ETHICS FOR ANIMAL EXPERIMENTATION

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PHYS-770

26th of February 2025

ANIMAL EXPERIMENTATION

Current status

- animal experimentation is a **controversial topic**, with both supporters and critics.
- most people agree that animal experimentation is **crucial** for scientific and medical progress.
  - to test and study new drugs, treatments, and medical procedures
  - to gain a better understanding of basic biological processes
- the **ethical considerations** surrounding this practice cannot be ignored

ANIMAL EXPERIMENTATION

- Its contribution to science
  - animals sharing many **biological and physiological similarities with humans**, making them **valuable models** for studying **human diseases and conditions.**
  - rats and mice have been used extensively in medical research because their **physiology and genetics** are similar to those of humans +  .
  - many medical treatments that are used today were first tested and developed using animal models.

Magnetic resonance spectroscopy in the rodent brain: Experts' consensus recommendations - PubMed (nih.gov)

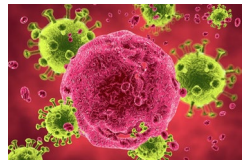
ANIMAL EXPERIMENTATION

- Ethical controversy
  - use of animals for **human benefit**.
  - ethical concerns surrounding the treatment of animals used in research.
  - many organizations and individuals advocate for the reduction or elimination of animal experimentation in favor of **alternative methods** such as computer modeling or in vitro testing.
  - while animal experimentation is **necessary** for scientific research, it is important to consider **ethical considerations** when using animals in research.
    - ensuring their **welfare**, exploring alternative methods, and interpreting the results carefully.

PROS AND CONS OF ANIMAL EXPERIMENTATION

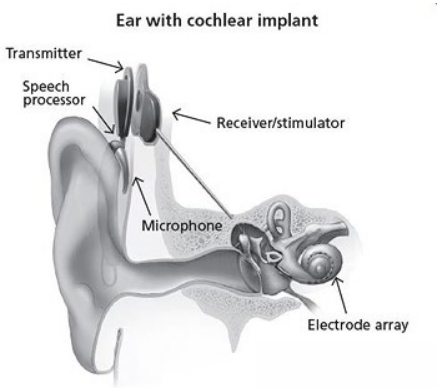
THE PROS OF ANIMAL EXPERIMENTATION

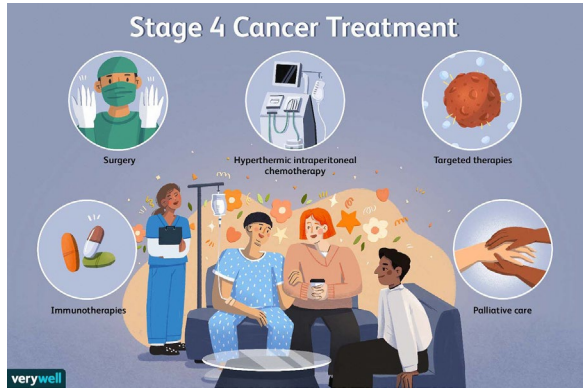
- Advancement in medicine
  - medical breakthroughs over the years:
    - Penicillin
    - Insulin
    - Covid-19 vaccines
    - HIV treatment



THE PROS OF ANIMAL EXPERIMENTATION

- Advancement in medicine
  - medical breakthroughs over the years:
    - Implants and medical devices
    - Cancer treatment



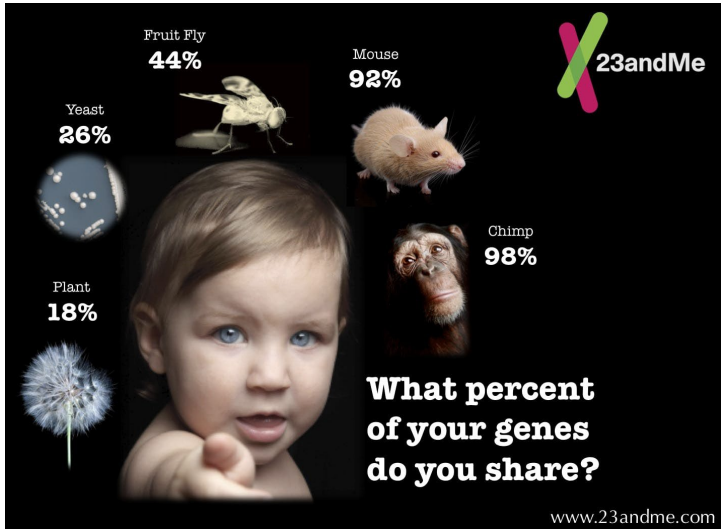


THE PROS OF ANIMAL EXPERIMENTATION

- Safety testing
  - drugs
  - cosmetics
  - household chemicals

THE PROS OF ANIMAL EXPERIMENTATION

- Basic research-understanding disease
  - animals share many **biological and genetic similarities** with humans, which makes them indispensable for understanding the basic biological processes and mechanisms of diseases
  - studying animal models, researchers can learn about the progression of diseases and develop strategies for prevention and development of new treatments and therapies



