

National Research Programme NRP 79

“Advancing 3R – Animals, Research and Society”

Call document



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What are National Research Programmes (NRPs)?

Research carried out by National Research Programmes consists of research projects that contribute to the solution of contemporary problems of national importance. Under the provisions of Article 10, paragraph 2 of the Federal Act on Research and Innovation of 14 December 2012 (version of 1 January 2018), the Federal Council selects the topics and focus areas to be researched in NRPs and mandates full responsibility for implementing the programmes to the Swiss National Science Foundation.

The Federal Ordinance on the Federal Act on Research and Innovation of 29 November 2013 (version of 1 January 2018, Article 3) describes the NRP funding scheme as follows:

¹ The National Research Programmes (NRPs) of the Swiss National Science Foundation (SNSF) are a means of generating and conducting coordinated research projects that pursue a common goal.

² Topics of research are generally appropriate for National Research Programmes if:

- a. Swiss research can make a significant contribution to the resolution of the problem;
- b. solutions require research contributions from multiple disciplines;
- c. research on the problem can be expected to produce research results that have practical applications within a five-year period.

³ In exceptional cases, an NRP may also be used for the targeted creation of additional research potential in Switzerland.

⁴ The following criteria are also taken into consideration in setting forth the topics of National Research Programmes:

- a. the programmes can provide the scientific basis for decision-making by the government and administration;
- b. the programmes can be conducted with international collaboration".

Summary

The new National Research Programme “Advancing 3R – Animals, Research and Society” (NRP 79) sets out two overarching goals on the basis of the 3Rs. From a bioscience technology perspective, it will devise and develop methods and instruments that, if systematically implemented and applied, will reduce the number of animal experiments and animals used in testing in university and private-sector research in Switzerland by a demonstrably significant amount. From a humanities and social science perspective, NRP 79 aims to examine in an innovative way the ethical, legal, social, historical, cultural and economic aspects of animal testing and the use of animals in science. The data and new findings obtained will provide animal welfare campaigners and proponents of animal testing with a shared basis for discussion that will drive forward societal discourse.

The NRP comprises three research modules:

Innovation: This module sets out to promote innovative research that will make a direct or indirect contribution to the effective application of the 3Rs in the real-world setting.

Implementation: Central to this module is a problem-driven approach intended to deliver information on barriers to the implementation of the 3Rs in various research areas, propose strategies for overcoming these barriers and also facilitate the application of existing knowledge.

Ethics and society: This module covers research into ethical, conceptual and societal issues connected with the 3Rs and the use of animals for scientific purposes in the context of the development of the relationship between humans and animals.

The programme will operate with overall funding of CHF 20 million and carry out research for a five-year period.

1. Introduction

Background

Experiments on and involving animals are an established and widespread feature of research. They can help elucidate biological and psychological processes and physiological functions, serve as a model for investigating diseases, for toxicological investigations and scientific training or improve our understanding of organisms and their ecosystems, thus contributing to conservation efforts. Beginning in the early 19th century, our knowledge about animals' biological functions, their psychological processes (motivational, cognitive, perceptual and emotional) and the factors that influence their natural behaviour have grown exponentially. One consequence of this knowledge is that ethical considerations have become more prominent, bringing vivisection and invasive animal testing, among other activities, under close scientific and societal scrutiny. In an attempt to address the dichotomy between the benefits of the knowledge that animal experimentation provides and the suffering that it causes, the scientists William M.S. Russell and Rex L. Burch set out the "Three Rs" in 1959.¹ The 3Rs are *replace*, *reduce* and *refine*, the objective being to replace animal testing by alternative experimental approaches, to reduce the number of animals used to the essential minimum, and to avoid exposing animals to unnecessary and disproportionate physical or other stresses by refining experimental approaches and providing more natural living conditions. The 3Rs also aim to improve the quality, information value and knowledge gained from biomedical research and to encourage researchers to search for new experimental approaches that deliver better-quality and more reliable results. Unlike animal rights-driven approaches, Russell and Burch only regard exposing animals to stress for research purposes as an ethical issue if such stress is unnecessary or avoidable.

Various efforts and initiatives to substantially reduce the number of animals used for experiments and to improve their welfare have been undertaken nationally and internationally over the course of several decades by enshrining the 3Rs in animal welfare legislation. After a period of drastic reduction of the number of animal experiments, they have been virtually stagnating in Switzerland in recent years^{2,3}. At the same time, scientists' awareness of the ethical component of animal experimentation has grown, animal ethics principles have been formulated and incorporated into national legislation, and there are indications that the relationship between humans and animals is changing. It is therefore unsurprising that public and scientific debate has gathered momentum once more. The dispute between people who criticise or are totally opposed to animal experiments and those who regard them as essential and advocate them seems to be particularly prominent. However, a much less polarised dialogue that avoids simple for-and-against stances and endeavours to build bridges is also taking place. Although misunderstandings and confrontations may play a role in these debates, they are part of the normality of an open, democratic society. It

¹ Russell, W. M. S., and R. L. Burch. 1959. *The principles of humane experimental technique*. Methuen.

