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RESEARCH AND ANIMAL EXPERIMENTATION IN SWITZERLAND: ALTERNATIVE METHODS

Animal experiments and so-called alternative methods are not two clearly separate paths in research: they are complementary and closely interdependent.

In silico, *in vitro* and *in vivo* are three complementary methods

Scientific research is based on various complementary methods, which contribute to the acquisition of new knowledge and the development of new therapies:

- *in silico* to study and predict the behaviour of a part of the organism by computer modelling;
- *in vitro* to study a part of the organism, for example by means of cell culture;
- *in vivo* to study a living, complete and autonomous organism in all the complexity of its functioning.

So-called alternative methods (*in silico* and *in vitro*) are preferred whenever possible for ethical, legal and economic reasons. They have great potential, but animal experiments (*in vivo*) remain irreplaceable if the organism is to be considered as a whole and with all its complexity. Cells, tissues and organoids can be cultivated today, but they are only a model of what happens in real life. After successful *in vitro* tests, additional *in vivo* tests must be carried out to confirm the hypothesis. The animal model is not completely reliable as a preclinical model for human diseases, but its record is positive, in particular in treating systemic diseases such as cancer or infections (e.g. with coronaviruses). Biomedical research needs animal experiments to understand the interactions between mechanisms, organs, chemical substances and other factors.

Alternative methods have priority

In Switzerland, all animal experiments are subject to an authorisation procedure, which ensures that the use of animals is only authorised if there are no alternative methods to achieve the intended purpose. For each experiment, the researcher must justify the choice of the animal model and prove that there is no alternative that would involve less constraint for the animals or that could be carried out without animals.

The use of animal models remains necessary today

There is a growing number of alternative methods generating reliable and robust results. However, in the current state of scientific knowledge, they do not allow the reproduction of whole organisms and diseases in all their complexity. The use of animal models remains necessary for research on serious diseases and for the development of new medical treatments and procedures that save lives and reduce suffering.

In the case of coronavirus, for example, no reliably tested vaccine can be used for humans without first being tested on animals. Animal testing is set to ensure that vaccines do not have undesirable systemic effects or undesirable side effects. Research is far from a situation where experimental vaccines could be tested sufficiently on cells for efficacy and safety and be given directly to the population at risk. This would be neither ethical nor legal.

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Rules require animal testing

For the safety of patients, the regulatory authorities for pharmaceutical and chemical products require prior animal testing. Potential therapies developed *in vitro* on cells are then selected on the basis of their efficacy and safety in animal models (preclinical research) and thus reviewed before moving on to human clinical trials.

Why animal experiments for basic research?

The aim of researchers is not to work on animals, but on disease patterns. Basic research aims to generate knowledge, without which applied research and the concrete results it produces could not be developed. Understanding the phenomena observed opens up prospects in essential and diverse areas such as the functioning of organs and cell systems, the development of neurodegenerative diseases, the mechanisms of cancer cell development, etc.

Alternative methods developed through animal research

Research is constantly making progress in the field of alternative methods. It is now possible to reproduce a tumour *in vitro* in three dimensions to test the best treatment combinations. The development of organoids will possibly replace the animal model in many research projects. Remarkably, this progress would not have been possible without animal research: the development of organoids is the result of research with animals, and mice have been used to find out how to breed intestinal fragments that can then replace animal experiments for certain purposes. Most cells are grown in environments of animal origin. The *in vitro* method does not necessarily mean that there are no animal components used.

No funds exclusively for animal research

The Swiss National Science Foundation (SNSF) does not distinguish between the use of alternative methods and the use of animal models when funding research projects. The criteria for funding are based on expected gain in knowledge, relevance and originality of the research question, suitability of the proposed methods for answering the question. The ethical and legal framework must be respected. The SNSF only funds experiments approved by the cantonal animal testing commissions. The researchers focus on answering the questions with the best models: sometimes with alternative methods, sometimes with an animal model, and usually with both. In 2019, 38% of SNSF's funding in the fields of biology and medicine was allocated to projects that use animal models, among other approaches. Large parts of these projects also use alternative methods.

Science is committed to the development of solid and relevant alternative methods

Whenever possible, researchers use *in silico* and *in vitro* methods. Alternative methods are developed with all available means, also to protect the animals. However, the development of suitable and reliable alternative methods takes time. Switzerland can and must invest even more in the development of alternative methods. However, it is essential that the funds invested in alternative methods be allocated on the basis of the quality of the projects and proof that the developed methods are sound and relevant.

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With the establishment of the 3R Competence Centre Switzerland (3RCC) in 2018, funds are available exclusively to promote and further implement the 3Rs principles, i.e. to replace animal models, to reduce the number of animals used and to refine methods used with animals in order to relieve or reduce pain and stress and improve their well-being. The members of the 3RCC are eleven Swiss universities and higher education institutions, the association of Switzerland's research-based pharmaceutical industry (Interpharma), the Federal Food Safety and Veterinary Office (FSVO) and the Swiss Animal Protection (SAP).

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.