

RESEARCH AND ANIMAL EXPERIMENTATION IN SWITZERLAND: THE 3Rs PRINCIPLE

William Russel and Rex Burch proposed the 3Rs principle in 1959 with the objective to protect the animals used in the context of research. The 3Rs principle has since then established itself internationally as the foundation of an ethical approach to research with animals and is an integral part of today's Swiss research landscape.

What is the 3Rs principle? ¹

1. **Replace animal research whenever possible**

Develop and encourage the use of methods in experiments or other scientific procedures that achieve a given purpose without using living animals or animal-derived material. Replacement methods include *in vitro* (in test tubes) approaches using cultured cells, tissues and organs (organoids), *in silico* simulation and computational methods (computer simulation) as well as testing strategies that take into account existing data. The development of the *lung-on-a-chip* technology to study pulmonary inflammation or of brain organoids to study the toxic effects of chemicals on brain cells are examples of replacement methods. It is also considered as replacement when researchers use animals that, "based on current scientific evidence, are not considered capable of experiencing suffering" including nematodes (roundworms) and insects.

2. **Reduce the number of animals involved**

Develop and encourage the use of methods that allow either comparable levels of information to be obtained using fewer animals in scientific procedures, or more information from the same number of animals. Reduction methods include the optimization of breeding programmes or the use of non-invasive imaging techniques. Other reduction approaches aim at improving experimental designs and biostatistical analyses to increase the reproducibility of animal studies and their relevance for humans and animals. The sharing among researchers from different institutions of animals, organs, tissues or cells from animals is yet another way to reduce the number of animals in research.

¹ <https://www.swiss3rcc.org/en/3rs-resources/what-are-the-3rs> and <https://www.blv.admin.ch/blv/en/home/tiere/tierversuche/3r-prinzipien.html>

3. ***Refine methodologies to minimise constraints***

Develop and encourage the use of methods which alleviate or minimise potential pain, suffering and distress, and which enhance animal well-being. Refinement methods include the improvement of housing conditions, handling methods, anaesthesia and analgesia, but also of health monitoring, euthanasia and the development of better tools to assess animals' suffering and well-being. Training programmes that allow researchers to better recognise animals' pain or distress, the improvement of pain management in animals undergoing surgery or the development of non-invasive interventions or monitoring are examples of refinement projects.

How is the 3Rs principle applied?

In research

Researchers must apply the 3Rs principle when asking for an authorisation for animal experimentation. This means that each researcher must:

- Use alternative methods whenever possible and demonstrate that there are no alternative methods for answering the scientific questions when an animal model is chosen;
- Justify the number of animals involved and reduce it as much as possible – e.g. through optimisation of experimental designs and sharing of animals or animal material;
- Use all procedures to improve the daily life of laboratory animals and apply appropriate methodologies to minimise constraints;
- Justify the necessity of working with an animal model, explaining the expected benefits for the society or the environment and clearly specify the constraints on the animal.

By developing alternative methods

In Switzerland, an authorisation for animal experiments can only be issued if there are no alternative methods available to achieve the research goal. Research is constantly making progress in the field of alternative methods. For example, tests to assess the health risks of chemicals, in particular their irritant potential on skin and eyes, which have until now been carried out on laboratory animals, are increasingly being replaced by alternative methods. These methods are also beneficial for the animals or the environment. A toxicity test recently developed in Switzerland, for example, uses cultured gill cells from fish to determine the acute toxicity of water samples and chemicals on fish. This is a crucial step, as until now there had been a lack of recognised alternatives to testing on live fish. However, in many fields, animal experiments remain indispensable for certain specific steps of the research project, particularly when the organism must be considered as a whole and with all its complexity.

In animal facilities

Reduction and refinement principles are also applied in animal facilities. The implementation of breeding plans and strategies as well as improved housing conditions and of handling methods contribute, for example, to reducing the number of laboratory animals and ensuring their welfare.

Swiss 3R Competence Centre

The Swiss research institutions are committed to apply the 3Rs principle. In order to promote and further implement it, eleven Swiss universities and higher education institutions conducting animal research together with the association of Switzerland's research-based pharmaceutical industry (Interpharma), the Federal Food Safety and Veterinary Office (FSVO) and the Swiss Animal Protection (SAP) founded in 2018 the Swiss 3R Competence Centre (3RCC).

The task of the 3RCC is to promote the 3Rs principle in Switzerland and to favour its implementation by funding and developing research, training and communication projects that advance the application of the 3Rs principle. Involving researchers, students and animal caretakers, the Centre organises workshops and conferences and develops training programmes on the 3Rs for Swiss institutions. It provides a network and communication platform where it shares good practice and up-to-date information on the 3Rs principle and on alternative methods to animal experimentation. The 3RCC also initiated a biostatistics task force, which aims to support researchers in the design and analysis of their studies. It lastly hosts the Swiss Culture of Care Group, which includes representatives of academic institutions and industry, veterinarians, animal welfare officers, animal caretakers and 3R coordinators. It is dedicated to promoting a culture of care and focuses especially on practical refinements in animal housing and husbandry.

As part of their in-kind commitment, the member universities employ 3R coordinators who promote the implementation of the 3RCC's research, training and communication strategy within their institutions and support the Centre in its activities. Within the 3RCC, member universities work closely with representatives of the animal facilities and animal welfare officers networks (Swiss Animal Facilities Network and Animal Welfare Officer Network) as well as with representatives of the Swiss Animal Protection, of the Federal Veterinary Office and of the pharmaceutical industry.

The 3RCC is the successor to the 3R Research Foundation Switzerland, which between 1987 and 2017 funded 146 3Rs projects worth CHF 18.8 million. The 3RCC funded 10 projects worth a total of CHF 2.5 million since its foundation in 2018. At least half of the projects the 3RCC financed so far aims to replace animals in research.

Combine complementary methods

According to a survey the 3RCC conducted, the primary motivation of researchers to apply the 3Rs principle and use and develop alternative methods is their concern about animal welfare. The second reason given is that they also want to improve the scientific quality of their research including the reproducibility and the relevance of their studies for humans and animals. The survey also showed that most researchers use more than one approach in parallel, combining the use of non-animal and animal procedures, a strategy that keeps the use of animals to a minimum. This is also reflected in the fact that, in a large proportion of the projects funded by the Swiss National Science Foundation in the fields of biology and medicine, researchers use alternative methods and animal methods side by side.

National Research Programme "Advancing 3Rs - Animals, Research and Society"

In 2021, the Federal Council launched a National Research Programme (NRP) "Advancing 3Rs - Animals, Research and Society" with a budget of CHF 20 million over five years. With its three research priorities (innovation; implementation: opportunities and obstacles; ethics and society), the NRP aims to reduce the number of animal experiments, replace them and reduce the strain on animals. It will be managed in close collaboration with the 3RCC.