HEXAXIM Environmental LCA

Technical summary report

01/01/2024

Contents

About Sanofi, Capgemini Engineering and ERM

Sanofi is a global healthcare leader focused on infant's needs, engaged in research, development, manufacturing, and marketing of health products, with a diversified offer of medicines, vaccines and innovative therapeutic solutions. By integrating an eco-design approach in its strategy, Sanofi aims to improve the environmental impact of its products. The company has committed to the following objectives:

- 100% of all new products will be eco-designed by 2025.
- 100% of vaccine syringes will be blister-free by 2027.
- The top 20-selling products will be eco-designed by 2030.

SANOFI ECO-DESIGN POLICY

- Sanofi has already executed some improvements in accordance its environmental policy for the production sites in France: Switch to 100% of renewable energies for electricity for both Marcy-l'Etoile (MLE) and Val-de-Reuil (VDR) (100% conventional electricity in 2017)
- 35% of biogas for Marcy-l'Etoile, 35% for Val-de-Reuil (100% natural gas in 2017)
- New packaging for the secondary packaging (CompactBox): the box is lighter and smaller in volume; the material of the blister was changed from PVC to cardboard

Capgemini Engineering as a brand of the Capgemini Group, is specialized in engineering and R&D services and helps the world's leading innovators design tomorrow's products and services thanks to its experts, laboratories, tools and managers in three main areas of specialization (Product and systems engineering, Digital & softwares and Industrial operations). Capgemini Engineering is committed to its customers, partners and employees in researching and developing innovative solutions for the energy transition and the fight against global warming.
Capgemini includes **LCA expertise in both industrial and digital systems** which regularly use several solutions to integrate LCA and eco-design into its projects. LCA expertise has been diversifying for over 10 years, producing environmental and social LCAs, life cycle optimization solutions and semi-automated LCA using AI, as well as dedicated LCA tools for customers. For years, Capgemini have had dozens of experiences in the LCA of digital solutions and industrial systems, and in the implementation of digital solutions to accelerate its customers' ecological transition.

With more than 50 years of experience, ERM (Environmental resources management) is the world's largest advisory firm focused solely on sustainability, offering unparalleled expertise across business and finance. ERM works with the world's leading organizations to help them set clear sustainability targets, measure progress and operationalize strategy through deep implementation and business transformation.
For the Hexaxim LCA, ERM has been a **key partner in the ISO critical review**.

1. General information

1.1 Study context and main goal

In 2023 Capgemini Engineering was commissioned by Sanofi to conduct the Life Cycle Assessment (LCA) of Hexaxim vaccine to identify its main environmental impacts, assess improvement levers already executed by Sanofi since 2017 and analyze further Eco-design solutions.

The goal of this study is also to assess several scenarios: different version (old version versus new version) and different markets (France *vs* other European countries where Hexaxim is distributed: Germany, Spain, Sweden, Norway, and Belgium).

1.2 Hexaxim vaccine

Sanofi Pasteur developed Hexaxim, a 6-in-1 pediatric vaccine for babies and toddlers aged from 6 weeks to 24 months used to protect and keep reducing the incidence of 6 infectious diseases around the world: Diphtheria, Tetanus, Pertussis, Hepatitis B, Poliomyelitis and invasive diseases caused by H. influenzae type-b bacteria.
Hexaxim development took more than 10 years and leveraged more than 24 years of experience of combination vaccines. It is the combination of best-in-class formulation and analytical sciences in the field of vaccines, combined with cutting-edge manufacturing knowledge.

1.3 Method

1.3.1 Standardized process

The LCA has been conducted according to the requirements of ISO applicable standards (14040/14044) which means it follows a strict standardized method and is internationally recognized. An external critical review was carried out by ERM (three iterations) to conform to ISO standards. The quality of the data collected during the life cycle inventory steps determines the quality of the LCA results. Data collection was carried out in an iterative way between Capgemini Engineering and Sanofi.

