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SCOPING ACTIVITIES

CG4: the impact of pharmaceuticals and other novel chemicals on wastewater

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Preamble

1 At the 43rd meeting of GESAMP in 2016 held in UN Environment's Headquarters in Kenya, Dr. Birguy Lamizana expressed the Division's concern on the possible impact of pharmaceuticals on marine environment and human health. She further inferred that UN Environment-GPA will be interested to partner with GESAMP to further investigate the issue. This interest in collaboration was further emphasized in the speech of the Director, UN Environment --GPA at the 43rd session of GESAMP. Felicia was then directed by the Chair to liaise with Birguy and UN Environment's Technical Secretary of GESAMP, Ms Joana Akrofi to develop a scoping paper on the subject.

Introduction

2 Pharmaceuticals also referred to as medicine, medication or simply drug is used to diagnose, cure, treat or prevent disease. www.ncbi.nlm.nih.gov-; http//en.wikipedia.org-pharmaceutical. Early day discovery of the first medicinal drugs came from natural sources and existed in the form of herbs, plants, roots, vines and fungi. Until the mid-nineteenth century, nature's pharmaceuticals were all that were available to relieve man's pain and suffering. The modern pharmaceutical industry traces its origin to two sources: apothecaries that moved into wholesale production of drugs such as morphines, quinine and strychnine in the middle of the 19th century and dye and chemical companies that established research laboratories and discovered medical applications for the product. (www.google.ng-origin of pharmaceuticals). The fact remains that from early to modern days of human evolution and civilization, human beings have always depended on pharmaceuticals for wellbeing, be it natural or synthesized from chemicals. With the stage of depending mostly on laboratory synthesized formulae and population explosion, there came up the issue of management of waste arising from both demographic and industrial processing of pharmaceuticals just like with any other form of waste. Also the need for scientific investigation on possible impact and sustainable management arose. Perusal of literature has presented evidence for the presence of pharmaceuticals in the terrestrial, river and estuarine environment and their possible impact to both the environment and human. Again it is evident that such researches have not been extended to the marine environment in a more generous manner irrespective of the trend of global population and industrial activity shift to coastal and marine environment, the direction of flow of effluent from the upland to the wet environment and ultimately to the oceans and seas in many cases and report of presence of these pharmaceuticals in some aquatic organisms and speculation that the salinity of the marine environment may encourage concentration of these products in different combinations there by placing the ecosystem and food chain more at risk of bioaccumulations. Further, little or no report on studies on this in the global southern countries of Africa, small island states amongst others are available in the literature.

3 Hence,the purpose of this proposal is to present the above situation and request that GESAMP approves and supports that more studies on the subject is carried out in the regions in the global south; that a comparative analysis is done on the trend of accumulation globally and that the research seeks for ways of more stringent treatment of this waste to prevent the risk.

Sources and trend

4 At this point, it may become imperative to question the sources of pharmaceuticals in the marine environment. This have been identified to be from both point sources such as industrial effluent discharge point and municipal waste directed to the coastal and marine environment and other diffuse sources as run of from upland

municipal waste streams including specific streams like medical and hospital waste and animal husbandry and horticulture. The introduction from ships, aquaculture have also been implicated. Gaw,S. et al.2014.

5 It is evident that cursory attention is being given to research on the sources, exposure, fate and potential impact of pharmaceuticals in the marine environment compared to terrestrial and rivers and estuarine environment there by leading to knowledge gap which is also polarised within the global south and north. According to. Hughes, S.R.et. al.2012. Over the last 15 years increasing attention has been paid to understanding the presence and impacts of pharmaceuticals entering or detected in freshwater ecosystems By contrast, significantly less attention has been paid to understanding releases of pharmaceuticals from sewage and other routes into coastal environments and their potential marine impacts. This is not surprising though as in the past more attention usually paid to terrestrial and rivers and estuarine environment s (resulting in more interest at achieving sustainable waste management for example) compared to coast and marine environment where it not for recent global marine environment protection global declarations as the paragraph of the outcome document of Rio +20"the future we want", SDG 14 on conservation and sustainable use of oceans and seas and efforts by nations to domesticate and implement the relevant IMO conventions on prevention of marine pollution by ships.

