PHARMACEUTICALS IN THE ENVIRONMENT

G4 Indicators : G4-EN26, G4-EN27
GRI Standards :
306-5 : Effluents and Waste

Sanofi focuses particular attention on the challenge of preventing pharmaceuticals from entering the aquatic environment. Pharmaceuticals may end up in the environment due to effluents from manufacturing facilities, medicines consumed by patients and then excreted, and the improper disposal of unused and expired medicines.

Our progress

Evaluating and minimizing emissions to the environment from manufacturing		
Implement an effluent assessment plan at manufacturing facilities	We proceeded with the implementation of a new risk-based program for managing emissions of active ingredients in wastewaters from pharmaceutical manufacturing plants.	On track
Define environmental thresholds for APIs	We continued to define environmental thresholds for APIs.	On track
Assessing the environmental impacts related to use of our products		
Conduct voluntary environmental hazard and risk assessments for APIs in drugs already on the market	We continued to conduct voluntary assessments on our legacy products.	On track
Encouraging the proper use and proper disposal of medicines		
Support targeted programs to take back unused and expired medicines	We have contributed to the implementation of take-back programs in many countries in Europe, Asia, North and South America.	On track
Develop programs to promote the proper use of medicines	We managed a platform for healthcare professionals and patients about the responsible use of antibiotics.	In progress
Contributing to advancing scientific research about Pharmaceuticals in the Environment (PiE)		
Develop and disseminate knowledge about pharmaceuticals in the environment	We have contributed to research programs with various stakeholders.	On track

I. BACKGROUND

Among the large number of organic compounds that may enter into the environmental media, pharmaceuticals have been a focus of attention for many years due to their biological activity and because of the evidence of their presence in the environment, generally at low concentrations.

Pharmaceutical substances may end up in the environment in various ways (Figure 1). The main source is considered to be the use of pharmaceuticals by patients. After pharmaceuticals are absorbed or administered, they are excreted by patients in the same form or they are transformed by the body into metabolites, which may be released into the environment through sewers and sewage treatment plants.

Other sources of discharge include emissions from manufacturing plants and the inappropriate disposal of unused or expired medicines.

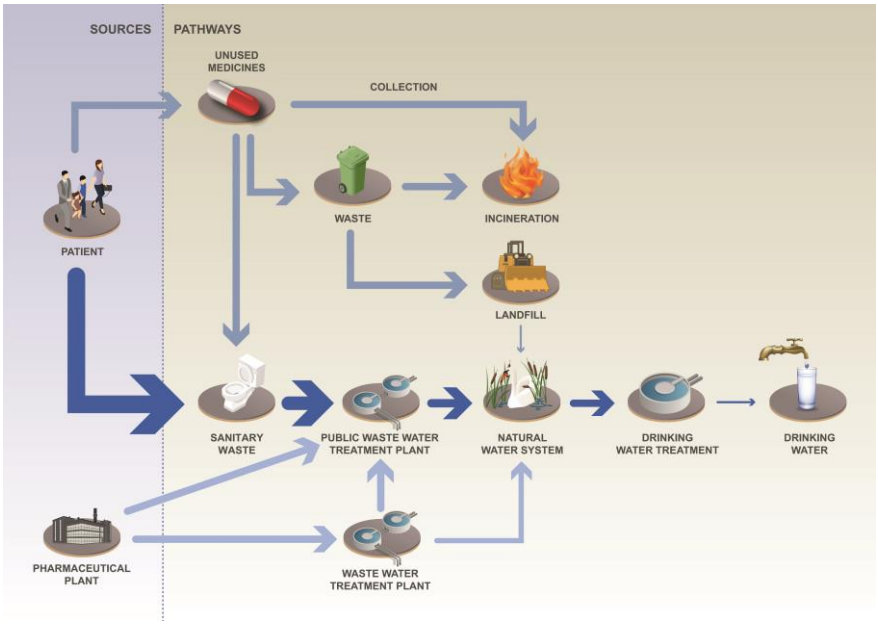

Figure 1. Main sources and pathways of pharmaceutical residues in the environment

With the improvement in analytical methods today it is possible to detect the presence of an increasing number of pharmaceuticals in the environment. Depending on the substances and where they are found, they may be present in very low concentrations in various environmental compartments, even in drinking water.

