ANIMAL PROTECTION

Executive Summary

As a diversified global healthcare leader focused on patients' needs, Sanofi is morally and legally obligated to ensure the quality, safety and efficacy of its medicines, vaccines, medical devices, and consumer healthcare products. Besides the regulatory requirements, the responsible use of animals is essential in the research and production process. Animals remain a small but an integral part of a comprehensive research and testing strategy that includes non-animal methods and clinical research.

Research involving animals poses dilemmas not only for scientists who use animals in medical research but also for society as a whole. At Sanofi, the consensus is that using animals for research is justified when there are clear benefits for human health and when the 3Rs principles (replacement, reduction and refinement of animal use) are applied.

As a key element of Corporate Social Responsibility, Sanofi commits to meet or exceed regulations and standards for the use of animals and to develop alternative approaches. Sanofi fully adheres to the 3Rs: Replacement, Reduction and Refinement of animals in Research. In this context, Sanofi uses animals only when a non-animal method is unsuited for the required use (replacement), with the smallest number necessary for quality science (reduction), and implements state-of-the-art practices to promote animal welfare and prevent animal pain and distress in housing and procedure conditions (refinement). Sanofi authorizes animal use only when the regulatory and scientific merit is established and under strict ethical oversight.

Sanofi promotes a culture of care which embraces responsible use of animals as a primary value and engages every employee working with animals. Whenever animals are required, Sanofi will provide high quality programs for care and use.

Any question could be asked to the Chief Veterinary Officer, please use the form available at the following address:
http://en.sanofi.com/contact/contact-form-chief-veterinary-officer.aspx

Summary table

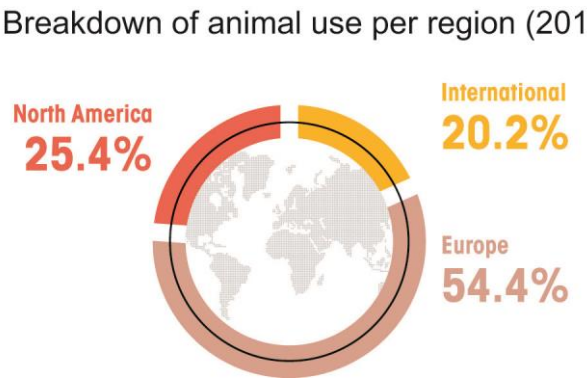
I. HIGH STANDARDS BEYOND REGULATIONS

In the last decades, major pieces of regulations and references (Europe, USA, China…) have been set up or updated taking into account the progress in animal welfare knowledge and the increased considerations of the protection of animals by the public (see chapter VII for references).

Biomedical research is a highly regulated area in the countries where Sanofi operates. The regulations include all the aspects surrounding the use of animals: personnel, facilities, studies and of course, the animals.

Examples of new obligations as defined by the European Directive 2010/63
• Ethical review and authorization of projects by independent authority • Publication of non technical summary of projects • Implementation and monitoring of the 3Rs • Enlarged list of covered species, including cephalopods and fetal forms of mammals • Inclusion of genetically-modified animals • Limitation of the use of non human primates • Training of the personnel and assessment of competencies • Appointment of a designated veterinarian • License for user establishments • Inclusion of animal breeders and suppliers

Local regulations are mandatory and compliance is monitored on a regular basis. All the sites are inspected by the national competent authorities usually every year. Over 80% of animal use takes place in the context of strict regulatory environments in Europe and Northern America. The others sites, dedicated to quality control of vaccines, are located in Asia and comply with their national regulations.