² Animal experimentation statistics issued by the Federal Food Safety and Veterinary Office (FSVO), <https://www.blv.admin.ch/blv/en/home/tiere/tierversuche.html>

³ Report on the statistics on the use of animals for scientific purposes in the Member States of the European Union in 2015-2017, <https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:52020SC0010&from=EN>

could even be argued that a continuous, shared negotiation process is essential to the ongoing development of scientific and normative standards.

The two fundamental positions in the debate can be summarised as follows: Having considered the implications, and in the knowledge that at least some animals in experiments are exposed to stresses, proponents of animal experiments regard them as necessary. The proponents further point to their requirement for investigating and understanding the mechanisms, underlying biological processes and particularly the causalities of pathophysiological change in an organism. Furthermore, they are adamant that complex interrelationships can only be elucidated and interpreted by addressing the research questions in cells, organ models (*in vitro*) and live animal models (*in vivo*). Some even doubt that it is possible to provide plausible and scientifically founded answers to fundamental issues using substitute techniques of the type advocated by replacement and are therefore sceptical of alternative methods of investigating complex *in vivo* processes.

Opponents of animal experiments contend that new developments in e.g. organ modelling or the increasingly advanced options provided by *in silico* computer-assisted simulation and recently developed experimental methods provide alternatives capable of replacing most harmful animal experiments. Limited applicability to humans of knowledge obtained from animal experimentation is frequently voiced, though highly contested. Accordingly, the scientific justification for animal experiments and exposing animals to stress for research purposes is disputed, with consequences for the legal and ethical legitimacy of such experiments.

The National Research Programme 79 “Advancing 3R – Animals, Research and Society” (NRP 79) aims to promote innovative ideas and constructive approaches for solving problems regarding animal experiments and their legitimacy. It should contribute to the application and development of 3R methods, bring transparency to the context of public debate and review the science-related ethical arguments – in a fact-based, cross-disciplinary and ethically reflected way. It also aims to create greater long-term attention and sustainability for research into all three Rs to ensure that awareness for animals, their needs and their protection is increased. By addressing scientific as well as societal and institutional factors, NRP 79 will encourage a critical investigation of the responsibility held by our society regarding animal research and take a reflective attitude to balance hopes to benefit from the knowledge generated by research on the one hand, and exposure of animals to considerable harm for this purpose on the other hand.

The 3Rs

In formulating the 3Rs – replace, reduce, refine – Russell and Burch set out to give empirical researchers a simple set of rules that would improve the way experimental animals are kept and used, thereby simultaneously increasing the quality, information value and knowledge obtained from research involving animal experiments. It was also Russell and Burch’s intention to encourage researchers to look for new experimental approaches and methods that would deliver results of even better quality. Back then, they defined the 3Rs as follows:

“Replacement means the substitution for conscious living higher animals of insentient material. Reduction means reduction in the numbers of animals used to obtain information of a given amount and precision. Refinement means any decrease in the incidence or severity of inhumane procedures applied to those animals which still have to be used.”

Since Russell and Burch first published their work on the 3Rs, researchers and authorities around the world have adopted replacement, reduction and refinement as essential guidelines for promoting the humane treatment of laboratory animals^{4,5}. However, the way each of the 3Rs is defined has undergone significant transformation since 1959 with multiple incongruent interpretations being used by various authorities, agencies and individuals⁶. For the purpose of this programme, the following working definitions were drawn from the EU directives (2010/63/EU), article 4, in order to have a coherent understanding and clarity of wording: **Replacement**: wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure; **Reduction**: the number of animals used in projects is reduced to a minimum without compromising the objectives of the project; **Refinement**: eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals, by refinement of breeding, accommodation and care, and of methods used in procedures.

To legitimise animal experiments by including further ethical considerations, it has been suggested that further Rs, such as replication, reproducibility, rigour, robustness, registration and reporting, should be added to the original three.^{7,8} Doing so would, in particular, increase the emphasis on the responsibility of researchers and also increase the focus on good laboratory practice. However, the extensive discussion on expanding the 3Rs into several Rs also conceals the danger of making an internationally established standard unwieldy. Irrespective of this, by legally prescribing a harm-benefit analysis. Switzerland and all EU Member States, for example, have tightened up the requirements for animal experiments above and beyond the 3Rs. The decision criterion “outcome-centred necessity” for evaluation of planned animal experiments, implemented in various legislations, puts further legal and ethical restrictions on the empirical scientists. This can be seen as an indicator that the 3Rs are not sufficient for evaluating and conducting animal experiments humanely.

Mandate

In March 2020, the Secretariat for Education, Research and Innovation (SERI) mandated the Swiss National Science Foundation (SNSF) to assess the feasibility of conducting a National Research Programme (NRP) to promote the 3Rs in research in Switzerland. At the same time, the SERI tasked the SNSF with developing a programme concept that would define the aims of the programme and the key research issues to be addressed. The National Research Council of the SNSF elected the

⁴ Hubrecht, Robert C., and Elizabeth Carter. 2019. “The 3Rs and Humane Experimental Technique: Implementing Change”. *Animals* 9(10):754.

⁵ Bayne, Kathryn, Gudde S. Ramachandra, Ekaterina A. Rivera, and Jianfei Wang. 2015. “The Evolution of Animal Welfare and the 3Rs in Brazil, China, and India”. *Journal of the American Association for Laboratory Animal Science : JAALAS* 54(2):181–91.