1.3.2 Environmental impacts indicators

The product environmental footprint (PEF) method[1] is a European Commission method to quantify the environmental impacts of products (goods or services) with **16 impact indicators**. It builds on existing approaches and international standards and enables to conduct studies that are more reproducible, comparable and verifiable, compared to existing alternative approaches. The Hexaxim LCA includes and studies all of the 16 environmental impact indicators (see appendix 4.2), but in order to make the results more accessible to non Eco-design experts, a detailed focus is made on **4 indicators selected for a pharmaceutical medicine**:

- **Climate Change** (kg CO2 equivalent): refers to the increase in the average global temperatures as a result of greenhouse gas (GHG) emissions. The greatest contributor is generally the combustion of fossil fuels such as coal, oil, and natural gas. The global warming potential of all GHG emissions is measured in kilogram of carbon 2 dioxide equivalent (kg CO2-eq), namely all GHG are compared to the amount of the global warming potential of 1 kg of CO2
- **Water scarcity**: direct and indirect use of water resources, both the water consumption measurable directly at the tap, and the water consumption that is invisible at our level but happens upstream during the production of materials or energy.
- **Abiotic resources depletion** (ADP ultimate reserves)[2]: non-living resources occurring naturally in the environment, not created or produced by man (e.g. water, light, minerals, metals).
- **Freshwater ecotoxicity**: measures the effects of " agents on ecosystems, whether they are agents of artificial origin (including drugs, endocrine drugs, endocrine disruptors, etc. or natural agents whose distribution natural agents whose distribution and/or cycles are modified by man in the different compartments of the biosphere.

In accordance with the ISO standards (14010, 14044), the ILCD Handbook[3] recommends a methodology for determining the quality of a data set. It defines the distinct levels of scoring that can be assigned to indicators, the robustness score (from Sanofi's EDDi tool method documentation) is ranking from I (most robust) to III (weakest). On the 4 chosen impacts for this study, Climate Change is ranked I on the robustness scale. The 3 other indicators, water scarcity, freshwater ecotoxicity and abiotic resources depletion are ranked III.

LCA is a metric-based methodology used to assess environmental impacts resulting from indicators as, for example greenhouse gas emissions, waste production, water, land, and energy use.

1.3.3 Scope of the study

A "cradle-to-grave" approach has been used for this study, which means environmental impacts are calculated over the life cycle of a product, including the 5 following steps:

1. **Production** includes production of the **Drug Substance (DS)** and the **Drug Product (DP).**
    - The production of the Drug Substance contains all the steps to produce the valences and their antigens:
        - Production of the raw materials: consumables, chemical substances, and solutions.
        - The production of the energy: electricity and gas
        - Cleaning products used for the cleaning process in Marcy-l'Etoile (FR: France)
        - Water consumption for Marcy-l'Etoile (FR)
        - Waste treatment of hazardous waste and liquid waste (effluents)
        - Transport of the Hepatitis B from Pilar (AR: Argentina) to Marcy-l'Etoile (FR)
    - The production of the Drug Product is done on a different site in Val-de-Reuil (FR) and contains the following step:
        - Transport from Marcy-l'Etoile (FR) to Val-de-Reuil (FR)
        - Production of the raw materials: consumables, chemical substances, and solutions
        - Production of the energy: electricity and gas
        - Waste treatment of hazardous waste and liquid waste (effluents)
        - Filling process: raw materials, energy, and water consumption
        - Waste treatment of vaccine loss

[1] Suggestions for updating the Product Environmental Footprint (PEF) method. Link to the EF3.0 Methodology: https://eplca.jrc.ec.europa.eu/LCDN/developerEF.xhtml
[2] This indicator is chosen over resources depletion (fossil fuels) in Sanofi's LCA, since fossil fuels resources are linked to climate change. It is preferred to have two really different indicators.
[3] ILCD Handbook, International Reference Life Cycle Data System (2010), JRC European Commission

All the raw materials involved in the production process can be summarized in the figure below.

