

ANIMAL PROTECTION

Research involving animals poses dilemmas not only for scientists who use animals in medical research but also for society as a whole. The current 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.

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.

I. STRONGLY COMMITTED TO THE 3Rs¹

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), in 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).

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. Ethics committees oversee 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 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. Good science requires that animals remain in good health and are subject to minimal pain or distress.

II. A COMPANY-WIDE POLICY ON ANIMAL PROTECTION

We developed a policy on animal protection to promote a shared vision of how animals are considered 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.

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.

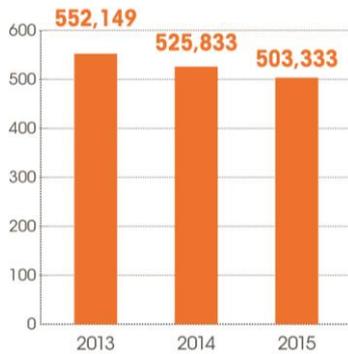
III. INDICATORS

1. Use of animals within our facilities

In 2014, we undertook the first comprehensive mapping of animal use within our facilities based on 2013 activities to ensure consistency and exhaustiveness of figures. In subsequent years, we renewed this comprehensive mapping of animal use within our facilities for 2014 and 2015.

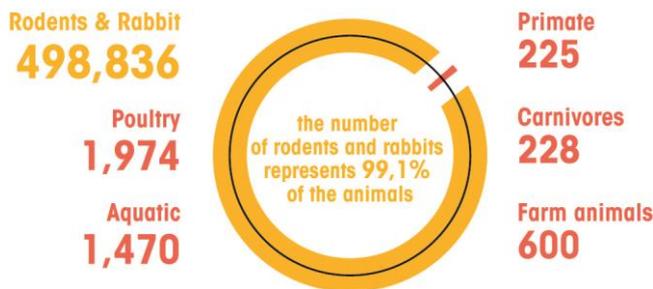
¹ THE 3Rs: Replacing use of animals with any other methods when a non-animal method is feasible, Reducing the number of animals necessary to ensure reliable, quality scientific results, and Refining techniques to promote animal welfare and minimize pain and distress.

Graph 1: Variation in numbers of animal used across the Sanofi Group, 2013-2015



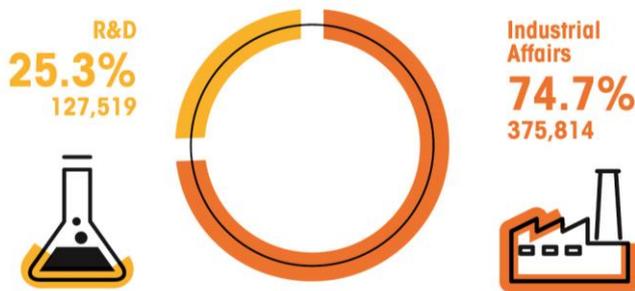
Use of animals in-house has steadily decreased over the last three years. The decrease is due to paying active attention to the 3Rs and to the focus of certain internal research and testing programs.

Graphs 2: Animal use per species (2015)



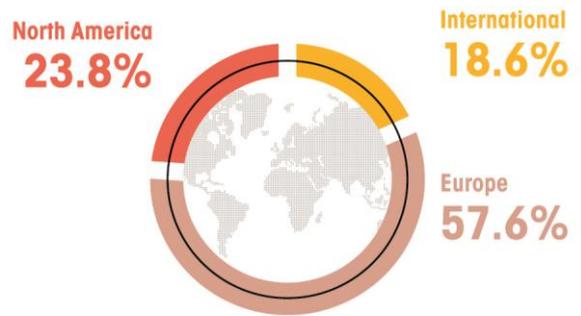
The majority of animals used (99%) are rodents and rabbits. Less than 1% are fish, poultry, farm animals, carnivores and non-human primates.

Graph 3: Breakdown of animal use per activity (2015)



In 2015, about 75% of animals were used to support our batch release activity to ensure the safety and efficacy of commercialized vaccines and drugs. About 25% of animals are used for research purposes.

Graph 4: Breakdown of animal use per region (2015)



Sanofi applies high standards globally. Over 80% of animal use takes place in the context of strict regulatory environments in Europe and Northern America.

2. Animal welfare inspections by responsible authorities

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.

3. Results of AAALAC accreditation site visits in 2016

The Sanofi Animal Welfare Steering Committee is committed to ensure the AAALAC accreditation of all our facilities using animals by 2020. By the end of 2016, 13 of our facilities that use animals had been AAALAC accredited. Newly accredited programs and re-accreditations in 2016 include:

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

4. Number of contract research organizations (CROs) and suppliers audited in 2016

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.

IV. ACHIEVEMENTS ABOUT THE 3Rs

In 2016 there were many examples of outreach within Sanofi and with external partners to increase awareness of the 3Rs. Below we provide several examples.

1. Rehoming dogs and horses with animal 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 (almost 100 horses) in collaboration with 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.

2. Sanofi Pasteur issues 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.

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

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.

4. Strong presence at the conference organized by the European Commission with 9 out of 35 posters on alternatives

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 seen at the European conference, "Non-Animal Approaches – the way forward," where Sanofi scientists presented nine of a total of 35 posters during the conference. Sanofi will continue to support the 3Rs through advancing science.

5. Our animal protection roadmap

- Improve transparency regarding animal use and the Integrated Research and Testing Strategy (3Rs)
- Accelerate the development of 3Rs programs with the support of senior management
- Continuous assessment of compliance with the Sanofi Policy on the Protection of Animals, beyond regulatory inspections and accreditation
- Ensure support to Sanofi sites by contributing to AAALAC accreditation and compliance of third parties (breeders, CROs, public institutions)
- Contribute to regulatory challenges, especially those related to the revision of the European Directive, and initiate a culture of openness
- Create a global ethics committee related to animal experimentation, reporting to the Sanofi Bioethics Committee

V. 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 2015 Report Update.