6 According to a UN Environment report, 40% of the global population live within 100km at the coast.www.un.org.natinfo.pop_coastal_areas.this will naturally translate to more waste and of cause pharmaceuticals in the marine environment. This will add more stress to the marine environment promoting the challenges already posed by climate change, marine litter and other emerging marine environment partubers.

7 Just like most anthropogenic substances introduced to the earth surface, fate apply to pharmaceuticals in marine environment though it may differ from that of same in fresh water environment. the fate here may be in form of adsorpsion,dispersion,accumulation in aquatic environment including organisms, decay and combination with other chemicals in the medium at different levels and formation of secondary compounds that may have potentiated or reduced or synergistic effects(50).In all these, salinity, seasonality and PH have been found to be important factors.

8 Geographical study spread shows that more work have been published in Europe, Asia and North America. The assessment of the concentrations of pharmaceuticals in coastal environments has been limited. Forty-nine studies have reported concentrations for individual pharmaceuticals and metabolites detected in estuarine and coastal waters. Only studies published since 2000 are considered. Seventy per cent of these studies have been published since 2010. The geographical breakdown for the studies is Europe (20) Asia (21), North America (6), South America (1) and Oceania (1) Gaw,S.et.al To date, 113 pharmaceuticals and pharmaceutical metabolites have been detected in coastal waters at concentrations ranging from 0.01 to 6800 ng l^{-1} with the maximum concentrations for 69 of these compounds exceeding the European Medicines Agency threshold for predicted environmental concentrations for surface waters of 0.01 µg l^{-1} Committee for Medicinal Products for Human Use (CHMP). 2006). Some authors claim this could be underestimated based on extraction procedure. Rate of accumulation of pharmaceuticals in different strata of the marine environment shows that the sediment is a reservoir for the accumulation of pharmaceuticals in marine ecosystems and can act as a secondary pollution source from which pharmaceuticals can be released by changes in environmental conditions such as salinity and pH Liang,et.al.,2013. Sediments can be resuspended during tidal changes and during storm events exposing marine biota to sorbed pharmaceuticals.

Twenty-two studies reporting sediment concentrations of pharmaceuticals for estuarine and marine environments have been published since 2000. In total, 62 pharmaceuticals and transformation products have been detected in marine sediments at concentrations up to 2 615 000 ng g^{-1} wet weight Gaw,S.et.al.2014.

9 Five hundred and fifty-nine pharmaceuticals have been detected globally in wastewater treatment plant effluent, influent, and sludge. Diclofenac was the most commonly detected pharmaceutical. Nearly as common were carbemazepine (an antiepileptic), sulfamethoxazole (an antibiotic), and ibuprofen and naproxen (analgesics). Ethinyl estradiol has been detected in all United Nations regions, as has the lipid-lowering drug clofibric acid (aus der Beek, et al., 2016).

> ” Upgrading wastewater treatment plants is expensive. Recommendations about the most effective and affordable techniques for removal would be useful; however even the best current technologies cannot remove all emerging pollutants at all times. Focusing on one compound at a time is impractical when mixtures of compounds could be far more dangerous than any individual emerging pollutant. A lack of standardized monitoring strategies worldwide and case-by-case approach to studies of impacts from pharmaceuticals and personal care products mean that there is no universal understanding of which wastewater treatment methods are 'best', or which emerging pollutants are 'worst"'. “Detection of pharmaceuticals in the aquatic environment has largely been reported in the USA, European Union, Japan, and Australia, because these affluent countries account for the vast majority of pharmaceutical consumption. In the European Union, pharmaceutical use is increasing 3-4% by weight each year. Because of this, the majority of action taken to address pharmaceuticals and personal care products in the environment has also been in these countries”.

