Pharmaceuticals in the Environment

GRI Standards:

304-2: Significant impacts of activities, products, and services on biodiversity

306-5: Effluents and Waste

PLANET CARE

At Sanofi, the dedication to improving people's lives goes beyond innovations in healthcare. As a global organization, Sanofi also bears great responsibility in caring for the planet. Every day, Sanofi is minimizing the environmental impacts of its products and activities while strengthening its business resilience in the face of environmental changes.

Through the Planet Care program, Sanofi sets clear goals and is mobilizing employees, partners to join in taking action for the planet.

- ***Fight climate change**: build the road to net zero emissions by 2045 with an intermediate carbon neutrality trajectory for 2030, on a 1,5°C science based emission reduction trajectory*
- ***Limit our environmental footprint and aim for circular solutions** by optimizing the use/reuse of resources and reducing impact of emissions*
- ***Improve environmental profile of products by** delivering eco-innovative products and by fostering a sustainable use of medicines*
- ***Mobilize our people for environmental sustainability** by promoting an environmentally conscious culture in the workplace*
- ***Engage our suppliers in our environmental ambitions by** sourcing responsibly and leading by example*

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1. Our commitments to PIE

Among the large number of organic compounds that may enter the environment, pharmaceuticals have been a focus of attention for many years due to their biological activity and evidence of their presence in the environment, although generally at low concentrations.
Pharmaceutical substances may end up in the environment in various ways (Figure 1). The use of pharmaceuticals by patients is considered as the main source. 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.

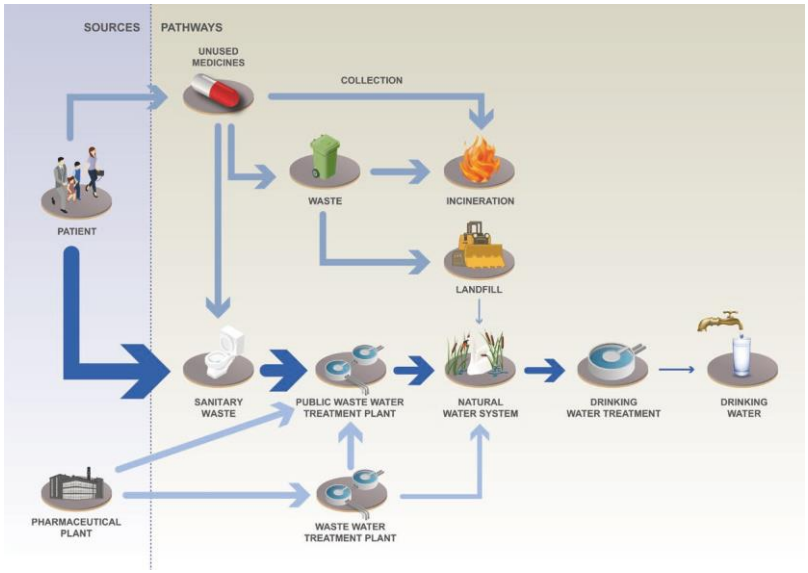


Figure 1. Main sources and pathways of pharmaceutical residues in the environment

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.

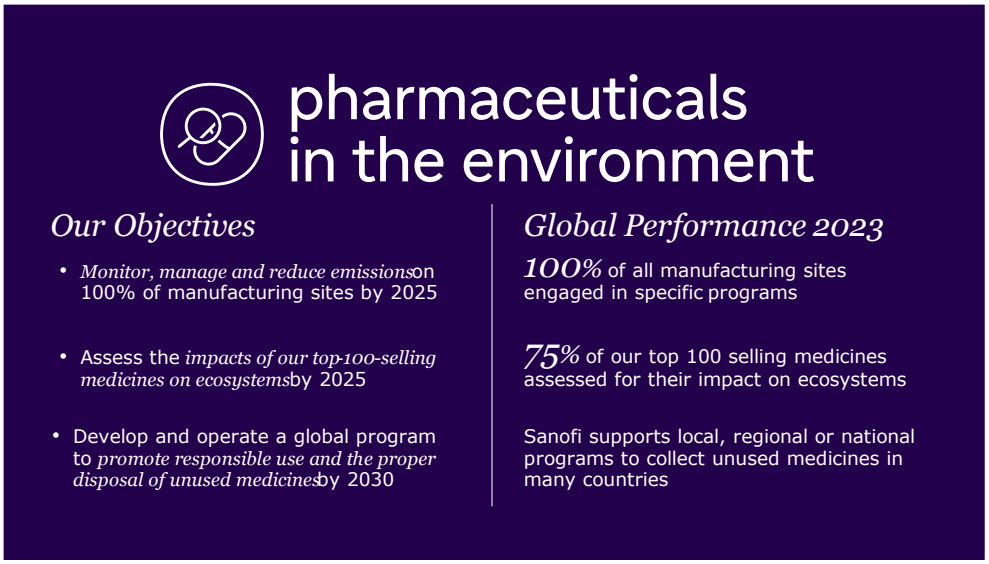
[1] "Targeted investigations conducted in the UK, the US and Australia found that pharmaceuticals are largely present in drinking water at concentrations several orders of magnitude (more than 1,000-fold) below the lowest therapeutic dose and largely below the calculated acceptable daily intakes. The 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.