Magnetic resonance spectroscopy in the rodent brain: Experts' consensus recommendations - PubMed (nih.gov)

THE PROS OF ANIMAL EXPERIMENTATION

- Environmental Impact
  - Animal experimentation is also used to understand the impact of environmental factors on living organisms.
  - Help researchers develop solutions to environmental problems and improve human health.

THE PROS OF ANIMAL EXPERIMENTATION

- Veterinary medicine
  - Animal experimentation is also used to develop new treatments for animals, including surgical techniques and therapies for diseases.
  - This can improve the health and well-being of animals and help advance veterinary medicine.

THE CONS OF ANIMAL EXPERIMENTATION

- Animals used in experiments can experience pain, suffering, and even death.
  - Treatment / handling.
- There are also concerns that animal models may not accurately represent human physiology or human diseases (e.g GBM – at date there is no animal model fully reproducing the human disease).
- Ethical considerations around using animals for human benefit, especially when alternative methods exist.

THE CONS OF ANIMAL EXPERIMENTATION

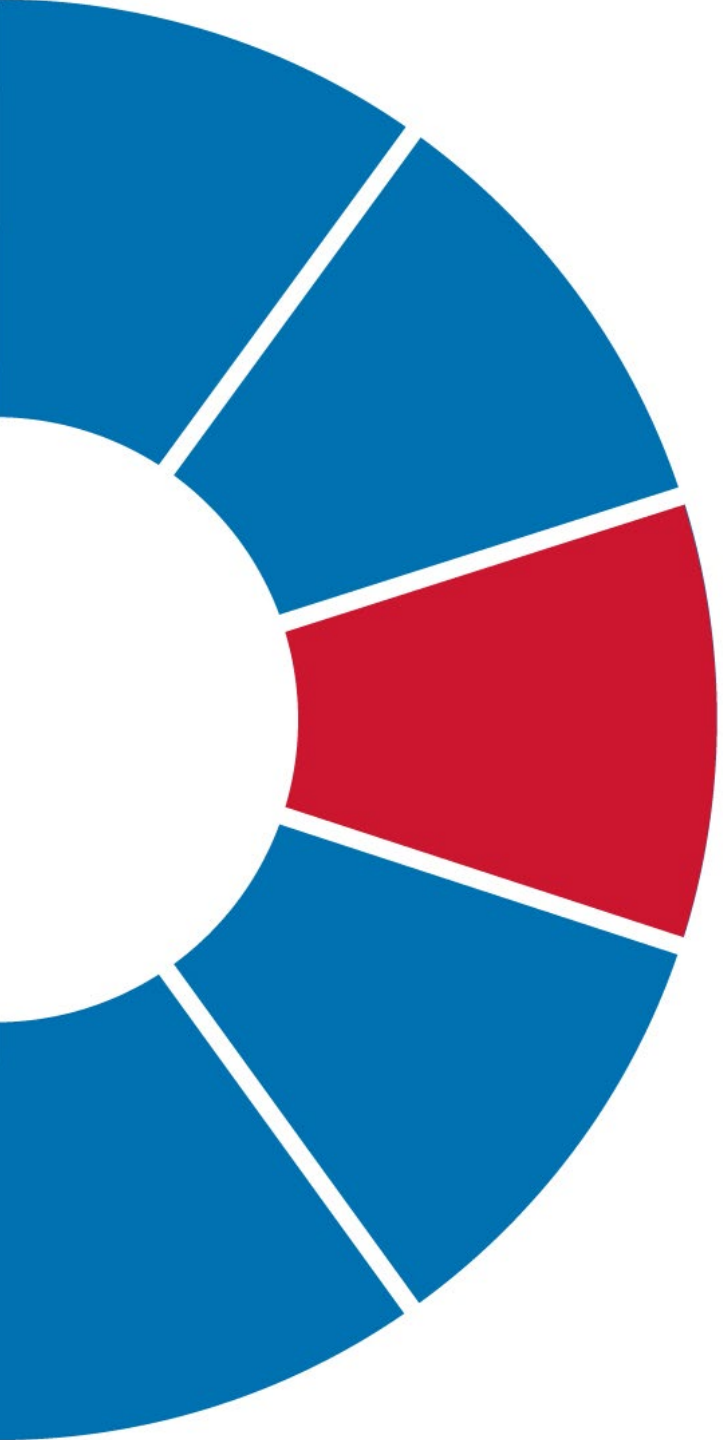
- Sometimes limited applicability to humans
  - Animals may not respond to drugs and other interventions in the same way that humans do.