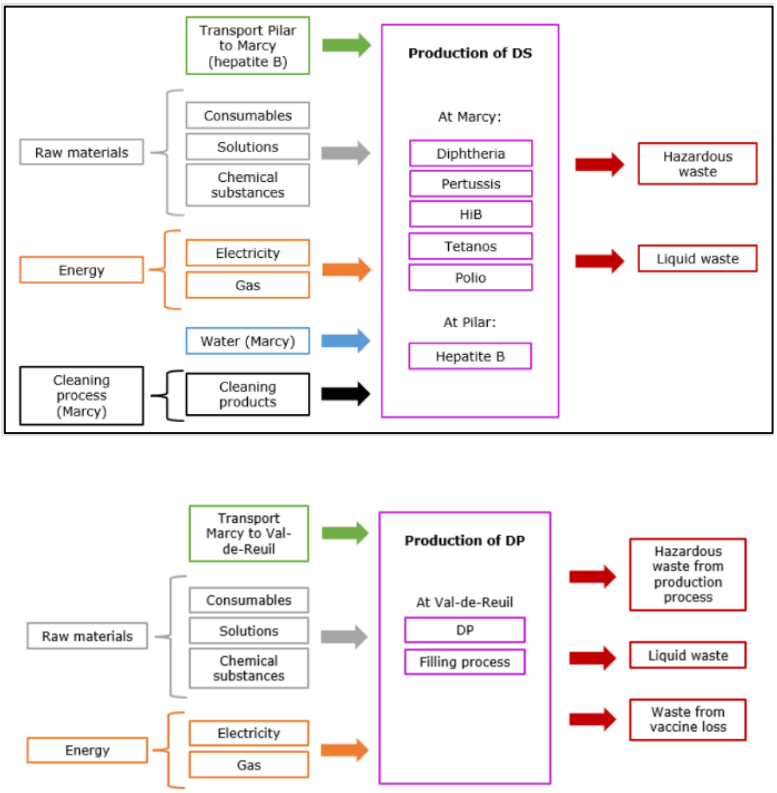

Figure 1. Flows for the production of the DS (up) and the DP (down)

2. **Filling and packaging process:**
    - In Hexaxim case it includes 3 layers of packaging
        1. Primary packaging, the syringe: glass barrel, tip cap, stopper, 2 needles and their plastic protections
        2. Secondary packaging: the box, leaflet and label
        3. Tertiary packaging: Packaging for transport (2 kinds):
            - Standard
            - Compactbox: new packaging used and implemented as a part of Sanofi's eco-conception policy (no more blister, smaller box, cardboard tray included)
    - Filling process corresponds to the step where the syringe is filled with the finished vaccine in Val-de-Reuil (FR). To ensure an administered dose of 0.5 mL of vaccine, it is necessary excute an overfill of the product. This step takes into account some loss of product.
3. **Storage & distribution:**
    - Storage: The vaccine is stored for an average of 3.5 months in a warehouse in Val-de-Reuil while awaiting shipping and then stored again at the distribution centers of the target countries. As Val-de-Reuil is also the distribution center in France, only one storage is considered.
    - Distribution: it is modeled for the 6 different markets. The distance includes:
        - the transport from Val-de-Reuil (VDR) to the distribution center of the country;
        - the transport from the distribution center of the country to the pharmacy;
        - The transportation of the infant from his home to the doctor (injection site).

- **Use phase** (combines the use and the end-of-life (specific to the use phase) of consumables):
    - Use of consumables: production of the raw materials of the consumables for the injection (cotton, adhesive plaster, antiseptic);
    - The energy consumption for the cold storage;
    - EoL of consumables: this step is considered in the use phase. This contains the EoL treatment of the cotton and the adhesive plaster, which are incinerated. The Sanofinvent

dataset used for the incineration of the plaster also includes the transport and the collection.

4. **End-of-life** (EoL): the assumptions for the end-of-life of the 3 packaging. Most of the materials are landfilled and incinerated according to the classification of the waste (hazardous vs. Non-hazardous) & local market average end-of-life treatment rates, which contains a mix of recycling, incineration, and landfill. It includes the collection and transport of waste.

The scope of study is wide and includes a large range of elements as the raw material production, the storage and distribution, the patient transportation or even the incineration. But it also discards some elements as animal quality test or batch records.

The results are also compared including and excluding the infant transportation (transportation to the vaccination center -pharmacy or doctor-) to better interpret the impact of each phase of the vaccine's production.

1.3.4 Functional unit (FU)

The Functional unit (FU) is the quantifiable reference unit which refers to a product, service or system whose impacts are calculated throughout the LCA (from Production to End-of-life). For example, a FU could be 1 liter of dairy milk, defined as the quantity investigated. Having a unique FU during the LCA enables an objective comparison between different products, services or systems.

The chosen FU is: **One infant treated over 1 year with the recommended course with the Hexaxim vaccine.**

The intended market of study for the reference scenario is France (3 doses of 0.5 mL or 1.5 mL).

Concerning the posology and administration, the recommended initial vaccination schedule is either two doses, given two months apart or three doses, given at least one month apart. A booster dose should be given at least six months after the last of these initial doses. Immunization must be carried out by intramuscular (IM) injection.

