THE ENVIRONMENTAL IMPACT OF PHARMACEUTICAL MANUFACTURING:

How does industry address its own waste?

INTRODUCTION

Pharmaceutical pollution is increasingly recognised as a threat to ecosystems and human health globally. Pharmaceuticals can enter the environment at all stages of their life cycle (production, use, and disposal), meaning they can ultimately end up in our drinking water as well as accumulate in vegetables and fish. Pharmaceutical residues have been detected in surface water, sewage effluents, groundwater, drinking water, manure, soil, and other environmental matrices globally.[1,2]

There is scientific evidence that even low concentrations of pharmaceuticals in the environment have harmful effects on animal and plant life, with effects include including: renal failure in vultures, impairment of reproduction in fish, or inhibition of growth of certain aquatic species.[3,4,5]

Critically, the discharge of pharmaceuticals into the environment has also been linked to the development of antimicrobial resistance (AMR), which is recognised by UN Environment as one of the biggest global public health concerns that we face.[6] Evidence shows that uncontrolled discharges from pharmaceutical manufacturing have devastating impacts on water systems as well as on people and animals coming into contact with the resulting resistant bacteria. This is especially true in India and China - where most Active Pharmaceutical Ingredients (APIs) for pharmaceutical products (including pharmaceuticals sold on the EU market) are manufactured.[7,8,9,10,11,12,13]

The production of APIs and finished dose antibiotics occurs in specific locations where point-source pollution results in incredibly high concentrations of APIs, encouraging the development of drug resistance. Recent studies from Hyderabad (India) reveal excessively high concentrations of pharmaceuticals exceeding maximum regulatory limits or safe exposure levels.[9] Exposure to environmental sources of antimicrobial drugs is placing vulnerable populations, such as pregnant women from low-income backgrounds at a higher risk for community acquired AMR.[14] Contamination of water sources with antimicrobial drugs (combined with the mass misuse of antibiotics and poor sanitation) has grave consequences in India, where an estimated 58,000 new-borns die annually from multidrug-resistant infections.[15]

Pharmaceutical manufacturing is a source of pharmaceutical pollution that is further exacerbated by poorly enforced environmental legislation in countries such as India and China.[16] Several studies show that polluting factories breeding resistant bacteria are exporting to EU markets and directly selling drugs to EU-based healthcare providers and buyers (e.g. German insurance companies).[17]

Furthermore, European patients are often not fully informed about pharmaceutical supply chains – packaging labels almost always refer to the final stage in the supply chain (where medications are packaged) as the manufacturing location, instead of providing information about where the APIs or the finished doses were actually manufactured. To increase transparency, patients and health professionals should have access to accurate information regarding the origin of drugs they use so that they can make an informed decision – knowing more about suppliers allows users to find out more about the environmental and social conditions under which the drugs were manufactured.[10]

Recognising the problems highlighted above, Health Care Without Harm (HCWH) Europe conducted a survey to identify best practice and gather information about how pharmaceutical companies manage manufacturing waste throughout their supply chains.

The survey was sent to the top 50 pharmaceutical companies worldwide (according to Pharmaceutical Executive's annual ranking)[18] and covered aspects such as waste and pollution management, environmental sustainability, governance, and transparency (page opposite). Participating companies were evaluated according to their responses, as well as any publicly available information. A traffic light system was used as an assessment tool with the following performance indicators:

Red – Low implementation/ no measures

Yellow – Average implementation of measures

Green – High implementation/ measures present

ASSESSMENT AREAS

A. ENVIRONMENTAL SUSTAINABILITY FRAMEWORK

- **What are the company's environmental policies?**
- **How are these policies implemented?**

B. SUPPLIER ASSESSMENT

- **Does the company require external suppliers to have environmental policies in place?**
- **How does the company verify that its suppliers' policies are being implemented?**

C. ENVIRONMENTAL GOVERNANCE

- **Is there a department in the company in charge of reducing its environmental footprint?**
- **What are the company's commitments in terms of reducing its environmental footprint?**

D. TRANSPARENCY

- **Does the company publicly report environmental monitoring data?**
- **Is the list of the company's external suppliers publicly available?**

RESULTS

Five companies participated in the survey.

