Swiss 3R Competence Centre

# Swiss 3RCC Application Guidelines for Project Grants

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# Introduction

The 3RCC is a non-profit association that promotes the principles of 3R (reduction, refinement and replacement of animal experimentation) in Switzerland and facilitates their implementation in life sciences, with a main focus on high quality research, education and communication.

The Swiss 3RCC was founded in March 2018 and is a joint initiative of academia, industry, regulators, the government and animal welfare associations. The partners include eleven universities and higher education institutions from Switzerland, the Swiss association of the pharmaceutical industry (Interpharma), the Swiss Federal Food Safety and Veterinary Office (FSVO) and the Swiss Animal Protection (SAP).

The 3RCC also benefits from the support from the Swiss State Secretariat for Education, Research and Innovation (SERI), as it represents a scientific centre of national importance working on a non-commercial basis according to article 15 of the Federal Act on the Promotion of Research and Innovation (RIPA). SERI as well as the Swiss Federal Office of Public Health (FOPH) are observer members of the 3RCC association.

The Swiss 3R Competence Centre aims at:

- Promoting high quality science and care for animals by subsidizing scientific projects of excellence and quality on the 3R principles.
- Developing a 3R education strategy targeted at different educational programs.
- Building a network and communication platform and providing up-to-date information on 3R alternative methods to animal experimentation to stakeholders and all those involved and/or interested on alternatives to animal experimentation.

The centre also monitors the progress made in the implementation of the principles of 3Rs in Switzerland. Finally, it offers its services to authorities, teaching bodies and any other interested parties willing to gain additional information on the principles of 3Rs and on alternative methods to animal experimentation.

Any specific questions regarding the Swiss 3RCC or the application process should be directed to the secretariat of the 3RCC at +41 31 631 5621, or by email at *secretariat@swiss3RCC.org*.

# 1. The 3Rs

## Replacement

*Methods which permit a given purpose to be achieved without conducting experiments or other scientific procedures on animals.*

Replacement methods can represent full or partial replacement methodologies, based on i) use of non-animal approaches including testing strategy, human data, *in vitro* methods, *in silico* and computational methods, physicochemical properties and non-testing data, and/or on ii) use of animals that, based on current scientific evidence, are not considered capable of experiencing suffering. This includes the use of most invertebrates (except Cephalopods and Decapods) and immature forms of vertebrates (embryonic and foetal forms of mammals, birds and reptiles before the last third of gestation or incubation, fish and amphibians before they can feed independently). Furthermore, it also includes the use of primary cells, tissues, or organs taken from animals killed solely for this purpose.

## Reduction

*Methods for obtaining comparable levels of information from the use of fewer animals in scientific procedures, or for obtaining more information from the same number of animals.*

Reduction methods include careful design and analysis of animal-based experiments so that fewer animals can be used, such as optimization of breeding programmes, experimental designs, statistical analyses, sharing of animals and animal material (organs, tissues, cells) as well as longitudinal instead of cross-sectional measurements (if balanced against any additional suffering caused by repeated measurements) and measures to reduce unexplained variation in the data (if balanced against any additional loss of external validity).

## Refinement

*Methods which alleviate or minimise potential pain, suffering and distress, and which enhance animal well-being.*

Refinement applies to all aspects of animal care and use, including housing conditions, handling methods, anaesthesia and analgesia, habituation to procedures, execution of procedures, monitoring of health and well-being, humane endpoints, and euthanasia. Refinement also includes the development of better (i.e. more accurate, reliable, sensitive) tools to assess suffering and well-being.

# 2. Swiss 3RCC funding program remits and eligibility criteria

## 2.1. General overview

The Swiss 3R Competence Centre publishes regular calls for funding research projects dedicated to the replacement, reduction or refinement of animal experimentation. High quality projects that have high impact on the 3Rs and bring benefits as compared to existing methodologies in term of e.g. reliability, relevance and animal welfare will be favoured. Each of the three Rs will be subsidised in a balanced manner by the 3RCC funding program. Collaborative and multi-centre projects are encouraged.

The 3RCC funding program addresses basic and applied research that support the development, optimization, application and implementation of new or modified 3Rs approaches, methods and technologies. The maximum duration of projects is 3 years although extensions in time are possible upon justification. The necessary ethical approvals (e.g., licenses for animal testing, for the use of embryonic stem cells, clinical studies, etc.) need to be in place for funds of approved projects to be released.

The calls for projects are in the form of **open calls** and **targeted calls** i.e., addressing specific challenges for the advancement of the 3R principles in Switzerland.

**Open calls** enable the funding of researcher-driven projects aimed at the development, optimization, application and implementation of the 3R principles. The open call scheme considers projects more widely than conventional research grant schemes. An example may be the introduction and testing of new educational concepts, usually not supported by traditional research funding. Since the advancement of the 3Rs requires the implementation and sometimes commercialization of 3R research results, researchers are also encouraged to apply for translational and bench-to-market projects.