⁶ Tannenbaum, J., and B. T. Bennett. 2015. Russell and Burch's 3Rs then and now: the need for clarity in definition and purpose. *J Am Assoc Lab Anim Sci.* 54(2):120–132.

⁷ Macleod, Malcolm, and Swapna Mohan. 2019. “Reproducibility and Rigor in Animal-Based Research”. *ILAR Journal* 60(1):17–23.

⁸ Strech, Daniel, and Ulrich Dirnagl. 2019. “3Rs Missing: Animal Research without Scientific Value Is Unethical”. *BMJ Open Science* 3(1): bmjos-2018-000048.

members of the Steering Committee on 3 November 2020. The Steering Committee will ensure the strategic management of the programme for its duration. NRP 79 will operate with an overall funding of CHF 20 million and conduct research work for a period of five years.

National and international research environment

Since 1 July 1994, Switzerland's Animal Welfare Act⁹ and Animal Welfare Ordinance¹⁰ have been geared to European Council Directive 86/609/EEC¹¹ of 24 November 1986 on the approximation of laws, regulations and administrative provisions of the Member States regarding the protection of animals used for experimental and other scientific purposes and Directive 2010/63/EU¹² of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. Recital (11) of Directive 2010/63/EU makes explicit reference to the 3Rs. Although these Directives provide a basis for uniform treatment of animal experiments and the statistical recording of such experiments throughout European territory, it is difficult or even impossible to make meaningful comparisons owing to inter-country differences in the statistics that are recorded. For example, animal testing that is classified as severity level 0 according to Swiss legislation (e.g. behavioural observations, removal of organs and tissue from dead animals) accounts for around 39% of all animal experiments in Switzerland and is recorded in the FSVO statistics. EU member states, however, do not report such experiments as animal testing. Instead, the use of animals for scientific purposes is only considered a procedure that falls under the directive, if "pain, suffering, distress or lasting harm equivalent to, or higher than that caused by the introduction of a needle, in accordance to good veterinary practices" is inflicted on the animal invasively or non-invasively; i.e. experiments that would be classified as severity level 1 to 3 in Switzerland. A further important difference is that the EU only counts animals once for statistical purposes, whereas Switzerland counts animals each calendar year, for the duration of the experiment.

In the last twenty years, most countries have added directives governing animal research in their national legislation. Furthermore, the majority have set up special centres that are generally made up of representatives of government and supervisory authorities, research and teaching, industry, animal welfare and animal protection groups. Norecopa, an online resource established on 10 October 2007, provides a comprehensive overview of activities, organisations, new approaches and guidelines connected with animal testing, the 3Rs and alternative methods in Europe and the USA¹³. These national centres are primarily engaged in training, advice provision, communication and networking. In a small number of cases, centres also provide research financing.

Following its establishment in 2018, the Swiss 3R Competence Centre received 64 and 96 submissions in response to its 2018 and 2019 calls for proposals respectively, and financed six projects in 2018 and four in 2019.

⁹ Animal Welfare Act, <https://www.admin.ch/opc/en/classified-compilation/20022103/index.html>

¹⁰ Animal Welfare Ordinance (in German), <https://www.admin.ch/opc/de/classified-compilation/20080796/index.html>

¹¹ 86/609/EEC, <https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=LEGISSUM:l28104&from=EN>

¹² 2010/63/EU, <https://eur-lex.europa.eu/legal-content/EN/TXT/HTML/?uri=CELEX:32010L0063&from=EN>

¹³ Norecopa, <https://norecopa.no/>

Although some initiatives and projects aimed at intensifying implementation of the 3Rs are already in progress, NRP 79 “Advancing 3R – Animals, research and society” sets out to point the way for systematic, comprehensive research of future options and the necessary, realistic advances, limitations and barriers of implementation, taking account of the change in relations between humans and animals over recent years. NRP 79 promises to provide a ‘reality check’ and important steps towards the thorough and effective implementation of the 3Rs, as well as a transparent basis for assessing where this approach may lead and where its opportunities and limitations lie.

2. Objectives and priorities of the programme

Swiss animal welfare legislation sets out detailed regulations on animal husbandry and research with animals. In terms of research involving animals, the Animal Welfare Act and the Animal Welfare Ordinance do not just govern the conditions under which laboratory animals are kept but, require application of the 3Rs – replace, reduce and refine – on the basis of Russell and Burch’s work in 1959. The 3Rs encapsulate efforts to *replace* animal testing by other experimental methods without using animals wherever possible, *reduce* the number of animals used in experiments and *refine* techniques so as to reduce the stress to animals.

The 3Rs are an integral part of national and international legislation on the use of animals in testing. The National Research Programme NRP 79 “Advancing 3R – Animals, Research and Society”, running until 2027, sets out two overarching goals on the basis of the 3Rs.

