

BIODIVERSITY AND BIOPIRACY

G4 Indicators: G4-DMA, G4-EN11, G4-EN12, G4-EN13, G4-EN14, G4-EN26

I. BACKGROUND

“Biodiversity,” or biological diversity, refers to the variety of life on earth. It encompasses three categories: genetic, species, and ecosystem diversity:

- Genetic diversity refers to the variation of genes within species.
- Species diversity refers to the variety of species within a region.
- Ecosystem diversity refers to the different communities or habitats found in a given location.

Biodiversity is vital to maintaining the balance of life on our planet. The world’s natural ecosystems are deteriorating at a rate unprecedented in human history. Preserving biodiversity and ensuring the sustainable and fair use of natural resources stand out as key issues worldwide. Today they are an essential part of any Corporate Social Responsibility (CSR) policy, and are considered critical topics for Sanofi.

The pharmaceutical industry places a great deal of importance on biodiversity, because natural resources are critical for the discovery and development of new drugs. Natural resources have valuable potential as sources for new chemical substances and active ingredients. Despite the decline in the use of natural products for drug discovery, biologists consider natural resources to be the treasure troves of pharmacopoeia in the 21st century, given the remarkable diversity of their substances and active ingredients.

1. Adhering to the principles of biodiversity preservation

Recognition of the Convention on Biological Diversity (CBD)

The Convention on Biological Diversity (CBD) entered into force on December 29, 1993 (and has now been ratified by almost all countries except the United States). It has 3 main objectives:

- The conservation of biological diversity
- The sustainable use of the components of biological diversity
- The fair and equitable sharing of the benefits arising from the utilization of genetic resources

Sanofi recognizes the CBD principles for obtaining and using natural resources, and stipulates that suppliers must comply with the CBD. Collaboration contracts set out conditions for sharing the benefits arising from the use of these resources.

For more information, see: www.cbd.int

The Nagoya Protocol

The Conference of the Parties to the CBD held their 10th meeting in Nagoya, Japan, drawing up what is referred to as the Nagoya Protocol. It was designed to contribute to the conservation and sustainable use of biodiversity.

This international agreement provides a legal framework to ensure the fair and equitable sharing of benefits arising from the utilization of genetic resources, directly addressing one of the three objectives of the CBD.

The Nagoya Protocol has been at the center of debate in the business world and society at large, and Sanofi has taken an active part in these discussions.

The Nagoya Protocol entered into force on October 12, 2014 and has now been ratified by 96 countries including the European Union. National legislation is being adapted to ensure compliance with this protocol.

Compliance with the local regulations stemming from the Nagoya Protocol requires coordinated efforts across all Sanofi entities. In 2015, a project team was set up to monitor the worldwide implementation of the Nagoya Protocol and to analyze its implications for our business, focusing on efforts to identify what biological materials are used in the discovery, development, manufacture and packaging of our products, and to document the originating country and acquisition date for these materials, in compliance with Sanofi’s own guidelines.

In 2016, the project team continued to create appropriate documents and policies regarding Nagoya. A dedicated intranet site designed for all Sanofi employees has been launched, aiming to raise general awareness about the Nagoya Protocol. In addition, some key departments were identified for specific employee awareness/training in 2017.

Questions remain to be answered concerning how the protocol is being implemented, and how companies can prepare themselves to satisfy the new requirements set out in the protocol. The interpretation of the protocol may also evolve according to feedback from the parties. For instance, one subject under

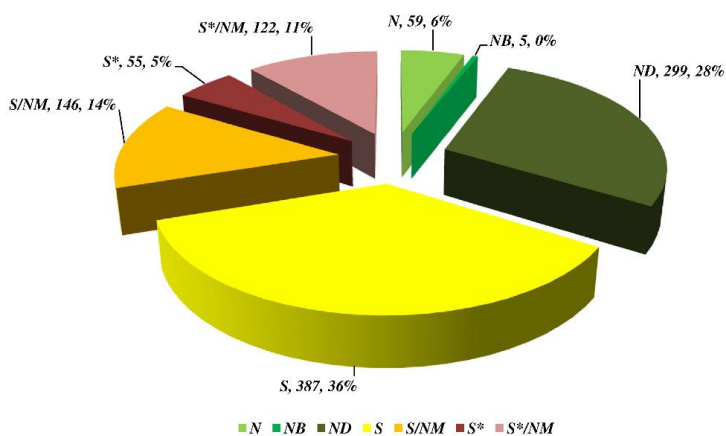
discussion is the use of digital sequence information on genetic resources.