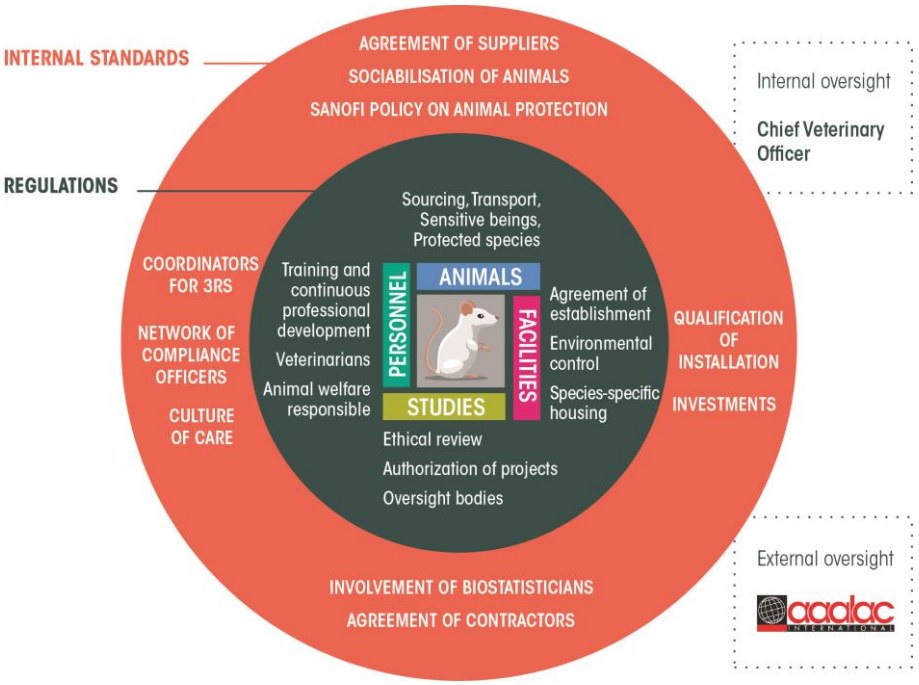


Moreover, in addition to the legal obligations, Sanofi has set internal standards to align requirements across the world and to ensure the high welfare considerations. All Sanofi sites look for independent accreditation of their animal care and use programs through recognized expert organizations such as AAALAC International.

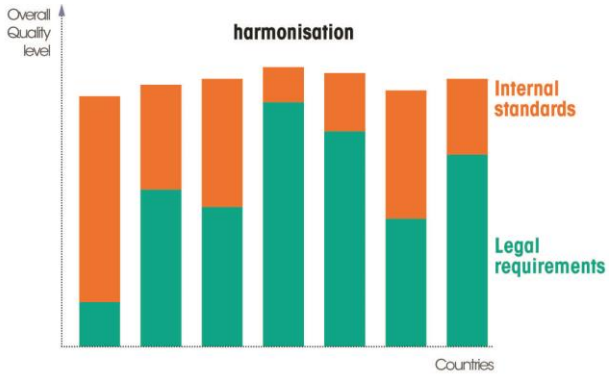
Sanofi applies the same principles to subcontractors and partners.

1. Animal use is highly regulated

Regulations are a first layer of obligations which are completed by specific standards developed by Sanofi (the second layer). Compliance with regulations and standards are ensured by the oversight of the Chief Veterinary Officer and by accreditation by AAALAC International.



Sanofi standards complement legal obligations by achieving high quality animal care and use programs. Legal requirements can differ from countries to countries; setting internal rules and principles contribute to increase the overall quality towards more harmonized high standards:



II. USE OF ANIMALS : A NECESSITY FOR THE BENEFITS OF PATIENTS

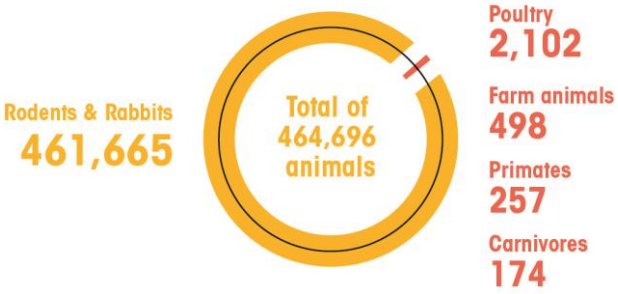
Sanofi is morally and legally obligated to ensure the quality, safety and efficacy of its medicines and vaccines. Although committed to developping and implementing non-animal methods, Sanofi believes the responsible use of animals remains essential in the research and production process. The most reliable scientific models should be used to the benefits of patients; those can be in silico (computerized modelization), in vitro (cells and tissues, including human tissues, biochemistry, microbiology…), in vivo (animal models), and in humans (clinical research and clinical trials).

