# PHARMACEUTICALS IN THE ENVIRONMENT

**GRI Standards :**

306-5 : Effluents and Waste

## EXECUTIVE SUMMARY

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. Through improved 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. Even though 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, 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.

Sanofi is committed to minimize the potential environmental impacts of our medicines through its Planet Mobilization Program, a strategic approach that covers the entire lifecycle of our medicines, from production to their use by patients. It involves all our stakeholders and encompasses several initiatives or programs developed below.

# TABLE OF CONTENTS

## 1. LIMITING PHARMACEUTICALS IN THE ENVIRONMENT: OUR PROGRESS

| Our objectives | Global performance 2019 |
|---|---|
| **Monitoring, management and reduction of emissions on** 100% of production sites by 2025 | 37% of production sites assessed; 75% of priority sites assessed |
| **Assess the environmental impact related to the use of our products** | 34% of Active Pharmaceutical Ingredients contained in our key marketed products assessed |

### Evaluating and minimizing emissions to the environment from manufacturing

- We continued to proceed with the implementation of our risk-based program for managing emissions of active ingredients in wastewaters from pharmaceutical manufacturing plants.
- We continued to define environmental thresholds for APIs.

### Assessing the environmental impacts related to use of our products

- We continued to voluntary expand our knowledge about the environmental fate and effects of our legacy products.

### Encouraging the proper use and proper disposal of medicines

- We have contributed to the implementation of take-back programs in many countries in Europe, Asia, North and South America.
- We managed a platform for healthcare professionals and patients about the responsible use of antibiotics.

### Contributing to advancing scientific research about Pharmaceuticals in the Environment (PiE)

- We have contributed to research programs with various stakeholders.

## 2. BACKGROUND

Among the large number of organic compounds that may enter into the environment, 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.

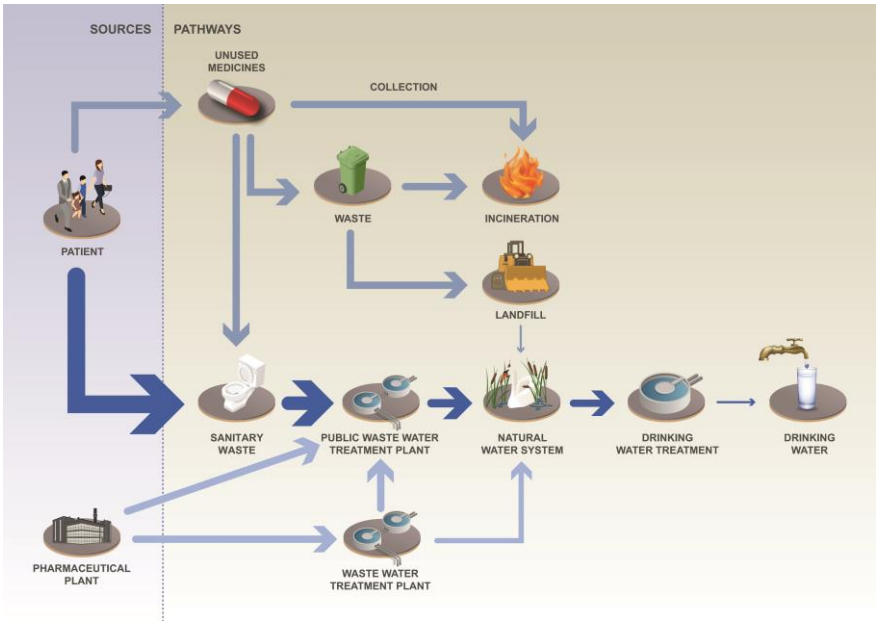


**Figure 1. Main sources and pathways of pharmaceutical residues in the environment**

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,

[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.

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.

## 2. 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.

## 3. HIGHLIGHTS

### 3.1. 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 external treatment stations in accordance with operating permits. The choice and performance of technologies for on-site 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 potential emissions of 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. Started in 2017, this new program is rolled out gradually at our different manufacturing sites. 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
- 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.

SANOFI is also engaged in the Industry roadmap for combating Antimicrobial Resistance. Together with the other AMR roadmap signatories we develop and implement measures to reduce environmental impact from production of antibiotics across our manufacturing and supply chain. This includes the definition and implementation of a common management framework and the application of shared environmental thresholds.

## 3.2. Assessing the environmental impacts related to use of our products

An environmental risk assessment (ERA) is 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

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

environmental risks. These assessments consider all available data and may lead to additional testing. Voluntary environmental assessments are preferably (but not only) conducted on our strategic marketed products. To date, such assessments have been conducted for 57 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.

## 3.3. Encouraging 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. Inappropriate use lead to unnecessary and avoidable emissions of pharmaceuticals in the environment. Fostering the proper use of drugs can in fact benefit the environment as well.

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.

Flushing unused drugs into sewer systems or throwing them in the trash or 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. Simple steps, taken by the consumer, can significantly reduce emissions contributing to environmental pollution.

We inform consumers about the safe disposal of unused medicines and we support programs that collect and properly dispose of unused drugs from patients.

- For many years, Sanofi has supported the development and implementation of local, regional or national programs to collect unused medicines in various countries such Belgium, Colombia, France, Greece, Japan, Mexico, Portugal, Spain, and North America. Programs may differ depending on countries.

[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).

### Our recommendations for users: How to properly dispose of your medicines?

Most importantly, do not dispose of unused medicines down the drain. That is, medicines should be neither flushed down the toilet nor poured down the drain.

Follow local disposal practices and use community pharmaceutical take-back programs where available. Disposal practices vary depending on the area.

In most European nations, unused medicines can be returned to the pharmacy for safe collection and disposal by incineration. In the United States and in many other countries, local take-back programs are probably in place through pharmacies or government or community waste treatment programs. Contact your pharmacy or local waste disposal agencies for more information if needed.

If no local take-back programs are available in your area, you can dispose of unused medicines in the household trash, taking measures to avoid accidental misuse or possible diversion for drug abuse. Render unused medicines undesirable and unrecognizable (e.g., mix them with household waste in unreadable packaging). Scratch out or remove any labeling identifying personal prescription information.

Do not forget a simple waste-reduction measure: whenever possible, try to obtain only the quantity of medicine you need. This will minimize the disposal of expired unused medicines later on.

## 3.4. 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 Document Center:*

- *Waste Management Factsheet*
- *Circular Economy and Ecodesign Factsheet*
- *Water Resource Management Factsheet*
- *Green Chemistry Factsheet*
- *Implementation of REACH Regulation Factsheet*
- *Soil and Groundwater Remediation Factsheet*
- *Antimicrobial Resistance (AMR) Factsheet*