- 1) From a bioscience technology perspective, it will devise and develop methods and instruments that will reduce the number of animals used in experiments in academic and private research in Switzerland (including animals used for environmental safety and toxicology testing) or that contribute to substantially reducing the stress, suffering and pain experienced by animals in experiments and in husbandries. *In silico*, *in vitro* and *in vivo* approaches may be used. In addition, it will explore the research issues that cannot (yet) be resolved without animal testing and the research issues for which non-animal-based models can deliver comparable or even better results. The NRP will also investigate whether the improved availability and comparability of human (and animal) health data will gradually make animal testing for medical translation purposes superfluous or at least give a boost to the 3Rs. Possible approaches for each of the 3Rs could be computer simulation and data analysis by artificial intelligence for ‘replace’, data sharing for ‘reduce’, and imaging methods and improved pharmacophysiological procedures in experiments or improved euthanasia procedures for ‘refine’. Projects can explore each of the three Rs, either individually or in combination. In addition to projects that aim to develop, validate or improve methods and instruments, it will also be possible to carry out implementation studies that investigate the practical benefits (impact) for the 3Rs.
- 2) From a humanities and social science perspective, NRP 79 also aims to examine in an innovative way the ethical, legal, social, historical, cultural and economic aspects of animal testing and the use of animals in science. The data and new findings obtained will provide opponents and proponents of animal testing with a shared basis for discussion that will drive forward societal discourse. Possible subject areas include society’s ideas on the relationship between humans and animals and how these are changing (in this and other areas of life), the issue of relevant moral attributes such as consciousness, experience of

pain and memory in different species, opportunities and risks in scientific and public communication, the review criteria and processes adopted by animal experimentation committees, the problems associated with outsourcing animal testing to countries with fewer regulatory requirements, or the analysis of the impact of animal welfare standards in Switzerland and other countries on medical and bioscience research. The findings obtained during the projects may – particularly at the synthesis level – contribute to advancing the 3Rs and to a more informed public debate on the sensitive issue of animal testing over the coming decades.

This translates into the programme’s degree of success in “advancing the 3Rs”, which will be assessed from the short-, medium- and long-term perspectives at research, institutional and policy levels:

- New and improved tools and methods that increase the probability of successful 3R implementation as well as validation of existing tools and methods;
- Strategies to overcome the barriers to implementation; establishment of a system for monitoring the introduction or use of available 3R methods; overcoming practical obstacles: training, publication requirements, data sharing, costs, project registration etc.
- Initiatives to encourage greater 3R ambition across all sector levels (e.g. acknowledgement of achieved 3R improvements, rewarding system, career benefits);
- Demonstrated uptake of 3R tools and methods at all levels; inclusion in training programmes and curricula, in academia and regulatory bodies;
- Initiatives to increase awareness of policy makers to promote alternative methods and adapt regulatory procedures and legal requirements;
- Innovative tools to raise societal awareness, and to promote dialogue between researchers and the citizens regarding normative issues of animal research.

Three modules and cross-module questions arise from these goals:

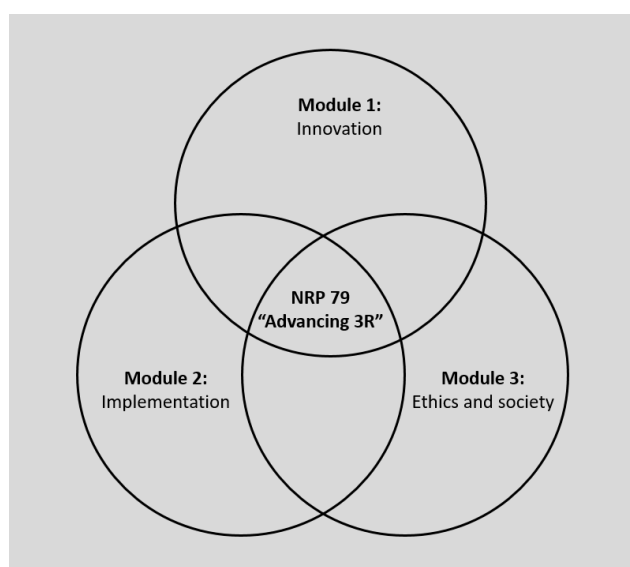
- Innovation: Module 1 sets out to promote innovative research that will make a contribution to the effective application of the 3Rs in the real-world setting.
- Implementation: Module 2 intends to deliver information on barriers to the implementation of the 3Rs in various research areas, propose strategies for overcoming these barriers and apply these strategies.
- Ethics and society: Module 3 covers research into ethical, conceptual and societal issues connected with the 3Rs and the use of animals for scientific purposes. This module further addresses animal research in light of the changes in human-animal relationship in Western societies and corresponding public perception-

In terms of **communication and knowledge transfer**, the goals of NRP 79 are to promote exchanges between research, researchers working with animals, social and philosophical scientists, and the target audience (e.g. policy makers, public administration, authorities, interest groups, NGOs and the public in general) of the programme throughout the duration of the NRP and, at the end of the programme, to support effective dissemination, so that the results and recommendations of the NRP are translated to the target audience.

3. Main research areas

Although the three focal areas (modules) – “Innovation”, “Implementation” and “Ethics and society” - are introduced and described individually, they should be regarded as interconnected and mutually interactive. For example, identifying obstacles to the implementation of the 3Rs (module 2) may impact the discovery of new methods (module 1); new trends in how the relationship between humans and animals is perceived (module 3) may remove certain obstacles (module 2); and new discoveries concerning 3Rs methodology (module 1) may impact the discussion on barriers (module 2).