THE CONS OF ANIMAL EXPERIMENTATION

- Cost
  - Animal experimentation can be expensive, both in terms of the resources required to conduct the experiments and the cost of caring for the animals involved.

THE CONS OF ANIMAL EXPERIMENTATION

- Alternatives
  - With advances in technology and science, there are now many alternatives to animal experimentation, such as in **vitro testing** and **computer modeling**.
  - BUT --- limitations and may not be suitable for all types of research or testing.
  - In some cases, animal testing are still necessary to fully understand the effects of a drug or intervention on living organisms before human trials can be conducted.
  - Use of alternatives to animal experimentation is not intended to completely replace animal testing, but rather to reduce the number of animals used in research and testing and to improve the accuracy and reliability of the results obtained.



ETHICAL PRINCIPLES

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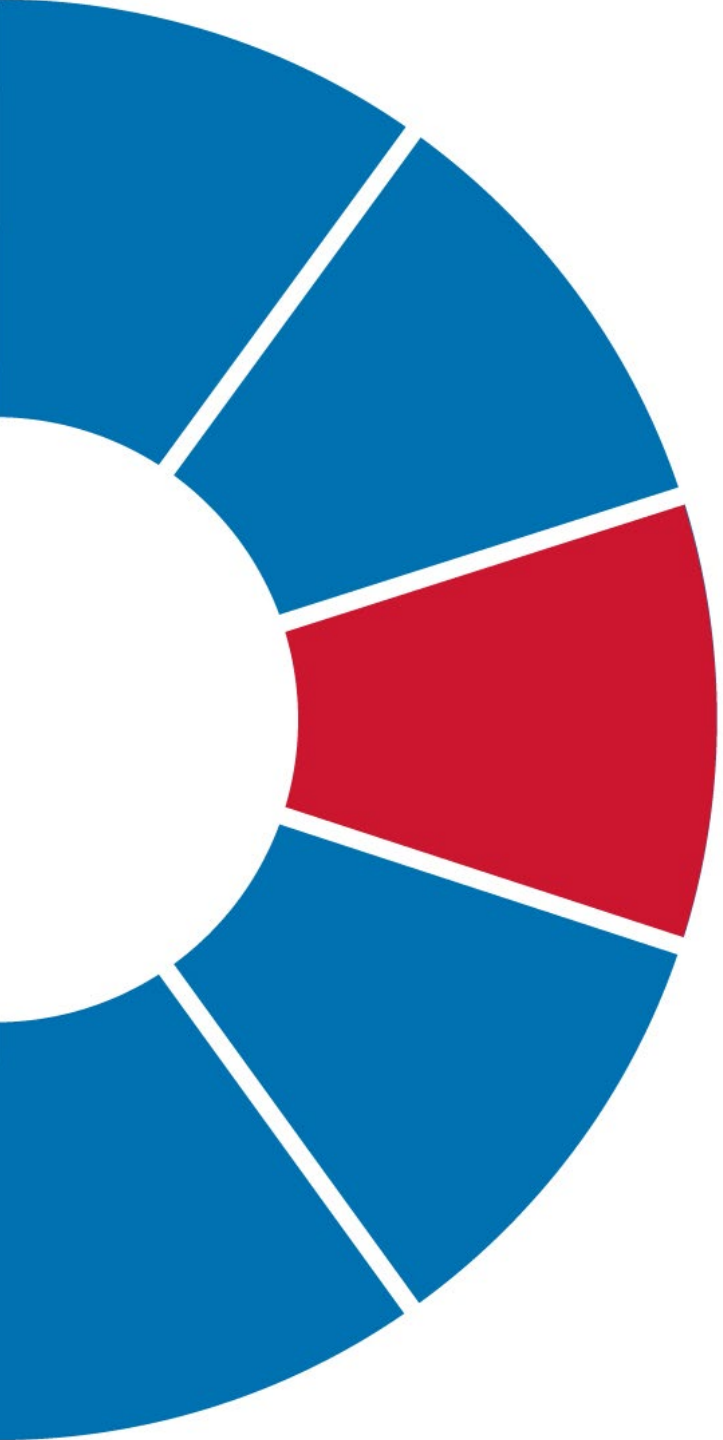
- Animal experimentation is guided by several ethical principles:
  - The 3**R**s: replacement, reduction and refinement:
    - **R**eplacement: which means that alternative methods should be used whenever possible.
    - **R**eduction: which means that the number of animals used should be minimized as much as possible. Researchers should only use the minimum number of animals necessary to achieve reliable scientific results.
    - **R**efinement: which means that the methods used should be designed to minimize animal pain, suffering, and distress. Researchers should use techniques that reduce pain and suffering, such as anesthesia and analgesia.