Fate

10 Gaw,S. et al. 2014 reported that according to their review researchers reported factors reported leading to increase concentrations of pharmaceuticals in seawater and sediment to include proximity to WWTP outfalls, higher effluent outflows, size of the urban area and population, the number of rivers discharging into coastal waters, the type of wastewater treatment, low mixing and dilution rates for WWTP effluents, the hydrodynamic flushing and residence time for confined water bodies, the type, scale and density of animal husbandry, and proximity to aquaculture. Typical municipal wastewater treatment plants are not designed with the goal of removing pharmaceuticals and personal care products effectively. In general, primary treatment by physiochemical methods such as coagulation and flocculation are unable to remove endocrine disrupting compounds and pharmaceuticals and personal care products from effluent streams (Bolong, et al., 2009; Gavrilescu, et al., 2015). Chlorination has also not been shown to be effective in removing the majority of pharmaceuticals. Activated sludge and other forms of biological treatment have shown varying rates of removal for pharmaceuticals, ranging from less than 20% to greater than 90% (World Health, 2014). More promising are advanced wastewater treatment processes, including ozonation, activated carbon and membrane nanofiltration and reverse osmosis, and advanced oxidation technologies. One promising option that is still being explored is the use of natural or constructed wetlands for treatment. Operational configurations of treatment plants and the type of compound they are aiming to remove influence the effectiveness of removal for each individual compound.

11 Many factors have been related to uptake and accumulation of Pharmaceutical in marine organisms by various authors such factors are: type of species and body-

tissue, gender and so on. These preferential uptakes have implications for ecotoxicological impacts and human exposure to pharmaceuticals via consumption of seafood, Sally eta.al

12 Field data for bioaccumulation of pharmaceuticals in marine organisms is limited. Field-derived bioaccumulation factors (BAFs) for pharmaceuticals in mussels from San Francisco Bay included dehydropnifedipine (290–764), carbamezepine (90–322), diphenhydramine (118–218), triamterene (57–71) and erythromycin-H_2O (11–54). The BAFs varied between sites by up to a factor of 7 Klosterhaus,S.L.2013 Bioconcentration factors (BCFs) ranged from 1300 to 1500 for uptake of 17α-ethinyloestradiol by mussels (*M. galloprovincialis*) harvested from Venice Lagoon, Italy Pojana,G2007 Field-derived BAFs for antibiotics ranged from 0 to 11 000 in shellfish collected from the coastal environment of Dalian in China. Based on the average BAFs, the authors concluded that sulfamethazine, sulfamethiazole, sulfamonomethoxine and doxycycline are potentially bioaccumulative and that sulfadiazine, sulfameter, sulfamethoxypyridazine and chloramphenicol are bioaccumulative in shellfish Na,G.2013.

Effects

13 Despite the limited number of studies, a wide variety of adverse effects have been reported for marine organisms with the effects being both test species and pharmaceutical specific. Examples of reported adverse effects for analgesics include reduced feeding rates Sole,M.2010 impacts on survival Guler,Y.2010, reduced mussel byssus strength Ericson,H.2010 and changes in immune response Sole,M.2010 and biochemical markers Gonzalez,M.2014. Studies have tended to focus on endpoints related to the therapeutic mode of action of the pharmaceutical. For example, reduced survival and developmental effects have been reported for anti-cancer drugs whereas studies on anti-depressant drugs have focused on neurobehavioural endpoints and spawning Bossus,M.C.2013 & Di Poi C 2013. The reported no observable effect concentrations (NOECs) and lowest observable effect concentrations (LOECs) ranged from several orders of magnitude above environmental concentrations to comparable to reported environmental concentrations.