This interdependence will shape the way the programme progresses and how the research groups collaborate and conduct research within the projects. NRPs organise and require attendance of symposia or summer schools and other forms of collaboration that will ensure a continuous dialogue at programme level between all the researchers involved in NRP 79.



Module 1 – “Innovation”

The following thematic clusters are expected to be investigated, but proposals that go beyond those are equally welcome:

- Innovations to advance the 3Rs specific to research areas and species:
 - Advancing existing and developing new 3R methods: cell lines, primary cells, stem cells, tissues, organoids, organs-on-chip, microphysiological systems, micro dosing, non-sentient animals, in silico, husbandry, etc.
 - Translating existing 3R methods into new fields
- Innovations to advance the 3Rs in general:
 - Advancing existing and developing new 3R methods that can be translated and used in various fields: e.g. statistical methodology advances in experimental

design to increase knowledge gain per animal used, innovative experimental designs and modelling strategies, biobanks, organ and tissue sharing, etc.

Innovations produced within this module may be eligible for support from Innosuisse for further development.

Project selection criteria are described under chapter 6 “Submission procedure and project selection”

Module 2 – “Implementation”

The aim of this module is to follow a problem-oriented approach leading to strategies that will make it possible to overcome obstacles to the implementation of the 3Rs.

The following thematic clusters are expected to be investigated, but proposals that go beyond those are equally welcome:

- Identification of challenges/barriers on the scientific, legal, economic, institutional and individual level, such as:
 - Methodological and scientific limitations of 3R strategies;
 - Challenges in aiming at replacing the “gold standard” animal experiment;
 - Practical barriers: education, publication requirements, data sharing, costs, etc;
 - Challenges in establishing 3R-friendly evaluation criteria of academic success;
 - Harmonisation of national and international statistics on experiments with animals, costs of animal experiments, severity levels, etc;
 - Adding value, e.g. by validating existing tools and methods;
- Instruments to identify 3R methods (e.g. 3R database or search tools) and assess 3R impact in a systematic manner;
- Developing strategies to overcome the barriers identified:
 - Top-down strategies: such as legal instruments and management tools and their potentials and limitations to translate the 3Rs into practice;
 - Bottom-up strategies: such as economic instruments and their potentials and limitations to translate the 3R into practice (incentives, benchmarking, credit systems, nudging, awards etc.).
- Gaining knowledge on committee work and legal procedures in order to improve implementation of the 3Rs;
- Research to identify measurable indicators of the advancements of the 3R approach;
- Translating 3R methods from one research area to other research areas.

Project selection criteria are described under chapter 6 “Submission procedure and project selection”

Module 3 – “Ethics and society”

The aim of the module is to research ethical, legal, social, historical, cultural and economic aspects regarding the 3Rs and animal use for scientific purposes, in light of the evolution of human-animal relationship. Even though this module provides space for theoretical reflection, e.g. on the relationship between humans and animals, it will encourage concrete deliberations or empirical studies that address specific issues contributing to our understanding of the constantly changing human-animal relationship and thus advancing the 3R approach.

The following thematic clusters are expected to be investigated, but proposals that go beyond those are equally welcome:

- Ethical foundations, methodological concerns, potentials and limitations of the 3R approach;
- Practical challenges of the 3R approach (e.g. applying the 3Rs; dealing with conflicts among the 3Rs; balancing the 3Rs etc.);
- Societal challenges of the 3Rs of ethical relevance in the broader sense:
 - Instrumental vs goal-oriented necessity: harm-benefit analysis;
 - National strategies vs. international developments;
 - The conceptual shift from animal experiments as a rule to animal experiments as an exception;
- The 3R approach in light of the evolution of the human-animal relationship;
- Acquisition of data about public perception of animal research and its future;
- Advancements and alternatives to the 3Rs and new ways of conceptualising humane animal experimentation that take ethical considerations into account;
- Developing innovative tools to promote research communication and public dialogue;
- Raising awareness and the quality of public debate (e.g. innovative tools to deal with the ethical dilemma, animal vs human rights, etc);
- Innovative tools to promote research communication and public dialogue.

Empirical studies including interventions that have measurable societal impact (stakeholders, experimenters etc.) as well as philosophical analysis, new policies or other analyses addressing significant problems in the field will constitute the main output of this module.

Project selection criteria are described under chapter 6 “Submission procedure and project selection”

4. Characteristics of NRP 79

Innovation and transferability to practice

The use of animals in research has long been an important topic, also in research funding. NRP 17, which was launched in 1988, already addressed alternatives to animal experiments. Since then, the research landscape has changed significantly. With the advancement of new technologies, including next-generation sequencing, 3D in vitro models, proteomics and bioinformatics tools, quantitative human biology data has become available; this has facilitated back-translation approaches that are expected to increase the translatability of animal to human data. The current call for proposals intends to take these changes into account. The aim is to bridge the gap between innovation and implementation. In addition to promoting 3R research, the NRP emphasises the relevance of implementing programme results in research projects involving animal experiments.

The development and implementation of new technologies may be jeopardised by premature disclosure (scientific or lay publications, printed or oral disclosure at conferences, workshops, etc). Please contact the technology transfer office of your institution before disclosing the results of your work. Protecting your research results should not delay research progress. For additional information, please consult (<https://switt.ch>) and ([Swiss Federal Institute of intellectual property](#)).