Considering the observed exposure levels, available data suggest a low risk to human health. A major study by the World Health Organization (WHO) concluded that at current levels of exposure in drinking water, adverse impacts on human health are very unlikely.[1] Concerns, have been raised, however, on the potential long-term environmental effects especially with certain classes of pharmaceutical products such as hormonal substances or antibiotics. Nevertheless, further research about the potential impact of combinations of pharmaceuticals, metabolites and other chemicals that may be present in low concentrations in the environment is necessary to improve our understanding of the potential long-term effects on the environment and human health.

[1] "Targeted investigations conducted in the UK, the US and Australia found that pharmaceuticals are largely present in drinking water at concentrations several orders of magnitude (more than 1,000-fold) below the lowest therapeutic dose and largely below the calculated acceptable daily intakes. The substantial margins of safety for individual compounds suggest that appreciable adverse impacts on human health are very unlikely at current levels of exposure in drinking water." Conclusions of WHO Pharmaceuticals in Drinking Water Report, 2012.

II. STRATEGIC APPROACH

Since 2010, Sanofi is committed to minimize the potential environmental impacts of our medicines. In view of growing public concerns about pharmaceuticals in the environment and the limited body of knowledge on the subject, Sanofi has strengthened its commitment through the Planet Mobilization Program. We have implemented a new strategic approach that covers the entire life cycle of our medicines, from production to their use by patients. It encompasses several initiatives or programs organized around 3 main pillars:

- Evaluating and minimizing the environmental impacts of manufacturing activities;
- Increasing knowledge of the environmental fate and potential impact of our products before and after their launch on the market;
- Encouraging and supporting the proper use and proper disposal of medicines by patients.

In addition we continue to contribute to advancing scientific research on this topic.

III. HIGHLIGHTS

1. Evaluating and minimizing emissions to the environment from manufacturing

At Sanofi, we are committed to continuously strive to make our processes safer to minimize environmental impacts. Industrial effluents (wastewater) are treated either at the sites' wastewater treatment facilities and/or at municipal treatment stations in accordance with operating permits. The choice and performance of technologies for effluent treatment are adapted to site-specific conditions. Effluents may undergo further treatment at the factory level or upon exit from the site, when required and appropriate. The company's manufacturing sites seek to adopt best practices.

Sanofi invests in technologies to improve wastewater treatment plants (WWTP) and minimize active pharmaceutical ingredients in effluents, but also seeks to limit effluent discharge upstream of the WWTP in order to reduce effluents at the source (i.e., upon exit from the factory).

Further to its commitment to minimize the impact on the environment of industrial sites, in particular the aquatic environment, the Group has implemented an environmental risk management strategy targeting pharmaceuticals in wastewaters. This strategy includes the following elements: assessment of pharmaceuticals in wastewaters and receiving water bodies ; setting of product specific environmental thresholds based on available data and standard methods ; characterization of environmental risks ; implementation of case by base risk mitigation measures from source reduction measures to end of pipe treatment solutions.

This strategy is progressively applied to all our manufacturing sites through business-specific programs. Its development and implementation started few years ago with a first program on eight Sanofi chemical manufacturing sites.[2] Further to this program we have proceeded with the implementation of a new program adapted to our pharmaceutical manufacturing sites. A first group of eight sites has implemented this new program in 2017. It will be rolled out gradually at the other sites in the coming years. These programs are supported by:

- a mass balance approach & tool to estimate emissions from production processes and characterize the related environmental risks;
- Specific analytical methods to quantify pharmaceuticals in wastewaters. These methods are developed and applied by our Sanofi Chemistry & Biotechnology Development Laboratory which is NF EN ISO/CEI 17025 accredited;
- Effect-based monitoring tools tested and applied in wastewaters and receiving water bodies;
- Substance-specific environmental thresholds used to characterize risks for aquatic ecosystems. Environmental fate & effects studies are conducted if necessary to address potential knowledge gaps.

[2] Chemical manufacturing sites: industrial sites where Sanofi manufactures the active ingredients in medicines marketed by the company or by third parties

2. Assessing the environmental impacts related to use of our products

An environmental risk assessment (ERA) is currently required for any new pharmaceutical product marketing authorization applications in the European Union, the United States and some other countries. While new drugs today are assessed for environmental risks, older drugs that are already on the market may have been studied less thoroughly, since regulatory requirements were not as stringent at the time they were launched.