2. Results and discussion

The main product studied is the 2023 vaccine with a syringe packaging (with all improvements since 2017). A complete analysis of this scenario is performed first (2.1), then scenarios analysis are done to evaluate the potential benefits of the changes implemented by Sanofi for the production (2.2).
Since 2017 Sanofi has made several changes regarding the production such as: reduction of water consumption, supply of Marcy-L'Etoile and Val-de-Reuil (VdR) site with renewable energy (RE), use of a mix of natural gas (NG) & biogas and the creation of a new secondary packaging for the syringe (CompactBox[4]).

2.1 Hexaxim LCA

2.1.1 Impacts of Hexaxim during its global life cycle

[4] CompactBox was fully implemented by end of 2023.

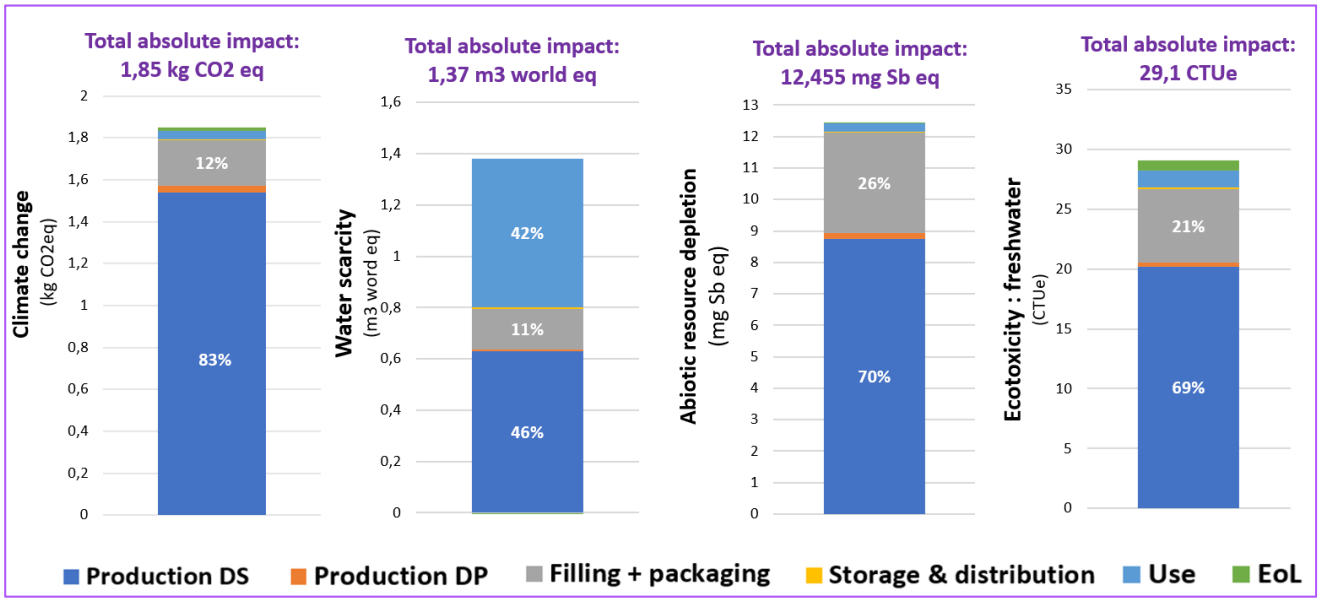

*Figure 2. Impacts of Hexaxim during its life cycle **without the infant transport** - Focus on 4 indicators*

During Hexaxim life cycle, the **production of the Drug Substance (DS)** is the most significant, especially in climate change (emissions of GHG), abiotic resource depletion and freshwater ecotoxicity. Its contribution is lower on Water scarcity where the **use phase** has a significant impact, due to the production of the cotton which requires an important consumption of water.
The other significant contributor is the **filling & packaging** phase, with the primary packaging for Abiotic resource depletion (production of the syringe with glass, stainless steel and rubber) and the secondary packaging for the other indicators (production of cardboard and paper).

2.1.2 Hexaxim environmental impact

The results highlight that depending on whether the patient transport is included or not, the impacts of Hexaxim during its life cycle are different.
When patient transport is included, the storage & distribution phase contributes the most or is the second contributor in all categories.

The treatment of 1 infant in France over a year with a syringe packaging generates 7.5 kg of CO2 eq when the infant transport is included versus 1.8 kg of CO2 eq when the infant transport is excluded. The data on infant transportation is a mix of transports totalling to an average distance of 8.5 km with 65% of transport by car (the rest being public transportation, bike, motor bike). Only the transport from the house of the infant to the doctor/vaccination center is considered. This quality of this data is low with high uncertainty on the available data/sources.