14 Pharmaceuticals are present in marine ecosystems as mixtures complicating risk assessments. These complex mixtures may contain a wide variety of pharmaceuticals and other contaminants as well as a number of compounds from the same class (e.g. quinolone antibiotics) or with similar modes of action (e.g. non-steroidal anti-inflammatories) Backhaus,T.2004. Additive effects have been reported for mixtures of pharmaceuticals on marine organisms. Delorenzo,M.E. et.al.2008 investigated the toxicity of six pharmaceuticals and personal care products to the marine phytoplankton species *Dunaliella tertiolecta* both singly and in binary mixtures and reported additive toxicity for a mixture containing simvastatin and clofibric acid. As mixture toxicity effects including synergistic effects have also been reported for freshwater organisms and cell lines Shnell S.Bols 2009, NOECs and LOECs derived from single substance testing may not be sufficient for deriving environmental quality standards Blackhaus,J,2000.

15 Marine food webs could either be directly affected through bioaccumulation of pharmaceuticals in the food chain to toxic levels or indirectly through the loss of a key species particularly sensitive to pharmaceuticals. The impacts of pharmaceuticals on primary producers such as phytoplankton is a key concern for marine ecosystems due to the potential follow on effects on nutrient cycling and availability of food for other organisms Delorenzo,M.E.2008. Similarly, endocrine disrupting compounds which impact growth and reproduction in fish have the potential to affect predator and prey

species Kidd,K.A.2014. the degree to which they are metabolized in the bodies of target organisms, in addition to their degradation rates and partitioning of the compound in sediments and the water column (Corcoran, et al., 2010). Some pharmaceuticals are partially metabolized Concentrations of pharmaceuticals detected in the aquatic environment are impacted by in the body of the target, others pass through completely without having crossed the gut wall and are excreted without any change. Concentrations of pharmaceuticals in wastewater also vary seasonally based on temperature, solar radiation, and precipitation rate (Deblonde,et al., 2011).

16 Some pharmaceuticals and personal care products have very high acute aquatic toxicity, while others elicit more subtle effects that are much more difficult to detect (Daughton & Ternes, 1999). Furthermore, some emerging pollutants may degrade very quickly, but still have the same level of impact as traditional priority pollutants that are both toxic and persistent because they enter the environment continuously over long periods of time (World Health Organisation, 2014).

17 Some areas are at greater risk than others. Densely populated cities where waste flows directly into nearby surface waters are at great risk, as are developed nations where pharmaceutical use is significant and growing rapidly. Even in remote areas, however, there is a potential for exposure to emerging pollutants. The persistent nature of many compounds means that they can be transported over long distances, and a diverse array of harmful substances disproportionate to the amount consumed locally have been reported in ecosystems of small island developing states. This is true of pharmaceuticals and personal care products, microplastics, heavy metals, and more (UN Environment, 2014).

18 Climate change may also lead to changes in distribution and effects of emerging pollutants. In areas with more intense rainfall, the frequency and severity of polluted urban storm flows is expected to increase. Flushing to water bodies of organic pollutants will likely increase along with it. Hot, dry summers and droughts will decrease river flow, reducing contaminant dilution capacity and elevating concentrations in some areas (Boxall, 2011).

> “It is likely that newly developed technologies will have both positive and negative impacts in this field. Companies are working to produce more 'pure' forms of drugs with only the desired enantiomers. This will make drugs more effective at lower doses and less active pharmaceutical ingredients will be excreted into wastewater. It will also mean that lower detection limits will be needed, as lower doses will potentially grow more potent, with greater environmental impacts. Cutting edge nano-technologies promise exciting improvements in health and other fields, but their impacts on the environment are still not well understood”

19 At this stage, expansion of research and improvements in monitoring capacity are the most important actions needed to address emerging pollutants. Comprehensive policies and regulations can then be developed to prevent harm from the most dangerous emerging pollutants, particularly to vulnerable populations. The precautionary principle should be emphasised, but only in careful and evidence-based ways. We must do our best to respond to emerging pollutants, while avoiding undue or unnecessarily expensive burdens on communities that are only now beginning to realize the benefits of pharmaceuticals and personal care products for human health and well-being.