ETHICAL PRINCIPLES

- **Scientific validity:** animal studies should be designed to produce reliable and relevant results that can advance scientific knowledge and improve human and animal health
- **Transparency and openness**: researchers should be transparent about their methods and results. They should share their data and findings with the scientific community and the public
- **Regulatory compliance:** researchers should comply with laws and regulations governing the use of animals in research. They should obtain appropriate approvals and permits, and they should ensure that their experiments are conducted in accordance with established standards and guidelines



REGULATORY FRAMEWORKS

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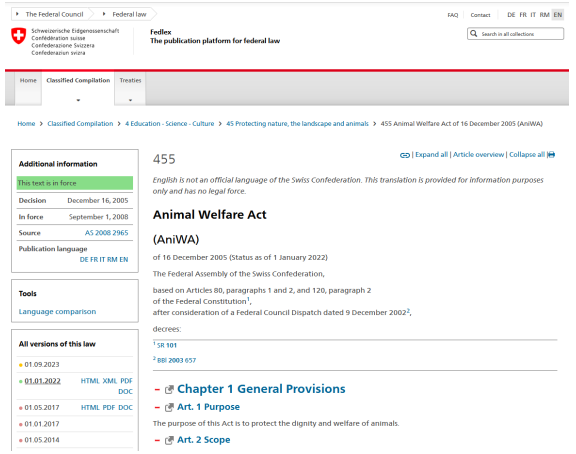
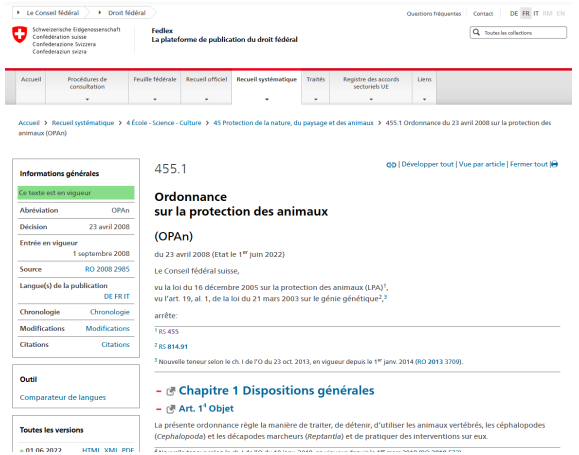
Swiss legislation

- In Switzerland, the regulatory framework for animal experimentation is based on the Animal Welfare Act (SR 455 Tierschutzgesetz/ Loi fédérale sur la protection des animaux (LPA, du 16 décembre 2005 (Etat le 1er janvier 2022))
- and its Ordinance on the Protection of Animals Used for Scientific Purposes (SR 455.1 Tierschutzverordnung/ Ordonnance sur la protection des animaux(OPAn) du 23 avril 2008 (Etat le 1er juin 2022)





REGULATORY FRAMEWORKS

Swiss legislation

- The legislation aims to ensure that animals used for scientific purposes are treated **ethically and with respect for their welfare**.
- The Act and its Ordinance require that any animal experimentation in Switzerland is approved by the cantonal veterinary office and must comply with the **3Rs** principles (Replacement, Reduction, and Refinement).
- Switzerland is a signatory to the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes.
- Swiss researchers conducting animal experiments must adhere to the guidelines established by the Swiss Academy of Medical Sciences, which provide additional guidance on the ethical use of animals in research.

REGULATORY FRAMEWORKS

- **Regulatory bodies and their responsibilities**
  - **Federal Food Safety and Veterinary Office** (FSVO): The FSVO is the national authority responsible for implementing the Federal Act on Animal Protection and its Ordinance on the Protection of Animals Used for Scientific Purposes.
  - The FSVO approves animal experimentation projects and monitors compliance with animal welfare regulations.