Promotion of junior researchers

NRP 79 also aims to increase research potential in the area of 3Rs and promulgate methods to replace, reduce and refine animal experiments in Switzerland by specifically promoting young researchers working in this area – not only in biomedical and natural sciences, but also in humanities and social sciences. On the one hand, the aim is to arouse the interest of young researchers with excellent projects but little experience in the field of 3Rs research and, on the other hand, to retain or attract young up-and-coming researchers who already have a track record in a relevant discipline. For this reason, NRP 79 introduces fellowships for post-doctoral researchers with initial experience in project management, who are particularly welcome to submit applications.

Within the framework of this fellowship, the research must be executed in Switzerland. Applicants should either have Swiss nationality or hold a degree from a Swiss university, or else be carrying out – or aiming to carry out – research in Switzerland. They must document that they will be hosted by an institution for the duration of the project and that the availability of the necessary scientific infrastructure is guaranteed. Written proof of support by the host institution is required at pre-proposal stage. The conditions favouring long-term integration of the applicant in the home institution need to be described.

In the context of this fellowship, the applicants can apply for their own salary, consumables and – where justified – for the assistance of a technician and/or a PhD student. The applicant's salary will be based on the standard salaries for corresponding positions at the home institution.

Additional requirements for this fellowship are as follows: The researchers must start the fellowship at the latest 5 years after obtaining their doctorate. Research topics should comply with the selection criteria defined in chapter 6 and with the goals of the programme. The proposed research

projects must be limited to a maximum of 48 months. This fellowship does not overlap with existing SNSF funding tools, since it is designed for more junior candidates with the aim of specifically promoting the research covered by the NRP 79. Similar SNSF funding tools are more selective and not linked to a particular theme.

International collaboration

In addition to strengthening 3Rs research at the national level, NRP 79 also intends to better embed and network this field of research at the international level. To this end, the NRP offers the possibility of support for research groups whose project is part of an ongoing international programme.

Inter-, multi- and transdisciplinary collaboration

NRP 79 calls for mono-, multi- and interdisciplinary approaches that, depending on the research question, draw on the perspectives of various disciplines from life science, medical sciences (human and veterinary medicine) and natural science, the humanities, social sciences, and engineering. Proposals with an inter- or multidisciplinary character embracing the goals of more than one module will be given preference.

Participating in NRPS implies participation in a number of programme-specific activities. Researchers should plan a minimum of 2 weeks for these programme-specific activities, organised by the NRP management team.

5. Practical significance and target audience

Within the framework of an NRP and its limited resources and duration, the scientific community will not be able to provide answers to all the questions raised by the scope of the programme. However, it will address many pressing questions and provide the first important evidence-based answers.

The practical benefits of the three modules can be summarised as follows:

- Propose innovative approaches to advance the 3Rs and to translate them into practice, including the immediate testing and validation of new 3Rs methods;
- Identify barriers and develop strategies to overcome problems of implementation; develop new scientific standards, procedures and evaluation criteria in order to promote the 3Rs;
- Propose conceptual analyses and empirically informed input as a basis to improve social dialogue and inform policy-makers.

6. Submission procedure and project selection

General conditions

Proposals are submitted and selected in a two-stage procedure: pre-proposals are submitted first, followed by an invitation to submit a full proposal if selected in the first evaluation round. Pre- and full proposals are expected to be submitted in English.

Research projects conducted under NRP 79 should last from a minimum of 36 months to a maximum of 48 months. NRP 79 will not fund the fourth year of PhD students' salaries in projects lasting under 48 months. Thus, projects lasting under 48 months and employing one or more PhD students must ensure their salaries are guaranteed for 48 months at project selection.

The average budget of a project is expected to lie between CHF 300,000 and 1,000,000. These figures are provided as a benchmark, and budgets below or above this range are not ruled out if the budget is sufficiently justified.

Collaboration with research groups in other countries is encouraged, provided the cooperation either generates significant added value that could not be achieved without cross-border cooperation or that it substantially enhances the proposed research with respect to content or methodology, or if the competencies of researchers from abroad are essential for the successful completion of the project. As a rule, the funding share requested for researchers abroad may amount to 20 – 50% of the requested research budget. For applicants from abroad, the norms and salary rates of the relevant country will be applied *mutatis mutandis*, with the SNSF maximum rates as the upper limit. In accordance with SNSF guidelines, overhead costs are paid directly to the home institution and under no circumstances directly at project level. Before submitting a proposal with a cross-border component, please contact the programme manager of NRP 79.

To allow for optimal coordination, approved projects must start no later than six months after the approval date.

The present NRP 79 Call document, the Funding Regulations of the SNSF and the General implementation regulations for the Funding Regulations provide the legal basis for the call. All forms, rules, regulations and instructions for the submission of proposals can be found on the mySNF web portal under 'information/documents' after selecting the corresponding NRP and creating a new application.

Only one call for projects is envisaged. However, in the event of significant thematic gaps in the coverage of the programme's objectives, a second call for projects may be launched.

Online submission on mySNF

Pre- and full proposals must be submitted online via the mySNF portal (www.mysnf.ch). Applicants need to register as mySNF users before they can submit an application. User accounts obtained in the past remain valid and provide access to all SNSF funding schemes. It is advisable to request new user accounts as early as possible via the mySNF homepage.

