

ANTIMICROBIAL RESISTANCE (AMR)

GRI Standards :

NA

EXECUTIVE SUMMARY

Antimicrobials are essential in the treatment of life-threatening infections and vital to the success of common surgical procedures. However, they are becoming less effective as a result of antimicrobial resistance (AMR), the ability of microbes to resist medicines designed to stop them. AMR has been identified by the World Health Organization as one of the top 10 health threats that the world is currently facing. By progressively limiting treatment options, it poses a risk to modern medicine, patient outcomes, and economic growth and can place a significant strain on healthcare resources.

The rise of AMR is driving an urgent need for collaborative action of pharmaceutical companies and other private sector actors, national governments, international bodies, healthcare professionals and patients. As a signatory to the Industry Roadmap for Progress on Combating AMR and as a member of the AMR Industry Alliance, Sanofi is committed to the fight against AMR. By developing new antimicrobial medicines and vaccines, managing our wastewater, enabling and expanding appropriate access to antimicrobials and vaccines, and promoting responsible use and disposal, Sanofi contributes to address the issue of AMR in a variety of ways.

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1. BACKGROUND

1.1. AMR: A Global Health Threat

Antimicrobial medicines,¹ including antibiotics, are essential in the management of life-threatening infections and vital to the success of most common surgical procedures and many treatments, such as chemotherapy, HIV and transplant medicines. However, they are becoming less effective as a result of antimicrobial resistance (AMR), the ability of microbes to resist medicines designed to stop them.² For that reason, AMR has been identified by the World Health Organization (WHO) as one of the top 10 health threats that the world is currently facing.³ This threat is intensified by the fight against the viral COVID-19 pandemic, as early studies suggest that severely ill COVID-19 patients are massively given antibiotics to prevent or treat secondary bacterial infections.^{4,5}

By progressively limiting treatment options, AMR poses a threat to modern medicine and global health security. It is estimated that more than 700,000 people already die from AMR every year,⁶ which is equivalent to the current population of Athens, the capital of Greece. If not addressed, the impact of AMR will become increasingly severe. For instance, routine surgeries such as hip replacements, diabetes complications, as well as injuries and cuts become harder to manage, and even life-threatening conditions, due to common infections that develop resistance to current antimicrobials. According to the UK AMR Review,⁷ without global action, an additional 10 million people will die every year from drug-resistant infections by 2050 - more than current deaths from cancer.⁸ As a consequence, AMR also constitutes a threat to economic growth: if not addressed by 2050, AMR could cause a global economic damage equivalent to the 2008 financial crisis,⁹ with eight trillion USD in global productivity losses per year by 2050, and a cumulative 100 trillion USD loss over the next 35 years.¹⁰

1.2. The Global Action Plan on AMR

AMR is driven by multiple interconnected factors across different sectors in which antimicrobials are being used. These sectors include human health, animal health, food, agriculture and the environment.¹¹ For that reason, and as a follow-up to the resolution adopted by the World Health Assembly in May 2014,¹² the World Health Organization (WHO), in collaboration with the Food and Agriculture Organization (FAO) and the World Organization for Animal Health (OIE), released in May 2015 a Global Action Plan on AMR¹³. Looking at the issue of AMR through a one-health approach – i.e. considering human health, animal health, agriculture and environmental aspects –, it defines 5 strategic priorities to tackle AMR: 1) awareness, 2) surveillance and research, 3) reducing incidence of infections, 4) optimizing antimicrobial use and 5) increasing investments in new medicines, diagnostic tools, vaccines and other interventions.

¹ An antimicrobial medicine is an agent that kills a germ or stop its growth. Antimicrobial medicines can be grouped according to the germ they act primarily against, eg. antibiotics are used against bacteria and antifungals are used against fungi.

² WHO defines AMR the ability of a microorganism (such as bacteria, fungi, viruses, and parasites) to stop an antimicrobial (such as antibiotics, antifungals, antivirals, antimalarials, and anthelmintics) from working against it. As a result, standard treatments become ineffective, infections persist and may spread to others." <https://www.who.int/health-topics/antimicrobial-resistance>

³ <https://www.who.int/emergencies/ten-threats-to-global-health-in-2019>

⁴ <https://www.pewtrusts.org/en/research-and-analysis/articles/2020/04/27/superbugs-in-the-news-how-covid-19-is-increasing-antibiotic-use>

⁵ <https://academic.oup.com/cid/advance-article/doi/10.1093/cid/ciaa530/5828058>

⁶ https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

⁷ <https://amr-review.org/>

⁸ https://amr-review.org/sites/default/files/160518_Final%20paper_with%20cover.pdf