REGULATORY FRAMEWORKS

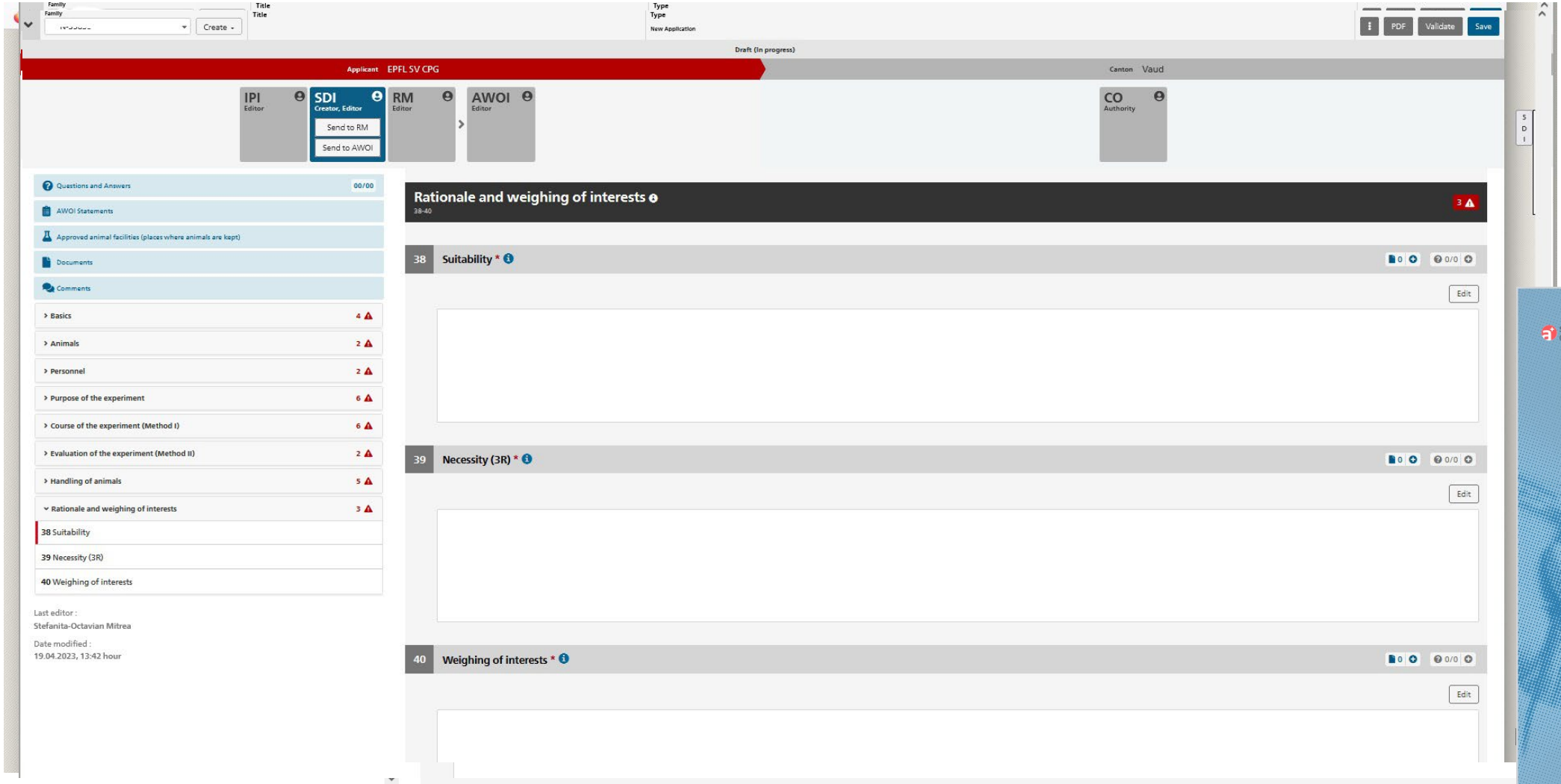
- **Regulatory bodies and their responsibilities**
  - **Cantonal veterinary offices**: The cantonal veterinary offices are responsible for issuing licenses for animal experimentation projects and ensuring that they comply with national and cantonal regulations.
  - Each canton has its own veterinary office, and the offices work closely with the FSVO
  - They carry out inspections for every new animal license and recurrent inspections ensuring the legal and smooth conduction of the experiments