Pre-proposals

The deadline for the submission of pre-proposals is 3 August 2021, 17:00 Swiss local time.

In addition to the administrative data that needs to be entered directly in mySNF, the following documents must be uploaded in PDF format:

- **Project description**
Applicants must use the template provided on the mySNF portal under 'information/documents' in their newly created proposal. The project description includes details about the project team and the module allocation as well as five key publications of third parties regarding the project and a research plan. The project description must not exceed 5 pages, including the cover page and references.
- **Short CVs and list of five key publications** of the applicants
The CVs and a list of publications (last 5 years only) must not exceed a maximum of two pages for each applicant. Links to full publication lists may be included.
- **Supplementary documents** (support letters, confirmation of cooperation or co-financing, etc.) can be uploaded to in the appropriate container in mySNF.

Project descriptions and CVs exceeding the indicated length will not be considered.

Full proposals

The deadline for submitting full proposals is expected to be 25 January 2022, 17:00 Swiss local time.

Besides the administrative data and the data management plan to be entered directly in mySNF, the following documents need to be uploaded in PDF format:

- **Research plan**
Applicants must use the template provided on the mySNF portal under 'Information/documents' in their newly created proposal. The research plan must not exceed 20 pages, including the cover-page, tables, illustrations and the list of references.
- **Short CVs and publication lists of all applicants**
The CVs must not exceed two pages each and must adhere to the guidelines in mySNF. Publication lists must be submitted according to the guidelines in mySNF. Links to full publication lists may be included.
- **Supplementary documents** (support letters, confirmation of cooperation or co-financing, ethical approval, etc.) can be uploaded to the appropriate container in mySNF.

Project selection procedure

The Steering Committee evaluates the pre-proposals and reaches final decisions based on the selection criteria outlined below. In the process, it may refer to assessments provided by national and international reviewers.

In the second stage of the submission procedure, the Steering Committee will invite the authors of the selected pre-proposals to submit a full proposal. In the invitation, the Steering Committee may include recommendations or set conditions for the full proposal. Authors who are not invited to submit a full proposal will be informed accordingly by means of a ruling.

Based on external reviews as well as on their own evaluation, the Steering Committee will recommend a selection of full proposals to be either approved or rejected by the National Research Council (Programmes division and Presiding Board) of the SNSF.

Selection criteria

The Secretariat of the Programmes' division checks whether the personal and formal requirements are met before forwarding the proposal for scientific review (cf. chapter 2 of the Funding Regulations of the SNSF). Pre- and full proposals that do not meet the personal and formal requirements will not be processed further.

Pre- and full proposals will be reviewed based on the following criteria:

- **Compliance with the goals of NRP 79:** Proposals must reflect the programme's objectives and research focus, as delineated in chapters 2, 3 and 4, and comply with the programme's overall framework. This criterion is eliminatory, particularly at pre-proposal stage.
- **Scientific quality:** Proposals need to be state-of-the-art and comply with international research standards in terms of scientific quality and methodology. Proposals must contain an innovative component and must be relevant to completed or ongoing research projects in the same field.
- **Inter- and transdisciplinary projects, addressing questions from two or more modules:** NRP 79 calls for mono-, multi- and interdisciplinary approaches that, depending on the research question, draw on the perspectives of various disciplines from life science, medical sciences (human and veterinary medicine) and natural science, the humanities, social sciences, and engineering. Proposals with an inter- or multidisciplinary character embracing the goals of more than one module will be given preference
- **Application and implementation:** The potential for practical application and the implementation of results is a key element of NRPs. Projects with relevance to politics, society and practice, as well as projects that aim to develop answers to current and upcoming challenges in the Swiss economy and society, are therefore given priority. The selection will also take into account whether the expected results from the programme can serve as a scientific basis for governmental and administrative decisions. Therefore, projects that go beyond academia by integrating stakeholder views, the general public or national authorities are very welcome. The success criteria must be clearly stated in the proposals.
- **Personnel and infrastructure:** Applicants must have a sound scientific track record in the field of the proposal. Adequate personnel resources and an adequate infrastructure must be secured for the project.
- **Response to comments:** The Steering Committee may address comments, suggestions or recommendations to the research teams when inviting them to submit a full proposal. The

implementation of such suggestions or recommendations will be assessed in the full proposals.

Schedule and budget

The following schedule is envisaged for NRP 79:

Publication of the call for pre-proposals	18 May 2021
Deadline, submission of pre-proposals	3 August 2021
Selection meeting	18 October 2021
Invitation to submit full proposals	2 November 2021
Deadline, submission of full proposals	25 January 2022
Selection meeting	12 April 2022
Final decision on full proposals	4 May 2022
Communication of decisions	18 May 2022
Start of research	mid-May to mid-November 2022
End of research	mid-November 2027
Publication of the programme synthesis	mid-November 2028

Research projects cannot be prolonged beyond the duration of the research phase of the programme and will submit their final scientific report at the end of the programme's research phase.

Research in NRP 79 will run for a period of 5 years with a total budget of CHF 20 million. The individual projects of NRP 79 can have a maximum duration of 4 years. After project selection, research work must start within 6 months of the date of approval.