2.2 Scenario analysis: old vs new version (Syringe presentation)

The syringe new version of Hexaxim (2023) was used as a base scenario, then compared to the syringe old version (2017) without the patient transport. The results correspond to the FU for France, namely: the treatment of one infant with the recommended course of Hexaxim vaccine in France (1.5 mL of Hexaxim or 3 doses). Results for other countries are provided in next chapter.

As highlighted in the graph below, the changes implemented by Sanofi lead to an overall improvement of the four main environmental impacts.

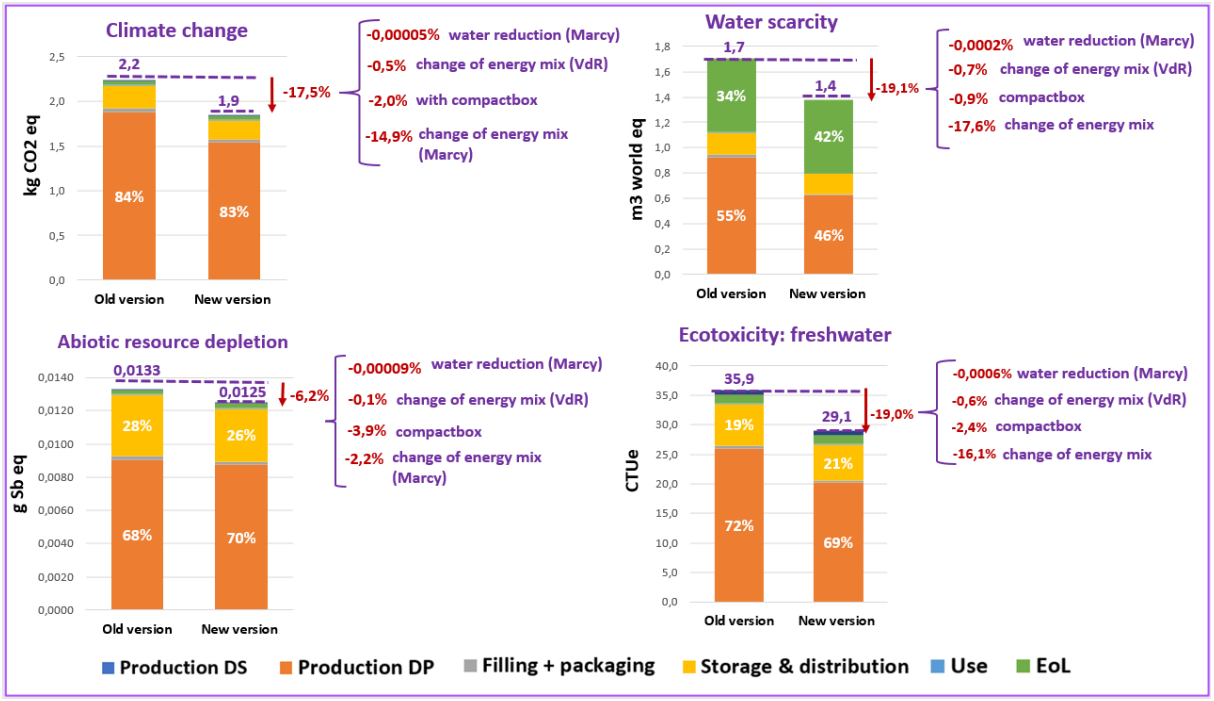

Figure 3. Scenario analysis old version (syringe 2017) vs new version (syringe 2023) without patient transportation

The reduction is most important for Ecotoxicity: freshwater, Water Scarcity and Climate change. Even if the benefits are less important for Abiotic resource depletion it is still significant.

- The **change of energy mix** is the highest contribution to the reduction of impact, from grid mix in 2017 to 100% renewable energy in 2023; and from 100% natural gas in 2017 to 70% natural gas & 30% biogas in 2023.
- Then, the **CompactBox** has benefits on every indicator, thanks to a reduction in weight (smaller box, replacement of PVC blister by a cardboard tray).

When looking at the other impacts briefly (so not only the four main indicators), we can note the changes implemented for the production processes lead to an overall improvement, except for Land use: +2%.

2.3 Impacts relative to several markets

Hexaxim is produced in France, but the vaccine is shipped all around the world. Sanofi is interested in assessing the impacts from different markets in Europe compared to France: Belgium, Germany, Spain, Norway and Sweden.
The results for the different market correspond to the following functional unit: the treatment of one infant with the recommended course of Hexaxim vaccine. Note that the FU consists of **4 doses for Belgium and 3 doses for all other countries**.