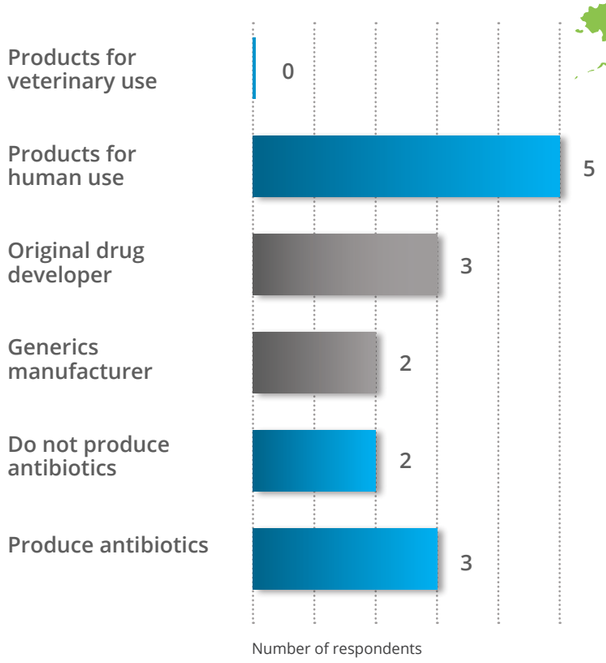
Three directly responded to the survey as drafted by HCWH Europe:

- AstraZeneca (AZ)
- GlaxoSmithKline (GSK)
- F. Hoffmann-La Roche (Roche)

Others compiled answers in their own format covering the areas of interest in the survey:

- Mylan
- Teva

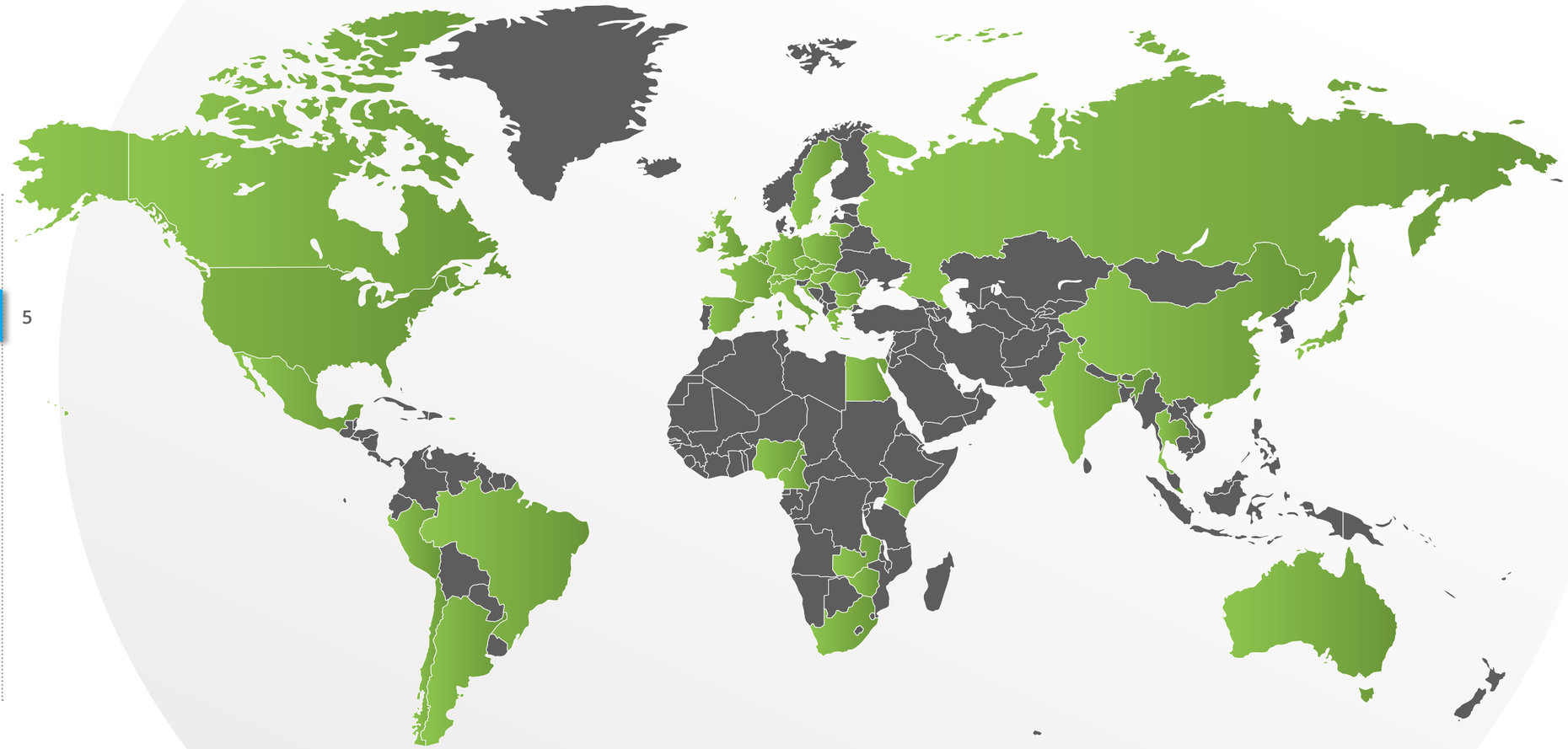
All the companies surveyed manufacture medicinal products for human use only, three develop original drugs, and three produce antibiotics.