Preliminary funding allocation among the various research modules and administrative activities:

Module 1 - "Innovation"	CHF 7.0 million
Module 2 - "Implementation"	CHF 5.0 million
Module 3 - "Ethics and society"	CHF 5.0 million
Administration, programme synthesis, communication and dissemination	CHF 3.0 million

The proposed amounts for the individual modules are based on the budget structure of the expected projects, allowing competition within the modules and a presumed success rate of 20% per module. Modules 1 and 2 are aimed at costly projects involving basic research and application- or implementation-oriented research. Module 3 will probably attract less expensive projects, given the lower cost of research in the social sciences and humanities. Cross-modular research projects will be financed by funds from more than one module.

If required, the Steering Committee may reassess the above funding allocation.

7. Contacts

For questions regarding the submission of pre-proposals and full proposals, please contact the programme manager: Marjory Hunt, nfp79@snf.ch or 031 308 22 22

For questions concerning salaries and eligible costs, please contact the Head of Finance: Roman Sollberger: roman.sollberger@snf.ch or 031 308 22 22.

Technical help with mySNF and electronic submissions

Hotline:

Tel. + 41 31 308 22 99 (Français)

Tel. + 41 31 308 22 00 (Deutsch)

Tel. + 41 31 308 22 88 (English)

Email: mynsf.support@snf.ch

mySNF Homepage: www.mynsf.ch

8. Actors

Steering Committee of NRP 79

Prof. Herwig Grimm, Messerli Research Institute, Department of Interdisciplinary Life Sciences, Veterinary University Vienna, Medical University Vienna, University of Vienna, Austria (President)

Prof. Thorsten Buch, Institute of Laboratory Animal Science, University of Zurich, Switzerland

Prof. Josep Call, School of Psychology & Neuroscience, University of St Andrews, Scotland, United Kingdom

Prof. Olivier Guenat, Medical Faculty, ARTORG Center, University of Bern, Switzerland

Prof. Marcel Leist, In vitro toxicology and biomedicine & Director, Centre for Alternatives to Animal Testing in Europe (CAAT), University of Konstanz, Germany

Prof. Christine Nicol, Royal Veterinary College, University of London, United Kingdom

Prof. Anna Olsson, i3S – Institute for Research and Innovation in Health, University of Porto, Portugal

Dr. Elisa Passini, Department of Computer Science, University of Oxford, United Kingdom

Prof. Markus Wild, Department of Arts, Media, Philosophy, University of Basel, Switzerland

Delegate of the Programmes division of the SNSF Research Council

Prof. Nikola Biller-Andorno, Institute of Biomedical Ethics and History of Medicine, University of Zurich, Switzerland

Representative of the Swiss Federal Administration

Dr. med. vet. Kaspar Jörger, Animal Welfare Division, Federal Food Safety and Veterinary Office (FSVO), Bern, Switzerland

Representative of Innosuisse

Dr. Wilma Lukas, W Life Sciences, Nyon, Switzerland.

Representative of the Swiss 3R Competence Centre

Dr. Jenny Sandström, Swiss 3R Competence Centre, Bern, Switzerland

Programme Manager

Dr. Marjory Hunt, Swiss National Science Foundation (SNSF), Bern, Switzerland

Head of Knowledge Transfer

N.N.

Glossary

For the purpose of this programme, the following working definitions were drawn from Article 4 of EU Directive 2010/63/EU to provide a coherent understanding and clarity of the terms used.

The 3R principles:

- **Replace:** wherever possible, a scientifically satisfactory method or testing strategy, not entailing the use of live animals, shall be used instead of a procedure;
- **Reduce:** the number of animals used in projects is reduced to a minimum without compromising the objectives of the project;
- **Refine:** eliminating or reducing to the minimum any possible pain, suffering, distress or lasting harm to the animals, by refinement of breeding, accommodation and care, and of methods used in procedures.

Harm: typically refers to pain, suffering and distress

Animal experiments/procedure: according to Directive 2010/63/EU, any use, invasive or non-invasive, of an animal for experimental or other scientific purposes, with known or unknown outcome, or educational purposes, which may cause the animal a level of pain, suffering, distress or lasting harm equivalent to, or higher than, that caused by the introduction of a needle in accordance with good veterinary practice.

Scientific research:

- (a) basic research;
- (b) translational or applied research with any of the following aims:
 - (i) the avoidance, prevention, diagnosis or treatment of disease, ill-health or other abnormality or their effects in human beings, animals or plants;
 - (ii) the assessment, detection, regulation or modification of physiological conditions in human beings, animals or plants; or
 - (iii) the welfare of animals and the improvement of the production conditions for animals reared for agricultural purposes;
- (c) for any of the aims in point (b) in the development, manufacture or testing of the quality, effectiveness and safety of drugs, foodstuffs and feed-stuffs and other substances or products;
- (d) protection of the natural environment in the interests of the health or welfare of human beings or animals;
- (e) research aimed at preservation of the species;
- (f) higher education, or training for the acquisition, maintenance or improvement of vocational skills;
- (g) forensic inquiries.

Animal:

- (a) live non-human vertebrate animals, including:
 - (i) independently feeding larval forms; and
 - (ii) foetal forms of mammals as from the last third of their normal development;
- (b) live cephalopods.

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