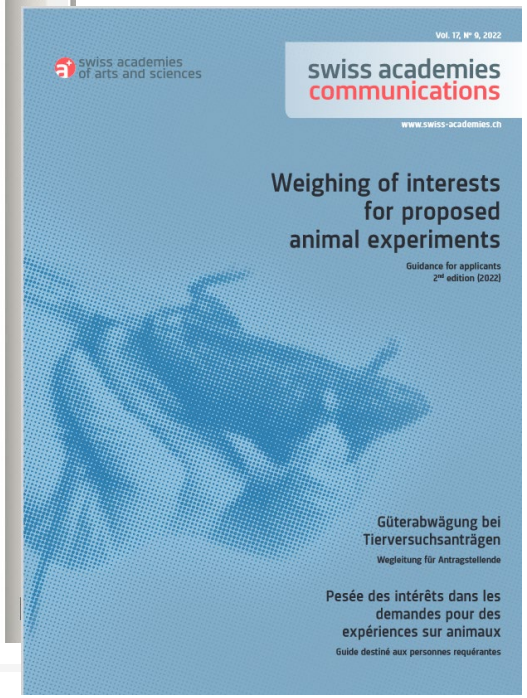
REGULATORY FRAMEWORKS

- **Regulatory bodies and their responsibilities**
  - **Ethical committees:** Every institution that conducts animal experimentation in Switzerland must have an ethical committee.
  - These committees are responsible for evaluating the scientific and ethical justifications of animal experimentation projects before they are approved by the veterinary office.

REGULATORY FRAMEWORKS

- **Obtaning a licence for animal experimentation**
  - Anyone wishing to conduct animal experiments must inform the cantonal authorities of this intention.
  - Applications have to be submitted using forms issued by the Federal Food Safety and Veterinary Office (FSVO)
  - The principal form is called Form A and is divided in several sections.
  - The filled form is verified by the animal welfare officer of the institution and then submitted and evaluated by the Cantonal Veterinary Authority office and by an Ethical Committee(2 commissions) that serve as regulatory bodies.





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SUITABILITY

- Reasons for selecting the animal model with regard to the experimental objective and depiction of scientific validity (i.e. construct validity, internal validity, and external validity) and reproducibility of the expected findings, if appropriate.
- Show the extent to which it is possible to generalise or extrapolate to other study conditions, populations of animals or species, incl. humans.

NECESSITY (3R)

- Reasoning why the intended aim of the experiment **cannot be achieved by methods that comply better with the 3R criteria**.
- Explain also why a method that does not require animals does not exist (**Replace**), why the experiment cannot be carried out with fewer animals (**Reduce**), and how all possibilities to reduce the strain on the animals are exploited (**Refine**)

WEIGHING OF INTERESTS

- Assessment of the application with regard to the balance between expected gains in knowledge or other results (interests) and the pain, suffering, harm, injury or anxiety inflicted (strain on the animals) in accordance with ethical considerations.
- For more details on the weighing of interests, see the “Explanatory notes to Form A” and the document “Weighing of interests in animal experimentation” [LINK www.blv.admin.ch].

SAMPLE SIZE

Statistical considerations for a parallel trial where the outcome is a measurement

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Request

0.05 Significance Level — 2 sided *(default is 0.05, two-sided)*

Standard Deviation of the outcome variable *(if known)*

Enter two of the following three values and the remaining value will be calculated

1. Total number of patients
2. 0.8 Power (usually 0.8 or 0.9)
3. Minimal detectable difference (specify one of the following):
   a. Difference in means
   b. 18 % Location of the mean of one treatement group in terms of a percentile of the other treatment group.

Calculate

Response

Calculation performed at: 22.01.2014 09:38:06

The provided parameters were: significance level (adjusted for sidedness) = 0.025, standard deviation = undefined, number of patients = undefined, power = 0.8, difference in means = undefined, location of mean in one group as a percentile of the other group = 0.82.

The variable calculated was the total number of patients.

A total of 40 patients will enter this two-treatment parallel-design study. The probability is 80 percent that the study will detect a treatment difference at a two-sided 0.05 significance level, if the true difference between treatments is 0.915 times the standard deviation.