In 2016, about 70% of animals were used to support our batch release activity to ensure the safety and efficacy of commercialized vaccines and drugs. About 30% of animals have been used for research purposes to better understand diseases and to assess the safety and efficacy of new drug and vaccine candidates.

Breakdown of animal use per activity (2016)

The majority of animals used (99%) are rodents and rabbits. Less than 1% are fish, poultry, farm animals, carnivores and non-human primates. The choice of the species is based on a scientific assessment and justifications are reviewed by the Site Ethics Committee responsible for the project approval.

Animal use per species (2016)



III. A COMPANY-WIDE POLICY ON ANIMAL PROTECTION

Animal are used at Sanofi in 15 sites located in 7 countries. We developed a policy on animal protection to promote a shared vision of the consideration of animals within the company. In support of our longstanding commitment to the 3Rs, the policy applies to all animals used by Sanofi for research, testing and the production of medicinal products, investigational medicinal products, vaccines, medical devices, nutraceuticals and active pharmaceutical ingredients. It also applies to breeders, suppliers and transporters of animals for research, testing and production purposes, as well as to external partners using animals under Sanofi's sponsorship.

15 sites in 7 countries

The use of animals is authorized only when regulatory and scientific merit is established, with strict ethical oversight. Our company-wide policy promotes a culture of care that embraces the responsible use of animals as a primary value so that, whenever animals are required, Sanofi and third parties develop quality animal care and use programs. The employees working with animals have been trained and must be committed to providing the best care and attention to the animals.

Good science requires that animals remain in good health and are subject to minimal pain or distress. The ethics committee ensures the oversight of the local animal care and use program.

1. Strong commitment to the 3Rs

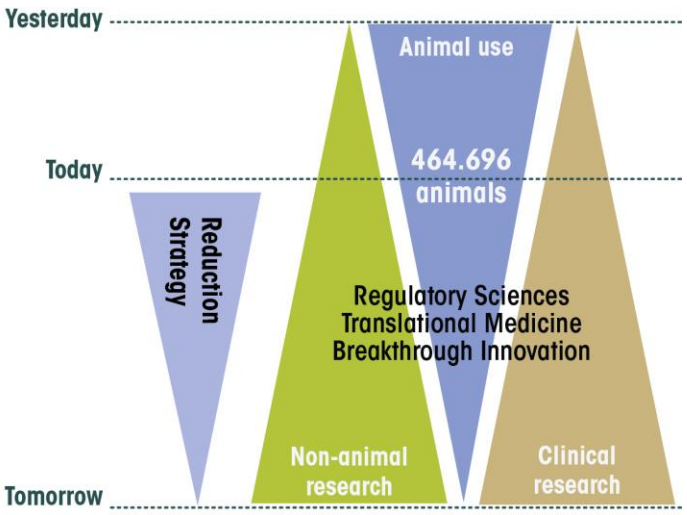
The 3Rs:

- Replacing use of animals with any other methods when a non-animal method is feasible,
- Reducing the number of animals necessary to ensure reliable, quality scientific results, and
- Refining techniques to promote animal welfare and minimize pain and distress.

For many years, Sanofi has sought to apply the 3Rs when using animals necessary for our research. Our approach is designed to use animals only when a non-animal method is not suitable for the required use (replacement), with the smallest number necessary for quality science (reduction) while implementing state-of-the-art practices to promote animal welfare and prevent pain and distress in housing, procedures and treatment (refinement).

Animals remain an integral part of a comprehensive research and testing strategy that includes non-animal methods (such as computerized models and *in vitro* testing) and clinical research. Animal use is also part of many regulatory requirements. For example, testing vaccines before batch release remains mandatory worldwide for public health reasons and use of animals is justified to ensure the safety and efficacy of commercialized vaccines. However, a strategy, relying on regulatory sciences, translational medicine and breakthrough innovation, has been developed to increase the proportion of non-animal methods, including clinical research, to reduce significantly the necessity to use animals in research and production.