All participating companies operate manufacturing sites in developed as well as emerging and developing countries (as defined by the IMF).[19] The UK, USA, Germany, Ireland, Canada, Australia, and Japan were the most frequently mentioned developed countries with manufacturing sites, whilst China, Brazil, India, Thailand, and Argentina were the most popular sites in emerging and developing countries.

LOCATION OF PARTICIPANTS' MANUFACTURING SITES

Argentina	China	Italy	Puerto Rico	Thailand
Australia	Czech Republic	Japan	Romania	UK
Austria	Egypt	Kenya	Russia	USA
Belgium	France	Lithuania	Singapore	Zambia
Brazil	Germany	Mexico	Slovakia	Zimbabwe
Bulgaria	Greece	The Netherlands	South Africa	
Cameroon	Hungary	Nigeria	Spain	
Canada	India	Peru	Sweden	
Chile	Ireland	Poland	Switzerland	



A. Environmental sustainability framework

All five companies indicated that they have implemented environmental policies or guidelines for managing and processing pharmaceutical manufacturing pollution. The comprehensiveness of these policies or guidelines, however, differs between the companies, as does their implementation.

Implementing widely recognised standards for manufacturing practice and environmental management is a common way for pharmaceutical companies to limit the negative environmental impacts of their manufacturing activities. One such example is the International Organization for Standardization's ISO 14001 certification, which requires an environmental management system to be in place and helps organisations improve their environmental performance.[20]

Among the study participants, two companies have all their sites ISO 14001 certified; the remaining three companies did not provided specific data for all of their manufacturing sites.

The ISO 14001 standard does not contain specific environmental performance criteria, but provides a framework for the holistic improvement of a company's environmental performance. Other measures are therefore usually taken (in place of or in addition to the ISO certification) to address the environmental impacts of manufacturing processes.

Examples of such measures listed by participating companies include:

- Written standards and procedures
- Environmental risk assessments
- Internal and quality audits
- Air emissions, water, and soil contamination controls
- Safe discharge programmes
- Waste management programmes
- Training of staff and suppliers

Waste and pollution management

Responsible environmental management requires controlling the amount of APIs entering the environment. In terms of waste and pollution management practices, all participants indicated having implemented hazardous substance management programmes, aimed at reducing hazardous waste.

To determine the potential environmental impact of APIs, all the participating companies monitor their facilities and evaluate the discharge of wastewater to surface waters.

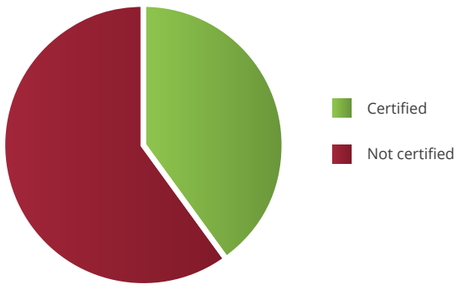
Three companies make use of Common Effluent Treatment Plants, which also collect and treat domestic sewage, and are not designed to specifically treat effluent from pharmaceutical manufacturing sites.[21] Notably, three companies indicated that they implement zero liquid discharge wastewater treatment systems at either their own sites or at their suppliers' sites. These systems have the potential to limit the discharge of liquid waste into the environment.[22]

Emissions to the air from manufacturing operations are also assessed at all five companies, but only two companies provided information about detailed measures taken to reduce air pollution at their facilities. These measures include containment and local exhaust ventilation, as well as the use of other air cleaning equipment (e.g. HEPA filtration, electrostatic precipitation, and/or carbon beds).