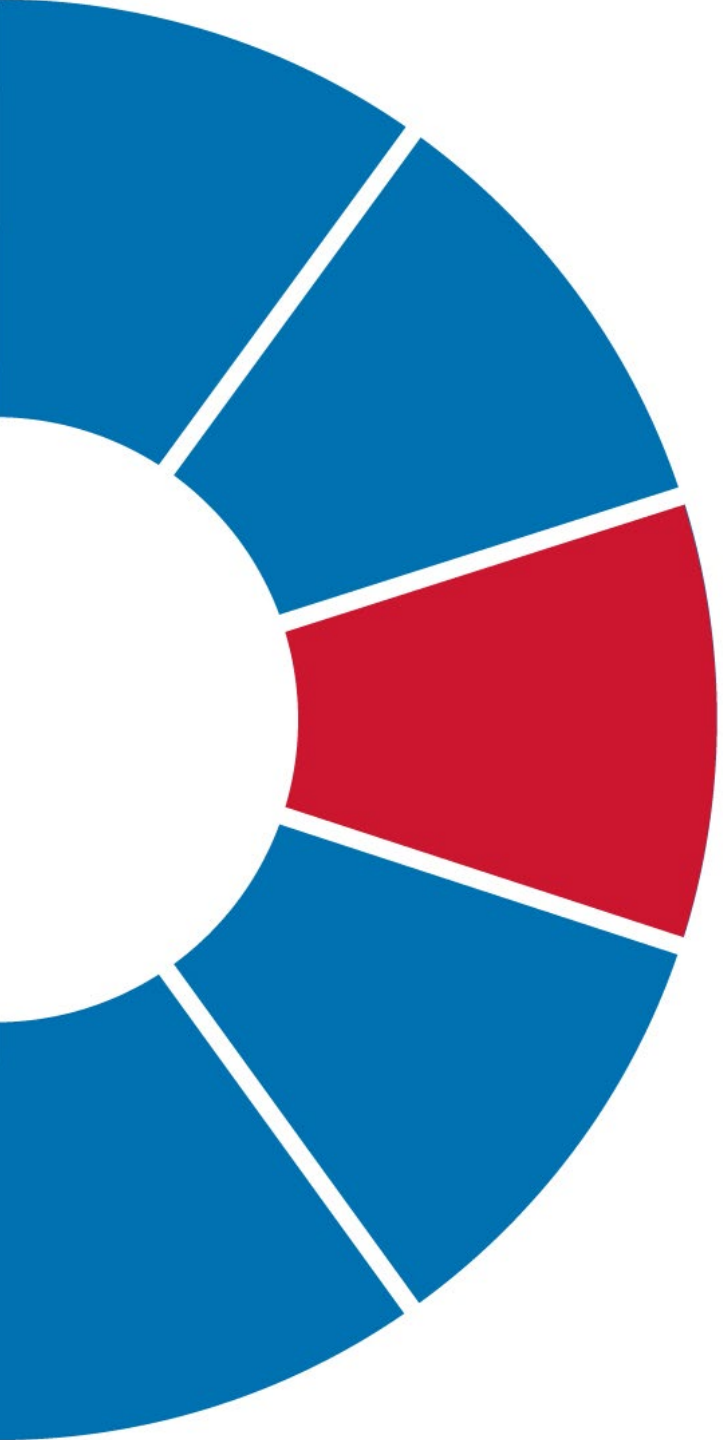
This software developed by David Schoenfeld, Ph.D. (dschoenfeld@partners.org), with support from the MGH Mallinckrodt General Clinical Research Center. Javascript version developed by REMorse.

These calculations are based on assumptions which may not be true for the clinical trial that you are planning. We do not guarantee the accuracy of these calculations or their suitability for your application. We suggest that you speak to a biostatistical consultant when planning a clinical trial. Please contact us if you have any questions or problems using this software

SAMPLE SIZE

Considerations -3Rs

- Longitudinal studies vs single time point
- End of experiment – ex-vivo studies
- Mutimodal and multiparametric studies
- Accuracy, precision, variability of the model



ALTERNATIVES TO ANIMAL EXPERIMENTATION

ALTERNATIVES TO ANIMAL EXPERIMENTATION

- **Are they enough?**
  - Alternatives to animal experimentation are not always exact, but they are constantly being improved and refined to provide better and more accurate results.
  - No single method can replace animal experimentation entirely, and a combination of approaches may be necessary to achieve the best results

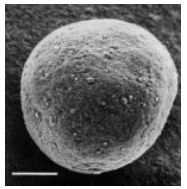
ALTERNATIVES TO ANIMAL EXPERIMENTATION

Examples of alternatives

- **In vitro testing**, involves testing on cells and tissues outside of the body, such as in a petri dish.
- While this method can provide valuable insights into the effects of drugs and chemicals on cells, it does not take into account the complex interactions that occur within a living organism.
- Therefore, in vitro testing is often used in combination with animal testing to provide a more complete picture of the potential effects of a drug or chemical.