Illustration of the Integrated Research and Testing Strategy towards the relative reduction of animals:



2. Ethical oversight

When animals are required to help ensure the safety or quality of medicines or vaccines, procedures are performed in accordance with regulations to involve minimal pain or distress. In every site, an ethics committee oversees animal care and use, including effective implementation of the 3Rs at the bench level. They weigh the objectives of the study and the likelihood of achieving the goals related to the protection and/or improvement of human health against potential animal welfare concerns. All research and testing protocols must be validated by the ethics committees, and their decisions are binding.

Members of the ethics committees include senior animal researchers, staff involved in the care and use of animals, at least one veterinarian, and an independent or lay committee member. Whenever possible, a biostatistician sits on the committee to make sure the study uses the smallest number of animals necessary to produce statistically valid results.

IV. OUR ANIMAL PROTECTION ROADMAP

To achieve Sanofi objectives of protecting animals, priorities have been defined and progresses are monitored on a regular basis. The roadmap defines the current axes for improvement:

- To improve transparency regarding animal use and the Integrated Research and Testing Strategy (3Rs)
- To accelerate the development of 3Rs programs with the support of senior management
- To continuously assess the compliance with the Sanofi Policy on the Protection of Animals, beyond regulatory inspections and accreditation
- To ensure support to Sanofi sites by contributing to AAALAC accreditation and compliance of third parties (breeders, CROs, not-for-profit institutions)
- To contribute to regulatory debates, especially those related to the review of the European Directive, and initiate a culture of openness
- To create a global ethics advisory body related to animal experimentation, reporting to the Sanofi Bioethics Committee, to address societal concerns about the use of animals

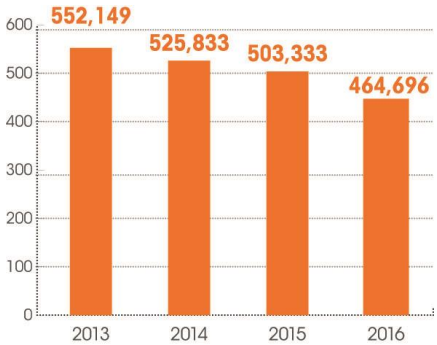
V. ACHIEVEMENTS ABOUT THE 3RS

There are many examples of outreach within Sanofi and with external partners to increase awareness of the 3Rs.
Below we provide several evidences of commitments and achievements:

1. Constant decrease of use of animals within our facilities

Every year, a comprehensive mapping of animal use in Sanofi facilities is conducted, evidencing a constant decrease of use of animals.

Evolution in numbers of animal used across the Sanofi Group, 2013-2016:



Use of animals in-house has steadily decreased over the last four years. The decrease is due to paying active attention to the 3Rs, especially for the quality control of vaccines prior to injection to patients, and to the focus of certain internal research and testing programs.

2. Rehoming dogs and horses with animal protection associations globally (at relevant sites)

Sanofi has a long history of rehoming dogs that are no longer required for research or testing. Over the last 20 years, more than 1,000 dogs have been made available for adoption at every location where dogs were used (Europe and United States). Recently, Sanofi Pasteur also developed a program to rehome horses (about 100 horses) in collaboration with GRAAL, an animal protection association. Sanofi partners only with animal associations that maintain the highest standards of animal welfare and ensures that animals are fully evaluated by veterinary staff prior to adoption and that the place where animals will be rehomed as also been evaluated.

3. Sanofi Pasteur issued two statements in 2016

In 2016, Sanofi Pasteur issued two statements to enhance awareness of the 3Rs.

One of the two statements concerns the general commitment of Sanofi Pasteur about the 3Rs and underlines that Sanofi Pasteur, with the support and commitment of its R&D Department, ultimately aims to eliminate all use of animals in the manufacture and inspection of vaccine batches on the market, in particular for its new vaccines, and to reduce the number of animals used in the development of new products.

The other statement, “Reduction of animal testing for vaccine release by Official Medicines Control Laboratories,” emphasizes that Sanofi Pasteur is committed to working with competent national authorities as well as international organizations to reduce, replace and refine the use of animals for testing purposes in a systematic way, based on science and a risk-based approach, and to work together developing and implementing alternatives to animal testing with the objective of continuing to deliver high-quality vaccines to people around the world in a reliable and timely manner.