Sanofi's biodiversity approach is summarized in Sanofi's position paper, which is available in our Download Center. This paper demonstrates that biodiversity and the fight against biopiracy are key issues for Sanofi, and establishes a clear position on combatting all forms of biopiracy.

These guidelines are consistent with Sanofi's human rights principles, specifically in regards to the fair and equitable sharing of the benefits arising from the use of genetic resources.

2. Biodiversity and the pharmaceutical industry: Origin of compounds

Over the past 30 years, 34% of the 1,073 small molecules (vaccines and biological products not included) that have been marketed worldwide have come from substances found in nature. These 1,073 new compounds may be broken down as follows:



N = Natural product

NB = Natural botanical product (in general these have been recently approved)

ND = Derived from a natural product; usually a semi-synthetic modification

S = Totally synthetic drug

NM = Natural product mimic

S* = Made by total synthesis, but the pharmacophore is/was from a natural product

Source: Newman, D. J. and Cragg, G. M. (2012) "Natural Products: A Continuing Source of Novel Drug Leads," in *Journal of Natural Products*, 75(3), pp.311-335. For more information, see:

<http://www.sciencedirect.com/science/article/pii/S0304416513000512>

3. Our strategic approach

Sanofi concentrates on three key issues relating to biodiversity:

- The controlled use of natural plant and wild animal species in research projects to discover new drugs
- Determining the fair distribution of benefits resulting from putting this type of resource on the market
- Ensuring the preservation of biodiversity surrounding Sanofi sites and beyond, particularly in fragile or protected zones

To translate our approach into action, Sanofi committed to:

- Verifying, prior to placing an order, that relevant plant species are not on the lists established by the Convention on International Trade in Endangered Species (CITES) of Wild Fauna and Flora. See www.cites.org
- Ensuring that all new relevant contracts are in line with the CBD and take into account the CITES convention and the International Union for Conservation of Nature (IUCN) Red List criteria;
- Ensuring that suppliers produce, if necessary, the official authorizations that allow them to collect the plants, animals or/and micro-organisms that have been ordered

Sanofi complies with local regulations. Regarding the preservation of protected natural areas surrounding the concerned sites, Sanofi carries out relevant environmental impact assessments.

II. ACTIONS

1. Natural substances used in R&D

The actions implemented to comply with the CBD and the Nagoya Protocol, as well as with Sanofi's position on biodiversity, focus on the use of natural substances to develop new drugs. They entail:

- Limiting the quantities of genetic resources used for research
- Identifying protected natural substances (CITES list) and finding alternative solutions
- Establishing contracts with suppliers, stipulating that they must comply with international conventions and national regulations on preserving biodiversity
- Adhering to the principle of sharing benefits generated by Sanofi with countries that give access to their natural resources, as well as with local populations having specialized know-how, whenever products made from natural substances are commercialized (see "Biopiracy" section, below)
- To facilitate these actions, Sanofi has developed and adapted a tool to manage strain collections and ensure compliance with the CBD and the Nagoya Protocol.

2. The creation of a Natural Product Center of Excellence

Sanofi and Fraunhofer-Gesellschaft, Europe's leading organization for applied research, announced the creation of a Natural Product Center of Excellence to accelerate the discovery and development of new therapies to treat infectious diseases, the second leading cause of mortality worldwide, accounting for 10 million deaths in 2011.

Under the agreement, Sanofi and the Fraunhofer Institute for Molecular Biology and Applied Ecology (IME) will collaborate to identify and optimize novel, naturally occurring chemical or biological compounds, mainly in the field of infectious diseases.

Sanofi is sharing its strain collection, one of the world's largest consisting of over 100,000 different micro-organisms, with Fraunhofer, and in addition brings its know-how in anti-infective research. A joint team of scientists is working together in the first Fraunhofer Natural Product Center of Excellence, to find new antibiotics to treat serious infectious diseases.

Access to Sanofi's natural product collection will also create value for other industries, with significant economic opportunities.

3. Collaborative partnership with Warp Drive Bio

In 2012 Sanofi R&D started to implement a new collaborative model for the use of natural products. Sanofi co-invested in Warp Drive Bio, which is an innovative biotechnology company focusing on proprietary genomic technology to discover drugs of natural origin.