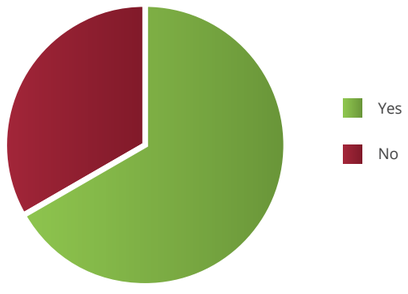
Finally, two of the three companies producing antibiotics confirmed that they take measures to limit their discharge, including discharge limits and specific wastewater treatment methods.

ENVIRONMENTAL SUSTAINABILITY

ISO 14001 certification of all manufacturing sites (5 respondent companies)



Companies producing antibiotics that take measures to limit their discharge (3 respondent companies)



B. Supplier assessment

The majority of responding pharmaceutical companies outsource their API production. Two companies provided responses showing that 10% and 40% of their APIs are produced in emerging and developing countries. Two further companies indicated that they use APIs produced in emerging countries, but no specific percentages were provided.

All five companies require external suppliers to have environmental policies for hazardous waste management, wastewater discharge, or air emissions as part of their Supplier Code of Conduct. In order to ensure environmentally responsible operations at supplier sites, all surveyed companies undertake inspections verifying compliance with environmental standards and examine appropriate authorisations on a regular basis. Three respondents specified how many audits/inspections take place at their or their suppliers' sites per year, and the other two companies indicated the number of audits that took place in 2017.

C. Environmental governance

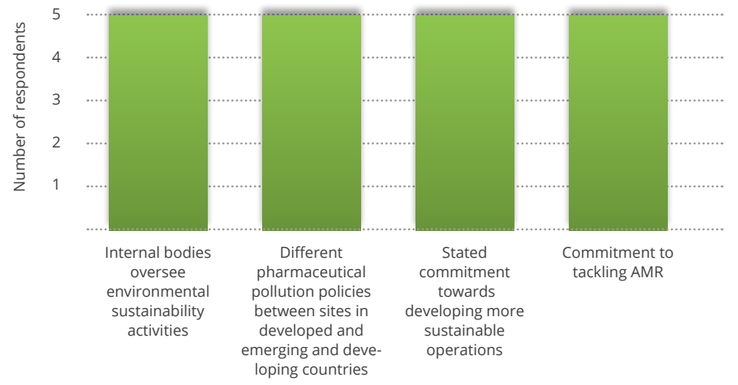
All companies reported having internal governance structures overseeing activities related to environmental sustainability at their manufacturing sites. These most commonly comprised safety, health, and environment departments, as well as sustainability and social responsibility divisions.

Examining governance practices in different parts of the world, participating companies indicated that their pharmaceutical pollution policies do not differ between manufacturing sites located in developed countries versus those in emerging and developing countries. Furthermore, aware of the environmental impacts of manufacturing activities, all surveyed companies have established specific goals and targets towards more sustainable operations. Some examples relevant to this study include: goals related to the quality of effluent discharges, safe discharge limits, the minimisation of waste, and unintended releases. Only two companies explicitly mentioned that they require external suppliers to follow their sustainability commitments.

Finally, all five companies recognise the threat posed by AMR; they fund relevant research (e.g. to develop new antibiotics and detection methods) and support measures to reduce pharmaceutical pollution. All surveyed companies are also signatories of the 2016 Davos Declaration, mobilising the pharmaceutical industry to accelerate efforts to reduce the development of antimicrobial resistance,[23] and are also part of the AMR Industry Alliance - a coalition initiated to provide sustainable solutions to curb AMR.[24]