E16 rat embryos - telencephalon,

3D organotopic brain cell cultures
Spheres (∅ => 0.5 mm)
with all types of brain cells.
(bar: 100 µm)



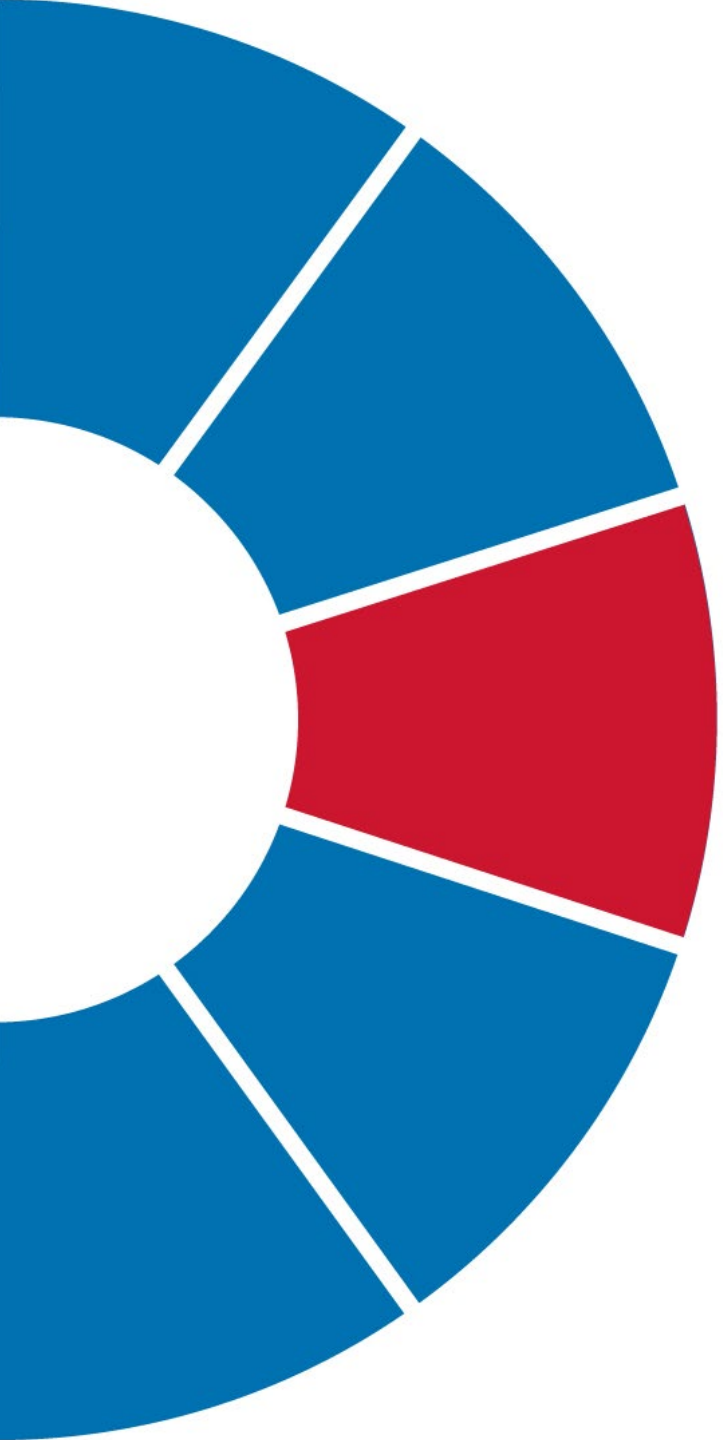
Prof O Braissant CHUV

Magnetic resonance spectroscopy in the rodent brain: Experts' consensus recommendations - Lanz - 2021 - NMR in Biomedicine - Wiley Online Library

ALTERNATIVES TO ANIMAL EXPERIMENTATION

Examples of alternatives

- **Computer modeling** is another alternative to animal experimentation, where mathematical and computational models are used to simulate the behavior of biological systems.
- While computer modeling can provide insights into complex biological processes, it is limited by the accuracy of the data used to develop the models.
- Ground truth



CONCLUSION

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- **Important to remember**
  - Animal experimentation is a **necessary** but controversial practice that requires ethical considerations
  - Ethical principles, such as the 3**R**s, guide animal experimentation, and regulatory frameworks ensure that it is **conducted ethically**
  - All animal experimentation are subject to Swiss and European legislation and controlled by the **regulatory bodies**

CONCLUSION

Important to remember

- Alternatives to animal experimentation exist, but they cannot always replace animal experiments.
- As we continue to explore scientific and medical advancements, it is important to balance the benefits of animal experimentation with the ethical considerations surrounding it.
- All animal experimentation should be carried on avoiding any effect on the **wellbeing of the animals** at any moment, which will be a benefit most importantly for the animals but as well for the outcome of the experiments.

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