⁹ <http://documents.worldbank.org/curated/en/323311493396993758/pdf/114679-REVISED-v2-Drug-Resistant-Infections-Final-Report.pdf>

¹⁰ <http://journals.plos.org/plosmedicine/article?id=10.1371/journal.pmed.1002184>

¹¹ http://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1

¹² http://apps.who.int/gb/ebwha/pdf_files/WHA67/A67_R25-en.pdf?ua=1

¹³ http://apps.who.int/iris/bitstream/handle/10665/193736/9789241509763_eng.pdf?sequence=1

After the release of the WHO Global Action Plan on AMR in 2015, the need to take action in order to limit the spread of antimicrobial resistance, was supported by other stakeholders in subsequent declarations and reports.¹⁴ Since then, the issue of AMR has been continuously gaining attention at the global level, as shown by its prominent position on the agendas of the United Nations,¹⁵ WHO,¹⁶ G7,¹⁷ and G20¹⁸ leaders' meetings in recent years. Encouraged by the WHO Global Action on AMR adopted in May 2015 and subsequent declarations and reports, 131 countries now have an AMR National Action Plan and 51 are in the process of developing one.¹⁹

2. SANOFI'S POSITION

As a leading pharmaceutical company, Sanofi participates in the fight against antimicrobial resistance. Sanofi encourages the collaboration with third parties like regulators, marketers, industry peers, international bodies or national governments, to address all the aspects of this issue. As a signatory of the Industry Roadmap for Progress on Combating AMR and as a member of the AMR Industry Alliance, we support the WHO's Global Action Plan on AMR, as well as the new AMR & Vaccines Roadmap under development. Sanofi's approach to combating AMR resistance is articulated around the following priorities:

- **Engaging in research and development to limit or prevent AMR:** Sanofi continues to invest in the development of new antibacterial medicines, as well as in AMR-relevant vaccines.
- **Preventing pharmaceuticals from entering the environment:** Sanofi is committed to minimize the potential environmental impacts, including the emergence of AMR, of our medicines through its Planet Mobilization Program,²⁰ a strategic approach that covers the entire lifecycle of our medicines.
- **Enabling appropriate patient access to antimicrobials and vaccines:** Sanofi supports efforts to broaden vaccine coverage to prevent infections and help optimize the use of antimicrobials. Sanofi also strives to increase access to our antimicrobial medicines for the patients who need them.
- **Preserving medical value of current antimicrobials through appropriate use and disposal:** Sanofi engages in initiatives to encourage the appropriate use and disposal of medicines, in particular by promoting responsible behaviour and sharing best practices among healthcare professionals and patients.

¹⁴ The private sector committed to "support measures for the prevention of infection along with conservation and appropriate use of all antibiotics" in [the Industry Declaration on AMR](#) adopted at the World Economic Forum in Davos in January 2016. The economist Jim O'Neill in his [landmark report](#) to the UK Prime Minister published in May 2016 and sponsored by the Wellcome Trust promoted the reduction of "the demand for antimicrobials so the current stock of drugs lasts longer". The priorities included in the WHO Global Action Plan on AMR relating to prevention and antimicrobials use were elevated at the United Nations level when Heads of States adopted a political declaration on AMR during the UN General Assembly of September 2016 in which commitments have been made to work at national, regional and global levels to adopt measures for strengthening appropriate antibiotic use in humans and animals.

¹⁵ https://www.who.int/docs/default-source/documents/no-time-to-wait-securing-the-future-from-drug-resistant-infections-en.pdf?sfvrsn=5b424d7_6

¹⁶ http://apps.who.int/gb/ebwha/pdf_files/WHA72/A72_R5-en.pdf?ua=1

¹⁷ <http://www.g7.utoronto.ca/healthmins/2019-health.html>

¹⁸ <http://www.g20.utoronto.ca/2019/2019-g20-health.html>

¹⁹ Marc Sprenger, World Health Organization, Overview of Global Action Plan – AMR & Countries National Action Plan. Presented in November 2019 at the "AMR Course – A One Health Challenge" co-organized by the Mériem Foundation and the University Paris-Diderot.