20 Widespread antibiotic resistance has been reported in fish, marine mammals and seabirds living in coastal waters including in the North Eastern United States

Rose,J.M.2009.Higher prevalence of antibiotic-resistant strains of bacteria has been reported for marine wildlife populations exposed to sewage Blackburn,Jk,20010 and there is evidence to suggest that the antibiotic-resistant bacteria present in seabirds are of human origin Bonnedah,L.J.2009. The presence of antibiotic resistance genes in marine ecosystems may be an indicator of ecological shifts occurring due to the presence of pharmaceuticals Delorenzo,M.E.2008.

21 Literature review has highlighted that human and veterinary pharmaceuticals and their transformation products (including metabolites) are present in coastal ecosystems.

22 Occurrence data for the marine environment are only available for a tiny fraction of the large number of pharmaceuticals currently in global use. There are extremely limited laboratory ecotoxicology data for the impacts of pharmaceuticals on marine organisms and a marked lack of field data. As for other ecosystems, a forward-looking prioritization approach is needed for the marine risk assessment of both generic and novel prescription pharmaceuticals. For example, such an approach has been successfully used for Tamiflu that involved defining both the predicted exposure concentration (PEC_{marine}) and predicted no-effect concentrations ($PNEC_{marine}$) to provide a prospective risk assessment Huchinson,T.H.et.al.2009.. For the $PNEC_{marine}$ to be reliable, it is important to consider the mode of action of the pharmaceutical, for instance, through the evaluation of Adverse Outcome Pathways in freshwater organisms and to extrapolate this to marine species Huchinson, T.H.2013. An Adverse Outcome Pathway is a conceptual framework for the link between exposure, the interaction of a contaminant at the molecular level within a cell and an adverse outcome or toxicological endpoint at the individual or community level.

23 As highlighted in reviews for pharmaceutical concentrations in freshwater Hughes,S.R.et.al2012 there is a marked absence of data for pharmaceuticals in marine environments in many regions (notably Africa, South America and small island nations in Oceania). These data gaps could easily be overcome by collaboration between well-resourced groups, with access to appropriate technology and validated analytical methods in developed countries, and local scientists in developing countries, at the same time providing valuable scientific and technical training.

24 There are insufficient data on the potential for impacts on higher trophic levels, either through trophic transfer of pharmaceuticals or indirect effects, such as limited availability of food, due to impacts on lower trophic levels including algae. For high priority pharmaceuticals, it would be desirable to extend the environmental assessment to include fish-eating birds and mammals as recently illustrated by Murray Smith,R.J.et.al.201.

Facts from perusal of literature

- Unwanted presences of anthropogenic pharmaceuticals have been established in the marine environment;
- Adverse effects of these pharmaceuticals have been recorded;
- The pharmaceuticals occur in combinations and can cause potentiated effects through bioaccumulation in the marine environment and aquatic ecosystem;
- Many factors can enhance the uptake of pharmaceuticals in aquatic the organisms such as gender, genetic configuration, body tissue mass and such can spell the rate and mode of bioaccumulation in the higher tropic level of the food we and food chain; and

- Paucity of data and research concerning concentration and impact on human and other organisms on the higher trophic level of the food chain/web and some regions of the world such as Small Island states, Africa amongst others.

Action requested of GESAMP

25 GESAMP is kindly invited to consider the facts so presented and approve a mapping study to investigate the presence of pharmaceuticals in the marine environment starting with those regions of the world were little or no research has been carried out in this subject area Such regions being suggested to be given primary concern are small island states, Africa and so on. Rapid assessment of the possible public health impact to human should be an integral part of the study, enhanced waste water treatment methods to prevent the entrance of pharmaceuticals into the marine environment, assay of pattern of accumulation in the marine environment and organisms amongst others.

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