ENVIRONMENTAL GOVERNANCE OF SUPPLIERS

ENVIRONMENTAL GOVERNANCE FOR OWN-OPERATED SITES



D. Transparency

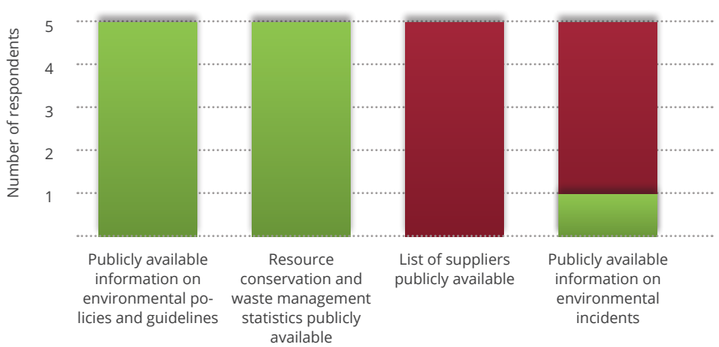
All surveyed companies make general information about their environmental policies and guidelines publicly available through their websites and relevant corporate documents (e.g. annual and sustainability reports).

All five companies also publish general statistics on their resource conservation (greenhouse gas emissions, and energy and water consumption), waste management (both hazardous and non-hazardous), as well as appropriate reduction or increase trends.

No company, however, provides site-specific information and none of the participating companies make their list of suppliers publicly available.

Only one company indicated that they publicly disclose information related to environmental incidents occurring at its manufacturing sites and the appropriate remediation.

TRANSPARENCY



CONCLUSIONS

Through its operations, the pharmaceutical industry has a substantial impact on the environment. Not only do pharmaceutical manufacturers have a critical role to play in addressing these issues, they also have a responsibility to foster environmental sustainability and reduce pharmaceutical pollution at source, throughout their supply chains.

With such a small sample size, and little publicly available information from pharmaceutical manufacturers, this study provides only a general introduction to the subject and is not intended to offer a representative sample or showcase best practices.

The limited response, however, demonstrates an industry-wide lack of transparency and reluctance to acknowledge the industry's responsibilities in terms of manufacturing to protect the environment from pharmaceutical pollution.

The results of this study show that although these companies frequently disclose general data related to environmental sustainability and governance, detailed information relating to specific measures taken to prevent pharmaceutical pollution at own-operated and supplier facilities remain unavailable to the public. There is a need for greater transparency from the industry in this regard. Increased transparency could encourage further responsible practices such as reporting environmental incidents, promoting extended environmental risk assessment, and/or driving technology investments.

Pharmaceutical pollution from drug manufacturing represents a global challenge that cannot be tackled without engaging the numerous stakeholders across supply chains. The EU has an important role to play in proposing ambitious legislation to deal with pharmaceutical pollution, including the global threat of AMR.

For example, the long-awaited Strategic Approach to Pharmaceuticals in the Environment[25] from the European Commission (which should have been published in September 2015 but has yet to be finalised) should call for the Environmental Risk Assessment (ERA) to be considered in the market authorisation process.[26]

Further measures, such as broadening the Good Manufacturing Practices (GMP) framework to cover environmental impacts of pharmaceutical manufacturing, or imposing stronger rules on Environmental Risk Assessments as part of market authorisations for pharmaceutical products, are imperative to curb the negative impacts of pharmaceutical manufacturing.

The problems associated with pharmaceutical pollution, however, seem to be neglected by key actors, including the industry and European legislators. For example, the Strategic Approach to Pharmaceuticals in the Environment is already three years overdue - it was originally scheduled for release in 2015. It is hoped that its publication will trigger more action from Member States and pharmaceutical manufacturers.

In the absence of action from regulators and manufacturers, it is imperative that civil society and the public continue to highlight this important issue and the need for appropriate action. To this end, HCWH Europe is committed to repeating this study in the future, in order to increase transparency and highlight gaps in both knowledge and legislation.

Safer Pharma
Safer medicine for a safer world

This study is part of HCWH Europe's Safer Pharma campaign, initiated to protect the environment from pharmaceutical pollution at all stages of their lifecycle. The campaign seeks to challenge the pharmaceutical industry to clean up its production and raise awareness within the healthcare sector about the impact of pharmaceuticals in the environment, encouraging rational prescription practices. It also aims to raise awareness amongst citizens about the impact of pharmaceuticals in the environment and the steps they can take to tackle the problem. For more information, please visit **www.saferpharma.org**.

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Health Care Without Harm (HCWH) Europe 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, economical, and political influence to create an ecologically sustainable, equitable, and healthy world.

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