All European markets selected have a **higher environmental impact than France**. As the contribution of the end-of-life is very small, the difference between the end-of-life treatment share has very little effect on the overall results.

In the countries with a posology of 3 doses (all except Belgium), **the difference of impact comes mainly from the storage & distribution stage**. The impact increases with the transportation distance: for Climate change there is a variation of +0,6% for Spain (1361 km) versus +1,6 % for Norway (1760 km).

The **electric mix of the country** (used for the storage at the distribution center) is also impacting the results. For example, the German distribution center is closer to Sanofi's French warehouse than the Spanish one, but the impact is higher on climate change for the German scenario. Indeed, a major part of the electricity in Germany is produced with coal, which translates to a higher climate change impact.

In other categories the difference of impact is smaller: less than 1% for Water scarcity and Abiotic resource depletion, between 1% and 1,1% for freshwater Ecotoxicity.

The impact of Belgium is the highest even though it is the closest country. We can note an increase between 33.6% (Water scarcity) and 34% (Ecotoxicity: freshwater) because the posology in this country is 4 doses, so one more dose must be produced.

Total per country excluding patient transport			France	Belgium	Germany	Spain	Norway	Sweden
Number of doses for one treatment			3	4	3	3	3	3
Climate change (kg CO2eq)	One product	Old version	0.75	0.75	0.76	0.75	0.76	0.76
		New version	0.62	0.62	0.63	0.62	0.63	0.63
		Comparison	-0.130	-0.130	-0.130	-0.130	-0.130	-0.130
		Number of meters travelled by car (Equivalent emissions)	-600	-600	-600	-600	-600	-600
		%	-17.46%	-17.40%	-17.15%	-17.37%	-17.24%	-17.23%
	Whole treatment (considering the number of doses)	Old version	2.24	3.00	2.28	2.25	2.27	2.27
		New version	1.85	2.48	1.89	1.86	1.88	1.88
		Comparison	-0.390	-0.520	-0.390	-0.390	-0.390	-0.390
		Number of meters travelled by car (Equivalent emissions)	-1792	-2390	-1792	-1792	-1792	-1792
		%	-17.40%	-17.33%	-17.09%	-17.31%	-17.17%	-17.17%
water scarcity (m3 world eq)	One product	Old version	0.57	0.57	0.57	0.57	0.57	0.58
		New version	0.46	0.46	0.46	0.46	0.46	0.47
		Comparison	-0.108	-0.108	-0.108	-0.108	-0.108	-0.108
		Minutes of shower (equivalent consumption)	-10	-10	-10	-10	-10	-10
		%	-19.10%	-19.06%	-19.04%	-19.05%	-18.98%	-18.59%
	Whole treatment (considering the number of doses)	Old version	1.70	2.27	1.70	1.70	1.71	1.74
		New version	1.37	1.84	1.38	1.38	1.38	1.42
		Comparison	-0.320	-0.430	-0.320	-0.320	-0.320	-0.320
		Minutes of shower (equivalent consumption)	-29	-39	-29	-29	-29	-29
		%	-18.85%	-18.96%	-18.80%	-18.80%	-18.74%	-18.36%
abiotic resource depletion (mg Sb eq)	One product	Old version	4.43	4.44	4.45	4.45	4.45	4.45
		New version	4.15	4.17	4.17	4.17	4.18	4.18
		Comparison	-0.274	-0.274	-0.274	-0.274	-0.274	-0.274
		µg of Gold (equivalent consumption)	-5	-5	-5	-5	-5	-5
		%	-6.18%	-6.16%	-6.15%	-6.15%	-6.14%	-6.14%
	Whole treatment (considering the number of doses)	Old version	13.28	17.76	13.34	13.34	13.36	13.36
		New version	12.46	16.66	12.52	12.52	12.54	12.54
		Comparison	-0.820	-1.090	-0.820	-0.820	-0.820	-0.820
		µg of Gold (equivalent consumption)	-16	-21	-16	-16	-16	-16
		%	-6.18%	-6.14%	-6.15%	-6.15%	-6.14%	-6.14%

3. Outlooks & limitations

3.1 Outlooks

This LCA shows the improvements of the changes that are part of Sanofi's Eco-design strategy. Some measures have already been taken to reduce the environmental impact and others will be implemented in the coming years.