²⁰ <https://www.sanofi.com/en/our-responsibility/planet-mobilization>

3. ACTIONS

3.1. Engaging in research and development to limit or prevent AMR

Sanofi maintains a pipeline of several antibacterial medicines to treat infectious diseases such as Tuberculosis. For example, we are collaborating with the US Center for Disease Control (CDC) for a Phase III clinical trial to create a shorter and simpler rifapentine dosing regimen for the treatment of latent and active tuberculosis (TB) compared to existing six-month treatments. Shorter and simpler regimens increase patient adherence to treatment, and thereby reduce the threat of the development of AMR against the medicine.

Sanofi also retains option rights to continue investing in the development and commercialization of the 10 infectious disease R&D assets that were transferred to Evotec in March 2018.²¹

Sanofi continues to invest in the research and development of new AMR-relevant immunization solutions, such as the RSV monoclonal antibody and pneumococcal conjugate vaccine, or improve existing ones, such as our influenza and DTP-HepB-Polio-Hib²² vaccines.

3.2. Reducing the impact of pharmaceuticals in the environment

The presence of antimicrobial resistant bacteria and related resistant genes (ARGs) in the environment is now well recognized for its role in the spread of antimicrobial resistance (Singer et al., 2016).²³ Sanofi continuously strives to make its manufacturing processes safer, to minimize pharmaceuticals entering the aquatic environment. 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 our commitment to minimize the impact on the environment of industrial sites, in particular the aquatic environment, Sanofi 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-case 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 a few years ago with a first program on eight Sanofi chemical manufacturing sites.²⁴ Further to this program, we have proceeded with a second program

²¹ Sanofi decided in March 2018 to transfer its infectious disease research unit to Evotec, excluding the vaccine R&D unit and related projects. Link to the press release: <https://www.sanofi.com/en/media-room/press-releases/2018/2018-03-08-07-46-35>.

²² Diphtheria-Tetanus-Pertussis-Hepatitis B-Polio-Haemophilus influenzae type B.

²³ Singer, A. C.; Shaw, H.; Rhodes, V.; Hart, A. (2016) Review of antimicrobial resistance in the environment and its relevance to environmental regulators. *Front. Microbiol.*, 7, 1728.

²⁴ Chemical manufacturing sites: industrial sites where Sanofi manufactures the active ingredients in medicines marketed by the company or by third parties

adapted to our pharmaceutical manufacturing sites and rolled out gradually since 2017. Our 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 Progress on Combating Antimicrobial Resistance.²⁵ 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.

3.2.1. Working with suppliers

We acknowledge that our environmental responsibility is extended all along the manufacturing lifecycle of our products, and with this purpose Sanofi is engaged in an increasing number of actions with our suppliers and subcontractors. Sanofi is actively working on different initiatives to reduce the release of pharmaceuticals in the environment, including:

- Onboarding of suppliers and contract manufacturing organizations (CMOs) on good practices in water management:
 - > As an active member of the Pharmaceutical Supply Chain Initiative (PSCI), Sanofi has invited our key API suppliers to attend seminars in China and in India in 2019, to inform on water-related issues including the release of pharmaceuticals in the environment.
 - > In late 2019, we initiated a new program to raise awareness on antimicrobial resistance, to clarify and strengthen our requirements, and to share related good practices on risk management with our partners.
- Health, Safety and Environment Audits (internal & external) of suppliers include questions on water and wastewater management. The risks identified are communicated to business for decision making.

For further information, please see our [Responsible Procurement Factsheet](#).

3.3. Enabling appropriate patient access to antimicrobials and vaccines

According to leading health authorities, improving appropriate access to medicines and vaccines is essential for limiting the spread of antimicrobial resistance. This is because taking actions on access can help prevent infections, optimize the use of antimicrobials and limit the use of substandard and falsified medicines.

²⁵ <https://www.ifpma.org/wp-content/uploads/2018/06/Roadmap-for-Progress-on-AMR-FINAL.pdf>

As a growing evidence base shows that vaccines' value towards AMR can be maximized by increasing uptake rates,^{26,27} health authorities in several countries and regions encourage the use of currently available vaccines more widely – including improved ones – to tackle AMR.^{28,29} For that reason, Sanofi continues to improve access to the AMR-relevant vaccines of its portfolio, such as Influenza, Meningococcal, Typhoid or DTP-Hib-Polio-HepB vaccines. We also maintain an extensive portfolio of mature products used to treat antibacterial or antifungal infections, of which half are on the WHO Essential Medicines List.