Sanofi is committed to minimize the potential environmental impacts of its medicines throughout their lifecycle. This commitment is reflected in our environmental sustainability program, Planet Care, by specific goals:

Limit our environmental footprint:
- by 2025, all production sites will have implemented a plan to monitor, manage and reduce emissions of pharmaceutical residues to reduce their potential impacts on ecosystems.

Improve the environmental profile of products:
- by 2025, the environmental impact of our top-100-selling medicines[2] will be evaluated, as well as all our new medicines on the market, regardless of regulatory requirements; and
- by 2025, pilot projects will be implemented for promoting further the sustainable use and responsible disposal of unused medicines, devices and packaging materials.

2. Performance



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; and
- we continued to define science-based environmental thresholds for APIs.

Assessing the environmental impacts related to the use of our products:
- we continued to voluntary expand our knowledge on the environmental fate and effects of our new and legacy active pharmaceutical ingredients.

3. Actions

Our strategic approach covers the entire life cycle of our medicines, from production to their use by patients. It encompasses several initiatives or programs organized around three 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 to market; and
- promoting the responsible use and the proper disposal of unused medicines.

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

[2] Based on turnover and number of units sold.

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 plants 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 for reducing 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, Sanofi has implemented an environmental risk management program targeting pharmaceuticals in wastewaters. This program includes the following elements: quantification of pharmaceuticals in wastewaters and receiving water bodies; setting of substance-specific safe discharge targets based on available data and standard methods; characterization of risks for aquatic ecosystems and other environmental compartments where relevant; implementation of case-by-base risk mitigation measures from source reduction measures to end-of-pipe treatment solutions.

This program is progressively implemented in all our manufacturing sites based on prioritization framework. It is supported by:

- a mass balance approach & tool to estimate emissions from production processes and characterize the related environmental risks;
- specific analytical methods allowing to quantify pharmaceuticals in wastewaters or receiving water bodies;
- substance-specific safe discharge targets used to characterize risks for aquatic ecosystems. Environmental fate & effects studies are conducted if necessary to address potential knowledge gaps; and
- effect-based monitoring tools tested and applied in wastewaters and receiving water bodies.

Sanofi is also engaged in the Industry Roadmap for Progress on 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 antibiotic manufacturing framework and an approach to establishing discharge targets for antibiotic manufacturing. These targets are intended to be protective of adverse effects to aquatic species and of antibioresistance promotion. We implement this framework in our antibiotic manufacturing sites. We also apply the AMR Industry Alliance[3] safe discharge targets in our risk-based program targeting pharmaceuticals in wastewaters.

For more information, see in our Document Center:

- *Antimicrobial Resistance (AMR)*
- *Water Stewardship*

[3] More information about the AMR Industry Alliance antibiotic manufacturing framework and discharge targets available on the AMR Industry Alliance website: https://www.amrindustryalliance.org/shared-goals/common-antibiotic- manufacturing-framework/

3.2. ASSESSING THE ENVIRONMENTAL IMPACTS RELATED TO THE USE OF OUR PRODUCTS

An Environmental Risk Assessment (ERA) is required for all pharmaceutical product marketing authorization applications in the European Union, the United States and some other countries. While new drugs today are fully 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, and new studies are often not needed unless marketed quantities will increase significantly.

Sanofi's commitment to prevent and mitigate environmental risks is central to our CSR and HSE policies. 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. These investigations cover both small molecules and biologics with dedicated testing requirements. 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; and
- 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 of our marketed products, and at evaluating the related 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 strengthen the management of potential environmental risks related to the use of our medicines by patients, Sanofi has voluntary launched in 2023 an EcoPharmacoVigilance pilot on 5 APIs. The aim of this pilot was to develop and test a process to identify and monitor potential environmental risks related to the use of medicines by patients in various countries around the world. Following this pilot phase, we plan to extend this process and to cover more products and countries in the coming years.

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 DISPOSALOF 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 leads 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, by promoting information and education for healthcare professionals and patients.

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 including Belgium, Colombia, France, Greece, Japan, Mexico, Portugal, Spain, Australia or North America. Programs may differ depending on countries.

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 (e.g. France) or by household waste for incineration (e.g. Germany). In the United States and in many other countries, local take-back programs are often in place through pharmacies, government or community waste treatment programs. Contact https://myoldmeds.com (US), https://healthsteward.ca (Canada), 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, regulators and we 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 research programs organized by the Innovative Medicines Initiative (IMI) on prioritization and risk evaluation of medicines in the environment (PREMIER), an industry roadmap to combat antimicrobial resistance (AMR Industry Alliance), and projects led by the Health and Environmental Sciences Institute (HESI), including concepts, tools, and strategies for effluent testing and thresholds for toxicological concerns.