a joint initiative of the

iii) Stockholm County Council (which provides public health care in the greater Stockholm region serving a population of about 2 million people), the state owned pharmacy chain Apoteket and the Swedish Pharmaceutical Industry Association. It has undertaken the environmental classification of pharmaceutical products

The Stockholm project is an example and tries to ensure that the least environmentally hazardous pharmaceutical is used. The fact that it has already gained that may be an example to promote international interest. The system also gained international attention, particularly in Germany, the

Netherlands, and Denmark shows that global coordination on this issue is warranted. Access to the system is open for anyone (in Swedish and English) on www.janusinfo.se.

~~The Stockholm County Council which provides public health care in the greater Stockholm region serving a population of about 2 million people, started a project 10 years ago aiming to provide an assessment of environmental negative impact for each pharmaceutical used in the national health care (16-18).~~

The rationale was that if health care staff, prescription providers and others, and patients were informed about the negative environmental impact of various medicines, they would be able to select the medicine with the least negative environmental impact among those available for their respective needs.

~~After a few years the national agencies and manufacturers of pharmaceuticals joined the project and extended the~~ The classification has now been extended to include not only environmental hazard but also environmental risk.

A complete classification of all medicines on the national market was reached in year 2010, and meanwhile the system had become accepted and used by most health care staff, not only in Stockholm but also in other parts of the country.

vii) National activity: In France a collection scheme for unwanted medicines operates. Cyclamed is a non profit programme which involves the collection of expired and non-expired unused drugs which patients bring back to the pharmacies for disposal and energy recovery. It involves the professionals involved in the drug supply chain (dispensing pharmacists, wholesale distributors and drug companies) who made a joint commitment to set up Cyclamed.

c) Gaps to be addressed:

-There are many gaps in the management of pharmaceuticals that need addressing, and a life-cycle approach is warranted, so that gaps are identified at all stages covering pharmaceutical production, manufacturing, use and disposal. There is a need to move from environmental risk assessment of a few drugs to a far more comprehensive environmental stewardship of pharmaceuticals across their entire life-cycle.

However, some specific issues are identified as needing attention. For example, more cost-effective (sensitive) environmental laboratory detection methods should be developed and a global surface water monitoring strategy applied to map the current global situation.

Furthermore, ~~there~~ there are currently no test methods to assess whether negative effects may occur in humans in later life ~~due to~~ after long term environmental diffuse exposure to multiple pharmaceutical residues in humans, both during ~~since~~ pregnancy ~~conception~~ and during ~~other~~ the vulnerable periods of development. Nor are there test methods currently in operation to assess the effects of such simultaneous exposure to multiple pharmaceutical residues in ~~an~~ aquatic microorganisms, or how they may affect many other ~~species~~ animals. Therefore, the precautionary principle must ~~be~~ guide ~~ing~~ policy responses to reduce exposures where possible.

- Consideration must be given to bioaccumulation in fish and other aquatic species, both to protect biodiversity and also to protect humans who utilise certain species as a food source. There is a need to evaluate the potential food used by humans, as well as to additive and synergetic effects between pharmaceuticals and other chemicals in the contaminated water. Consideration also needs to be given to designing pharmaceutical chemicals which do not have adverse effects in the environment with consideration of their environmental fate i.e. provide for degradation in the environment, exclude formation of active metabolites and degradants, etc.

d) Extent to which the issue is of a cross-cutting nature

The global problem posed by the pollution of surface water (as well as groundwater, drinking water, tap water, and to some extent farmland and soil), with chemicals of pharmaceuticals origin and their residues is well-known to scientists in the field. Policy makers are starting to promote action.

However, very little is being done made to tackle-meet the problem on a global basis.

A strong interest from SAICM on this issue wshould therefore be a highly significant positive contribution to all those who strive to make the future world less polluted with chemicals.-

Pharmaceuticals are synthetic chemicals belonging to a wide group of different chemical families and they were typically not and may also react differently in the environment as are not conceived or designed to enter in the environment. As there are thousands of different synthesized chemicals present at the same time in the environment, many different interactions may occur and the effects result of these multiple exposures in humans and wildlife to nature are not sufficiently studied or understood.

Documented evidence shows that some pharmaceuticals enter and persist in the environment, some are endocrine disruptors (synthetic hormones) and some are designed to kill bacteria and viruses (antibiotics). These may affect microorganism and wild-life in severe and unexpected ways. Little is known on the possible negative effects and impacts of WEPPPs in humans and the environment caused by by diffuse and widespreadsystematic exposure, for long periods of time, especially during the vulnerable periods of development.

Describe the proposed cooperative action

With the objective of improving understanding among policy makers and other stakeholders of the risks posed by Widespread or Environmentally Persistent Pharmaceuticals-Persistent Pollutants – WEPPPs- to human health and the environment and of promoting actions to reduce these risks, it is proposed that an international project on W-EPPPs be established to undertake the following. This SAICM initiative will build by building on existing activities, in particular those of the European Commission, UN Agencies (Project under UNDP, UNEP, UNFPA, UNOPS, and WHO) and including the Swedish experience.

- A synergy should be developedbuilt with the EDCs-(endocrine disruptors) strategy. Such a synergy would be useful, because as many actions are similar and target the same actors. International actions which are needed at a global level, in order to tackle this emerging policy issue, include for points to similar actors and to built international actions and regulations to tackle a new and emerging policy issue at global scale, for example (but are not limited to):

- i) ~~The provision of Provide~~ up-to-date information and scientific expert advice to policy decision makers and others responsible for chemicals risk management, for the purpose of identifying or recommending potential measures that can contribute to reductions in exposures and / or effects from WEPPP, *inter alia* through timely updates. ~~For example, there is a need for a global data-base on relevant research projects and results.~~
- ii) Requesting ~~IPCS~~ to produce a document on the “state of the science”, with the involvement of relevant experts ~~and including the knowledge already available from experience gained under the auspices of recent initiatives of based on the experience and already existing knowledge as well as based on the experiences of the the~~ European Commission, Sweden, Germany and others, as well as in the recently started UN Interagency green procurement project.
- iii) Providing ~~information on options for prevention of pollution, including during the tools for the manufacturing of pharmaceuticals, such as like~~ chemical substitution or modification of processes (Cleaner Production Management)
- iv) Raising ~~awareness and facilitating~~ information exchange and networking, *inter alia* through regional and sub-regional workshops / discussion forums and a dedicated website that links to relevant information sources.
- v) Providing ~~international support activities to build capacities in countries, in particular developing countries and countries with economies in transition, for assessing WEPPP issues in order to support decision making, including prioritization of actions, e.g. through guidance and training tools / activities involving relevant expertise.~~
- vi) Creating ~~an international network of scientists, risk managers, and others that are particularly concerned with WEPPP issues to facilitate information exchange, discussion forums and mutual support in research and advice on translation of research results into control actions and reduced exposures.~~

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