The initiatives to lower the environmental impact should consider the main hotspots, such as the production of the DS or the optimization of infant transportation.
Even if infant transportation is not something easy to control for Sanofi, it possible to think of improvements such as: injections being done during mandatory visits to the doctor included in the health journey of the child, or a reduction of the number of injections needed, increasing the patient protection. When excluding the infant transport, the DS production is the most important contributor.

Sanofi is on the right track and has already done some work concerning the energy consumption of its production sites, such as changing natural gas to biogas, switching to renewables energy, and decreasing the energy consumption needed to produce each dose. It is possible to go further by switching to 100% biogas or using more solar and wind electricity instead of hydro powered one.

A deep dive into the circular economy world can also be a good way to reduce the emissions of the raw materials used for production or even of the different packaging types. By re-using or recycling some of the materials used, such as for example the cardboard boxes used as secondary and tertiary packaging, Sanofi will be able to decrease the impact of Hexaxim.

In **France**, our new eco-designed Hexaxim presentation with **1 PreFilled Syringe** has **- 17% carbon emissions** compared to **its previous version,** saving approx. **130 gr CO_2-eq per box**, **the same as driving your car on 0.5 km[5].**
It also allows saving approx. **110 l of water eq. per box which is similar to a 10-min shower[6]** or **300 µg of Sb eq. per box which represent 5,8 µg of Gold[7]**.

These potential environmental reductions are thanks to:
1# **Energy sources substitution** for heat and electricity :**100%** of the **electricity from french production sites** are from renewable sources and **35%** of the **heat** is produced thanks to **Biogas instead of Natural Gas**.
2# secondary **packaging** optimization: replacing **3.6 g of PVC** and **7 g of Cardboard** by a **9 g of cardboard** (including the **reduction of weight of the box).**

In France changing the packaging of one box Hexaxim with 1 PFS has helped to lower all environmental indicator (except for land use) and in particular **-2 % carbon emissions** compared to **its previous versionon the whole life cycle and – 9 % on the packaging impact,** saving approx. **15 gr CO_2eq per box**, **the same as using an electric bike on more than 1,3 km (France)[8].**

3.2 Limitations of the study

With a view for transparency, here are some limitations which need to be considered regarding the study. Even if some limitations might not have a big impact on the results, the following must be mentioned[9]:

- **Chemical substances:** 10 substances were modeled with generic approximations (due to a lack of data on their production process). A sensitivity analysis was performed by replacing the generic approximations with a "worst case scenario" approximation. In this case, the datasets were replaced by "market for adipic acid" for organic chemicals and "market titanium dioxide" for

[5] source : Comparateur carbone | Impact CO_2 (impactco2.fr) – visited on January 29th 2024 –4.6 km per kg CO2-eq by car
[6] source : Ableitner, Liliane & Schöb, Samuel & Tiefenbeck, Verena. (2016). Digitalization of Consumer Behavior – A Descriptive Analysis of Energy Use in the Shower. 11 L/min for Switzerland used for all European countries
[7] source : abiotic depletion potential (ADP): elements (ultimate reserves) no LT value for "Gold in ground" : 52 kg Sb-Eq / kg
[8] source : Comparateur carbone | Impact CO_2 (impactco2.fr) – visited on January 29th 2024 – 10.71 gr CO2-eq per box and 93.48 m per gr CO2-eq by electric bike
[9] The other limitations are presented in the appendices.

inorganic chemicals. Then the calculations were started again. The overall variation in the results is minimal, less than 1%. However, it is good to bear in mind that some of those substances have a very complex production process: it is possible that even the worst-case scenario dataset underestimates the impact.

- **Consumables**: in this study the model for the consumable used in the manufacturing production of the DS & DP is the part with the highest uncertainties and the lowest reliability. But it can be improved with direct data from suppliers and the verification of quantities in the production processes for the solutions.
- **Biogas**: the impact of the biogas is underestimated as the model only contains its production. There are also emissions of biogenic carbon and methane during the use phase due to the incomplete combustion of the gas that have not been modeled.
- **Chosen indicators**: as precised in the methodology, 3 of our 4 chosen impacts are ranking III (low) on the robustness scale, so it is recommended to take extra caution when analyzing the results.