Sanofi's commitment to prevent and mitigate environmental risks is central to our CSR and HSE policies. Guided by our ECOVAL committee of in-house experts, we have established a sound governance system for assessing the potential impacts of our products on the environment throughout their lifecycle:

- The environmental fate and effects properties of our new drugs are investigated during their development. An Environmental Risk Assessment is conducted as required by applicable regulations. This assessment considers environmental fate and effects information as well as all other relevant information generated during drug development and follows applicable ERA regulatory guidance documents.
- Sanofi has implemented a voluntary program to evaluate its legacy products, that were brought to market prior to enactment of the ERA requirement. This program aims at increasing knowledge about the environmental fate and effects or our marketed products, and at evaluating the related environmental risks. These assessments consider all available data and may lead to additional testing. To date, voluntary environmental assessments have been conducted for 50 compounds at Sanofi.

Today an increasing number of Sanofi products, both on the market and in development, are manufactured using biotechnology, such as therapeutic proteins. These products are considered to have no significant environmental effects and are potentially less harmful to the environment after use by patients.

3. Encouraging the proper use and proper disposal of medicines

Encouraging and supporting the proper use and proper disposal of medicines. Medicines are not ordinary consumer goods. At each link in the healthcare chain, professionals, public authorities, patients and the public must be informed about the proper use of medicines, which is essential to ensuring their safety and efficacy. While proper use of medicines benefits patient health primarily, it also includes an environmental dimension. Fostering the proper use of drugs can in fact contribute to limiting emissions of pharmaceutical substances into the environment due to inappropirate use. In the recent years, Sanofi has been engaged in initiatives to encourage the proper use of medicines, in particular by promoting information and education for healthcare professionals and patients.

- The responsible use of antibiotics: Each year in France, nearly 160,000 people contract infections caused by bacteria that are multi-drug resistant, meaning they are resistant to a range of antibiotics. Among these patients, 12,500 die[3] from a multidrug-resistant bacterial infection. From 30 to 50% of antibiotic prescriptions in France are inappropriate[4], which exacerbates the emergence of resistant bacteria. The massive consumption and, at times, unjustified use of antibiotics over decades has contributed to this situation. Moreover, antibiotics are the focus of growing concern due to their potential impact on human health and the environment, which needs to be studied and assessed. Sanofi is committed to supporting the responsible prescription and use of antibiotics, and supports healthcare professionals and patients through a dedicated website about the appropriate use of antibiotics: www.antibioresponsable.fr

Throwing unused drugs in the trash or flushing them into sewer systems when household waste is not treated in an environmentally responsible way constitutes a gateway into the environment. Sanofi is committed to encouraging the proper disposal of unused medicines. We support targeted programs that collect unused drugs from patients and inform consumers about their safe disposal.

- Sanofi has supported collection programs for unused medicines in many countries including Belgium, Brazil, Colombia, France, Greece, Japan, Mexico, Portugal, Spain, and North America.

[3] *Report of the Special Working Group for the Preservation of Antibiotics.* Jean Carlet, Pierre Le Coz, June 2015 (in French).
[4] *CMIT. Bon usage des anti-infectieux en ville et à l'hôpital.* In E. Pilly: Vivactis Plus Ed; 2014, pp. 597-602 (in French).

4. Advancing scientific research by collaborating with other stakeholders

As part of our commitment to advancing knowledge about pharmaceuticals in the environment, we have formed research collaborations with academia, and work closely with pharmaceutical trade and research associations. We also share this knowledge with other stakeholders as appropriate.

We continue to participate in collaborative programs and initiatives by pharmaceutical trade groups, academia, organizations and other stakeholders to expand scientific knowledge in this area and to better assess and limit emissions of pharmaceuticals in the environment. These include a research program organized by the Innovative Medicines Initiative (IMI) called the Intelligent Assessment of Pharmaceuticals in the Environment (iPiE), an industry roadmap to combat antimicrobial resistance, and projects led by the Health and Environmental Sciences Institute, including concepts, tools, and strategies for effluent testing and thresholds for toxicological concerns.

For more information, see in our Documents Center:

- *Waste Management Factsheet*
- *Circular Economy Factsheet*
- *Water Resource Management Factsheet*
- *Disposal of Unused Medicines and User Recommendations Factsheet*
- *Green Chemistry Factsheet*
- *Implementation of REACH Regulation Factsheet*
- *Soil and Groundwater Remediation Factsheet*