The Warp Drive Bio team created a platform for identifying potential drug candidates using microbiology, next generation sequencing, cutting-edge bioinformatics, and chemoinformatics. Warp Drive Bio's integrated process pairs a "genomic search engine" and customized search queries that enable natural products that are hidden within micro-organisms to be identified on the basis of their distinctive genomic signature. Sanofi has given Warp Drive Bio access to its strains library and natural product expertise.

The collaboration was expanded and reshaped in early 2016 to include oncology programs. In late 2016, Warp Drive transferred responsibility for the aminoglycoside antibiotic program, leaving Sanofi to run preclinical research needed to get one of the aminoglycoside antibiotic candidates into human testing.

4. Natural substances used in industrial production processes

Inventory of natural substances used as Active Pharmaceutical Ingredients (APIs)

Regarding plant and animal substances used in manufacturing sites, an inventory has been initiated in collaboration with the Procurement, Global Risk Management, Industrial Affairs and CSR departments. This inventory consists of reviewing our databases in order to identify APIs originating from plant- and

animal-based natural substances, which are used for industrial purposes, and identifying the associated suppliers.

Suppliers were asked to provide additional information on location and crops of origin of these substances.

In 2013, Sanofi launched a review of the active substances used at production sites for industrial purposes. This process is performed yearly. According to the information collected to date, no plant or animal included in the CITES lists (appendices I, II and III) are used in our production activities.

5. Preserving biodiversity around Sanofi sites and beyond

Sanofi understands the importance of biodiversity for the pharmaceutical industry. As a global healthcare partner, we are committed to safeguarding the environment. Sanofi pursues many initiatives designed to preserve biodiversity at our sites, in the surrounding areas and beyond.

In 2014, an independent consultant undertook a desktop-based mapping of the biodiversity sensitivity of our 116 industrial sites. The evaluation was based on six criteria:

- Proximity to a natural/semi-natural area
- Proximity to a restricted and/or classified sensitive area
- Proximity to wetlands
- Potential to be integrated into an ecological network
- Potential presence of sensitive species/habitats
- Anthropogenic pressure

In 2016, we undertook a more in-depth analysis by identifying the potential endangered species of mammals, birds and amphibian that may be close to these industrial sites. Initial results indicate that only seven sites (off which five are in Europe) being in an area with high sensitivity to biodiversity. This study contributes to the company's environmental program, called Planet Mobilization, which includes a component on biodiversity. We seek to refine the knowledge of our sites' environment through local biodiversity studies, starting first with sites identified as being in areas sensitive to biodiversity. More globally, initiatives to protect and promote biodiversity that involve employees located at all our sites are also considered.

Three of Sanofi's industrial sites (Swiftwater in the U.S., Vertolaye in France, and Csanyikvolgy in Hungary) are located in environmentally-protected zones where environmental regulations are more stringent. These sites are under particular scrutiny. For example, since 2002 Csanyikvolgy, located near the border of a National Park, has been working with a local expert to regularly survey lichen and plants around the site in relation to sensitivity to air pollution; no negative impacts have been reported.

In addition to complying with the CBD, Sanofi defined its own biodiversity approach in 2010. We want to take tangible steps that make a difference, such as limiting the environmental impact of our activities around our sites worldwide.

For more information, see Sanofi's Position Paper on Biodiversity and Biopiracy in our [Download Center](#). See also the Convention on Biological Diversity: www.cbd.int.

A global project: Plan Bee®

With the aim of preserving and protecting biodiversity at our sites worldwide, Sanofi launched the **Plan Bee®** project on early September 2015.

Because of pesticides use, pollution, contamination by parasites, climate change, and the development of Asian hornets, 30% of beehives die each year in France. In addition, 44% of bee colonies in the US disappeared in 2016 due to colony collapse disorder (CCD), which also affects humans since approximately one third of the food in our diet originate directly or indirectly from bee pollination. Pollinating insects are essential for the economy, food safety and sustainability.

Plan Bee® consists of setting up small-scale sentinel hives on Sanofi sites. Supported by departments such as Real Estate, HSE, CSR and Site Facilities, this project provides a unique opportunity for employees to become actively involved in their environmental ecosystem and in biodiversity protection and management.

By the end of 2016, **Plan Bee®** had been rolled out at 23 sites worldwide (19 in France, three in the US, and one in Belgium) for a total of 60 installed hives. Many sites are still in the early phases of the project, but already more than 250 employees have volunteered time for **Plan Bee®**. In 2016, 256 kilograms of honey were collected.