4. CSR award for the 3Rs: 2,000 rabbits saved annually by using a cell-based assay to replace a bioidentity assay for batch release of insulin glargine

In 2016, for the second time, an internal global award was developed to provide internal recognition of Sanofi’s commitments to the 3Rs and to foster innovation in this field. A total of 15 submissions were received by the jury, a noteworthy achievement to increase awareness about the 3Rs.

The Sanofi Research and Development Department partnered with Industrial Affairs to develop and validate an *in vitro* test that replaced an *in vivo* test in rabbits. This project involved an extensive effort over several years to ensure equivalency of the test. This new test eliminated the need to use over 2,000 rabbits every year. In late 2016 the team was

awarded the Hessian Animal Welfare Research Award from the Hessian Ministry of Environment, Climate Protection, Agriculture and Consumer Protection in Wiesbaden.

Based on these groundworks, in 2017, the US Pharmacopeia published a new testing guideline for comment with the cell-based bioidentity assay as an alternative to the rabbit bioassay, which will become at disposal of any insulin manufacturers.

5. Strong presence at the conference organized by the European Commission

Sanofi shows its strong commitment to the 3Rs by participating in several conferences and publishing scientific advances to further animal welfare. An example of Sanofi's impact could be reported at the European conference, in Brussels, December 2016, "Non-Animal Approaches – the way forward," where Sanofi scientists presented nine of a total of 35 posters during the conference (available online). Sanofi will continue to support the 3Rs through advancing science.

Active collaboration with other pharmaceutical companies and competent authorities fosters the development of good practices and alternative approaches across biomedical research. For example, Sanofi contributed to the EFPIA brochure: "Putting animal welfare principles and 3Rs into action."

VI. INSPECTIONS, ACCREDITATIONS, AND AUDITS

1. Inspections in 2016

Regulatory inspections at Sanofi's animal facilities are performed on a regular basis by national and local authorities and results are in compliance with animal welfare laws and regulations; no major issues have been reported.

2. AAALAC accreditation of our sites

The Sanofi Animal Welfare Steering Committee is committed to ensure the AAALAC accreditation of 100% of our facilities using animals by 2020.

By the end of 2017, 13 sites are accredited on a total of 15.

a) Accreditations

In 2017, the site of Hyderabad, India has obtained its first accreditation by AAALAC international.

b) Reaccreditations

5 sites have been reaccredited in 2016, and 2 in 2017,

In 2016:

- Sanofi Pasteur IA, Toronto, Canada
- Sanofi R&D and Sanofi Pasteur R&D, Boston area, United States
- Sanofi R&D, Frankfurt, Germany

- Sanofi IA, Frankfurt, Germany
- Sanofi R&D Vitry and Alfortville, France

In 2017 :

- Sanofi Pasteur, IA and R&D, Marcy-L'Etoile, France
- Sanofi Pasteur, IA, Val de Reuil, France

3. Number of contract research organizations (CROs) and suppliers evaluated in 2016

Third parties are periodically assessed by Sanofi laboratory animal experts to ensure compliance with the principles of the policy on the protection of animals.

In 2016, 59 contract research organizations (CROs) or academic institutions and 21 vendors underwent evaluation and were determined to meet requirements to comply with Sanofi's animal protection principles.

VII. REFERENCES

- ETS 123—European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes.
- European Directive 2010/63/EU of the European Parliament and of the Council of September 22, 2010, on the Protection of Animals Used for Scientific Purposes.
- United States Animal Welfare Act (Title 7 U.S.C 2131–2159) and United States Animal Welfare Regulations, CFR, Title 9, Chapter 1, Subchapter A, Part 1-4.
- Institute for Laboratory Animal Research—Guide for Care and Use of Laboratory Animals (8th Edition, 2011).
- Federation of Animal Science Societies—Guide for the Care and Use of Agricultural Animals in Research and Teaching (3rd Edition, 2010).
- EFPIA: Putting animal welfare principles and 3Rs into action. European Pharmaceutical Industry 2016 Report Update.