To ensure access to our products, Sanofi takes a multi-prong approach:

- **Innovation and Patent Management** – As a research-based pharmaceutical company, Sanofi is committed to the discovery, development, and provision of health solutions and will continue to work with key partners to leverage our expertise to ensure greater access for patients globally. Sanofi is committed to socially responsible patent management in developing countries.
- **Availability** – Without strengthened regulatory bodies, secure supply chains and delivery services, access to quality products can be compromised. Sanofi is committed to sharing expertise with local stakeholders to ensure effective registration, production and supply of medicines and vaccines for patients globally, as well as fighting against falsified medicines.
- **Affordability** – Even when patients have access to adequate care, cost can be a key impediment to receiving health products. Sanofi is committed to developing innovative business models and to working with governments and other partners to address issues of affordability.
- **Quality Care and Patient Support** – Sanofi believes that enhanced patient pathways, alongside better and wider use of existing technologies and well-trained human resources, are critical to ensure the efficiency and sustainability of health systems. Sanofi is engaged to contribute to capacity building and patients' empowerment for better care management.

For further information, please see our [Access to Healthcare Factsheet](#).

3.4. Preserving medical value of current antimicrobials through appropriate use and disposal

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 contributes to limiting the spread of antimicrobial resistance. Inappropriate use leads to unnecessary and avoidable emissions of pharmaceuticals in the environment. Fostering the proper use and disposal of drugs is essential in preserving their medical value.

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. For example, between 30 to 50 percent of antibiotic prescriptions in France are inappropriate,³⁰ which exacerbates the emergence of resistant bacteria. Each year in France, close to 160,000 people

²⁶ Kwong JC, Maaten S, Upshur RE, Patrick DM, Marra F. The effect of universal influenza immunization on antibiotic prescriptions: an ecological study. *Clin Infect Dis*. 2009;49(5):750-756. doi:10.1086/605087

²⁷ Knight GM, Clarkson M, de Silva TI. Potential impact of influenza vaccine roll-out on antibiotic use in Africa. *J Antimicrob Chemother*. 2018;73(8):2197-2200. doi:10.1093/jac/dky172

²⁸ Weiner LM, Webb AK, Limbago B, et al. Antimicrobial-Resistant Pathogens Associated With Healthcare-Associated Infections: Summary of Data Reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2011-2014. *Infect Control Hosp Epidemiol*. 2016;37(11):1288-1301. doi:10.1017/ice.2016.174

²⁹ <https://www.who.int/antimicrobial-resistance/national-action-plans/library/en/>. See also:

https://ec.europa.eu/health/amr/sites/health/files/antimicrobial_resistance/docs/amr_2017_action-plan.pdf; <https://www.mhlw.go.jp/file/06-Seisakujouhou-10900000-Kenkoukyoku/0000138942.pdf>; <https://www.cdc.gov/drugresistance/pdf/threats-report/2019-ar-threats-report-508.pdf>

³⁰ CMIT. Bon usage des anti-infectieux en ville et à l'hôpital. In E. Pilly: Vivactis Plus Ed; 2014, pp. 597-602 (in French)

contract, and 12,500 die of, infections caused by bacteria that are multi-drug resistant.³¹ The massive consumption and, at times, unjustified use of antibiotics over decades has contributed to this situation. 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, 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 the danger of antibiotics entering the aquatic environment. 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 as Belgium, Colombia, France, Greece, Japan, Mexico, Portugal, Spain, and North America. Programs may differ depending on countries.

As part of our stewardship efforts, Sanofi is also committed in engaging in surveillance initiatives. We are active in a long-term AMR surveillance program focusing on *S. pneumoniae* in France, covering 10 antibacterial products and including 400 health facilities. Our partner, the National Reference Centre for Pneumococci (NRCP) with the French Regional Pneumococcal Observatories, shares the results of the program through peer-reviewed journal articles.

4. ADDITIONAL INFORMATION

For more information, see other Factsheets in our [Document Center](#):

- Pharmaceuticals in the Environment
- Water Resource Management
- Responsible Procurement
- Continuity of Activities and Supplies
- Access to Healthcare & Access to Vaccines

See also:

- AMR Industry Alliance Website: <https://www.amrindustryalliance.org/>
- Industry Roadmap for Progress on Combating AMR: <https://www.ifpma.org/wp-content/uploads/2018/06/Roadmap-for-Progress-on-AMR-FINAL.pdf>
- Antimicrobial Resistance Benchmark 2020 Report: https://accesstomedicinefoundation.org/media/uploads/downloads/5e43ebfba86d8_Antimicrobial_Resistance_Benchmark_2020.pdf

³¹ Report of the Special Working Group for the Preservation of Antibiotics. Jean Carlet, Pierre Le Coz, June 2015 (in French).