Initiatives implemented locally at our sites

Sanofi sites are implementing a wide range of programs to preserve biodiversity in the areas surrounding their facilities, such as initiatives to plant trees and other plant life in India, Spain, Brazil, the US, Panama, Ireland, Italy and Russia, among others.

Here are some examples of initiatives implemented worldwide:

At our Waterford site in Ireland, “La Marche”

Enabling future planning for business development required the creation of a wildlife pond to provide a breeding and hibernation habitat for a protected species, the common frog (*Rana temporaria*), which inhabits a wetland area on site. We took advantage of this opportunity to incorporate a Slí na Sláinte 1.7km walking track.

Taking on board the imperative of protecting the frog population in the wetlands within our landbank and the aspiration to develop a pleasant walking route that would encourage daily outdoor exercise, the Health, Safety & Environmental team developed a project to create a pond and walkway around the frog habitat. This conserves the protected ecosystem and species but also enhances the area and makes it more accessible on a clearly marked pathway. The Irish Heart Foundation-designated Slí na Sláinte (Path to Health) makes walking outdoors simple, satisfying and safe. At Waterford, the route features an eco-friendly “outdoor room” with benches and potted lavender. In developing the model, the team were very aware of the need to deliver return on investment and to minimize expenditure. In this context, the idea was developed of delivering the project in partnership with voluntary bodies. These included the Red Cross and Scouting Ireland, both of which had Genzyme personnel involved locally. To further boost employee buy-in, we invited volunteers from the site team to take part in the physical works at

weekends. In all, 200 people from the company and community volunteered at various stages. A naming competition boosted interest and generated the “La Marche” brand. There is a real sense of ownership and the habitat and related walking route are impeccably maintained year-round. All materials used in the works were environmentally-friendly, safe, sustainable and durable.

At our Brazilian headquarters site

A local partnership was established in 2016 with an NGO which aims to plant 15,000 native trees of the Atlantif Forest. Internal actions of engagement to environment issues will be conducted in 2017 with employees. This is a five-year project. The production of native seedlings of the Atlantif forest was carried out in 2016; the planting will take place in 2017.

At our Mount Pleasant (Tennessee, US) site

As part of the remediation of former manufacturing site, 10 acres of wildflowers were planted in areas disturbed during reprocessing of aluminum oxide. The wildflower mix was chosen to enhance the local pollinator environment. Seeds were planted in late 2016 and should bloom in 2017.

At our Panamá site

Sanofi joined the “Alliance for a Million” of the National Association for the Conservation of Nature (Ancon, in Spanish), which aims to reforest one million hectares over the next 20 years to convert Panamá into a country of low-carbon emissions with a better quality of life.

Through the Alliance, Sanofi undertook to plant one hectare of the Camino de Cruces National Park and provide maintenance for the next five years. This commitment kicked off in September 2015 with an activity in which each one of Sanofi’s partners attended the planting of a full hectare of the Camino de Cruces National Park. It is important to highlight that this National Park was created in 1992 with the purpose of talking about the ecosystems and the species of tropical forests.

The main objectives of the Alliance are environmental recovery, creation of biological corridors and limiting the effects of climate change by planting trees that regulate the biological cycles and protect our watersheds.

At our sites in Hungary

Our Csanyikvölgy site is located near a conservationist forest, the purpose of which is to preserve nature and the environment around the forest. Our Csanyikvölgy site seized the opportunity to become a bird-friendly workplace in the framework of its innovation program (CSIP). In mid-2016, as a first step, it worked with the agency in charge of forest protection to install bird feeders, sand baths and various types of drinking basins on site. Initiatives to save birds are ongoing all year long, and results are expected in the long-term.

In addition, our Ujpest site planted some oxytrees, which are special trees that grow very rapidly. Their huge leaves produce more oxygen than any other deciduous tree. To protect birds, birdbaths were set up on the site and silhouette stickers were applied to windows to prevent birds from flying into the windows.

6. Biopiracy

Biopiracy refers to the commercial utilization of endemic resources and local know-how without sharing the profits with the communities or countries that are the source. The CBD and the Nagoya Protocol describe the principles governing such utilization, although national regulations vary to a great extent.

From now on, each time Sanofi will investigate the use, for R&D purposes, of a new product isolated from natural sources, a due diligence will be performed to comply with the CBD and the Nagoya Protocol. This commitment aims to safeguard against biopiracy.