Other limitations as effluents, water consumption, energy mix, are presented in the appendices (see appendix 4.3)

4. Appendices

4.1 Glossary

AB: Activity Browser
BE: Belgium
DC: Distribution center
DE: Germany
DP: drug product
DS: drug substance
EoL: end-of-life
FU: functional unit
LCA: Life Cycle Assesment
MLE: Marcy-l'Étoile
NG: natural gas
NO: Norway
RE: renewable energies
SE: Sweden
SP: Spain
VdR: Val-de-Reuil

4.2 Sixteen indicators selected for the LCA

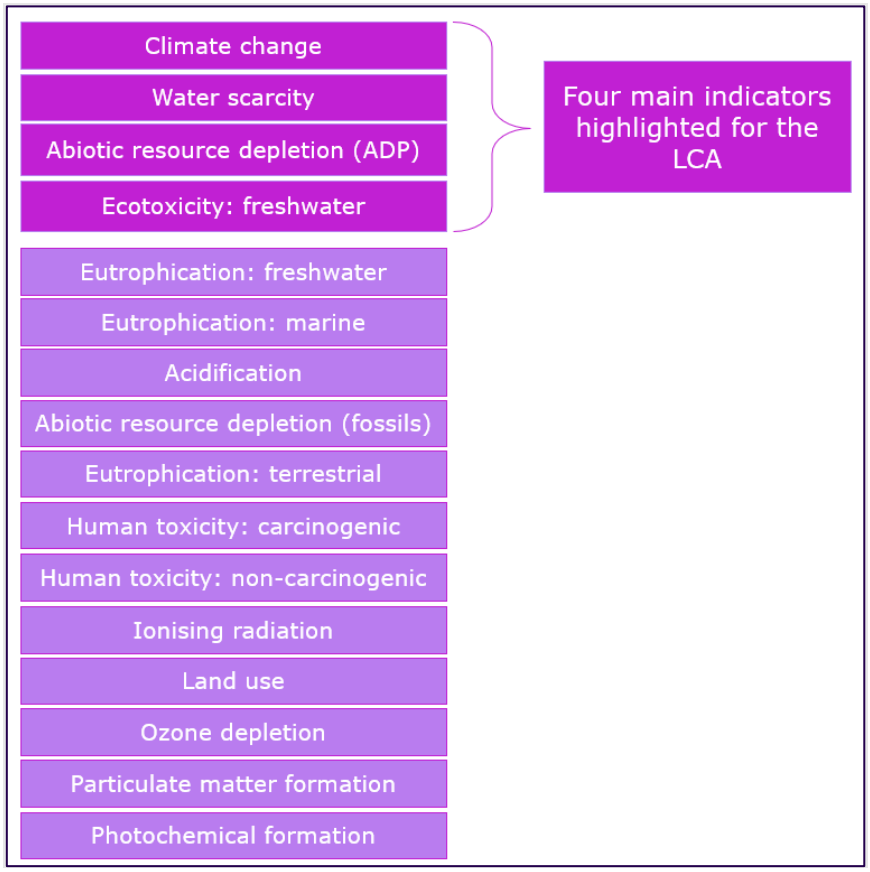

Figure 4. Sixteen indicators studied, according to the product environmental footprint (PEF)

4.3 Other limitations

Five more limitations should be considered for the LCA results:

- **Effluents**: the calculations were performed only for the 2 or 3 first levels of the production process of each valence Some solutions/production steps in lower levels also have effluents that could be added for a better model
- **Water consumption**: there is a decrease of water consumption between 2017 and 2022 at the Marcy-l'Etoile (FR) site which could be linked to a decrease in production and/or to water saving measures Therefore, there is uncertainty about the benefits linked to this as they could be null. In any case the benefits are negligible.
- **Renewable energy mix**: there is some uncertainty regarding the representativity of the energy mix used as Sanofi's renewable mix is not known and as there is no information on the assumptions that were taken to model this dataset for this study (the dataset is based on an Ecoinvent one and then has been modified in the Sanofi's database).
- **Energy mix**: the ecoinvent datasets for the conventional energy mix in France are dated from 2018 (close enough to the 2017 mix). However, the same dataset is used for the new version of the product (energy consumption from 2021 and 2022) as it is the only dataset available. The French energy mix has changed a little over 4 years (decrease of the nuclear and coal share and increase of the wind, solar and gas shares). The mix used for the new version is not fully representative of the mix of 2022, hence there is an uncertainty regarding the benefits of the change of energy mix that could be higher or lower.
- **Ecoinvent**: for this study, the 3.8 version of the Ecoinvent database was used. As Ecoinvent releases a new version of their database every year, the latest one being the 3.10 version. The 3.8 version was released in 2021, thus the data might not be the most up to date.