**Targeted calls** aim at solving long-standing problems and/or existing gaps regarding the application and advancement of the 3R principles. Topics of the targeted calls will be outlined in detail in the published call by the 3RCC.

## 2.2. Eligibility criteria

**Lead applicant eligibility**

- Lead applicants should be a Swiss-based researcher who can demonstrate that they will direct the proposed research and be actively engaged in carrying it throughout its duration. Applicants must be active in research-related activities at an eligible institution (see below) in Switzerland at least 50% of their time at the time of submission.
- The minimum formal qualification required is a graduate degree, although it would normally be expected that the applicant has been awarded a PhD, or is a MD or Dr. Med. Vet.
- Applications involving *less experienced* researchers should be made in collaboration with a more senior colleague.
- Lead applicants may already hold a grant from the Swiss 3RCC and other funding bodies for research related to the topic for which new funds are being sought. It is important that applicants state whether any financial support from another body is already provided.
- Lead applicants may only have one project lead application under consideration by the 3RCC during a call. There is no restriction on whether this proposal or others are under consideration by other funding bodies, but this should be clearly stated and described in both the cover letter and in section 12: Application Finances of the project proposal.
- Lead applicants are responsible for finding a host Research Organisation who will act as their employer and will manage the administration of the Project Grant for its full duration.
- Applicants or those employed by the 3RCC project grant may spend up to 6 months at a research institution abroad, yet this must be indicated in advance in the "Project Plan" section of the application.

**Lead institutional eligibility**

The 3RCC funding applies to public and non-profit research institutions including e.g.,

- Public Swiss Universities
- Swiss Federal Institutes of Technology
- Swiss Universities of Applied Sciences
- University (associated) Hospitals
- Non-commercial research centres outside the higher education sector.

Collaborative and multi-centre projects are encouraged including international collaboration as well as collaboration with private/industry/SME research groups. However, the lead organization should be a Swiss-based public research institution and funding will be allocated to Swiss-based lead institutions only. Industry partners may participate with in-kind contributions to the project.

In case of any doubt in eligibility, please contact the 3RCC office.

## 2.3. Funding scheme

Funding is provided on a yearly basis with 90% of the total budget funding equally distributed during the duration of the project, whereas the remaining 10% is withheld until the final report is accepted by the 3RCC. In the cases where the total project duration is not in whole years (e.g. 18 months), the project funding is allocated proportional to the time remaining.

For example for a 3-year project, the following settlements would be made:

| **Time** | **Payment** *(percentage of total budget)* |
|---|---|
| Upon signature | 30% |
| Year 1 *(12 months after signature)* | 30% |
| Year 2 | 30% |
| Approval of final report | 10% |

In case of an 18-month duration project, a first settlement of 60% of the total budget would be given at the official start of project, a second settlement of 30% after 1 year, and the remaining 10% after acceptance of the final report.

Infrastructure costs will *not* be covered by this grant.

# 3. How to apply

Applicants to the Swiss 3RCC Funding Program are required to complete and submit the standardised application form, which can be downloaded from the 3RCC website. Section 4 of this document provides guidance on completing the guided application form.

By submitting the application, lead applicants are confirming that the information given in the application is complete, that it has been discussed with those responsible at the hosting institution, and the contents have been agreed upon by all co-applicants. Applicants commit to their active engagement in the project and are responsible for its overall management, and agree to administer the project funds if selected.

- Completed applications should be sent in a single email to secretariat@swiss3RCC.org
- All documents should be submitted as PDF files. All application files, except for the cover letter, may be combined into a single PDF.
- All required documents should be clearly labelled and added as email attachments.
- Failure to complete mandatory fields on the application form and to submit all required attachments are likely to result in the rejection/ return of the application.
- Text word limits are indicated for each section and must not be exceeded.
- The entirety of the application must be written in English.
- The use of acronyms should be kept to a minimum.

## Resubmissions

- The 3RCC does not allow resubmission of previously unsuccessful proposals, unless explicitly invited by the Scientific Advisory Board during the previous evaluation. Proposals identified as uninvited resubmissions will not be further processed.
- Where a resubmission is invited, a cover letter summarising any revisions made must accompany the proposal. Please note that our willingness to accept a re-submitted proposal in no way implies that funding will be forthcoming.
- Proposals similar to any previously declined application and having no explicit invitation for resubmission will not be considered unless substantially revised. In these cases, the 3RCC expects applicants to recognise the similarity to their previous submission and explicitly

note the major revisions in the cover letter. Our resubmissions policy is part of a suite of demand management measures, to help alleviate pressure on all involved with our peer review process.

# 4. Completing the application

## 4.1. Basic overview

- Project Title: Please provide your own title for the project. This should be both clearly descriptive and concise.
- Indicate which of the 3Rs your project most closely target.
- Keywords: include up to 10 keywords that are most relevant to your project proposal.
- Project Duration: The maximum funding period for the Project Grant is 36 months. Applicants are encouraged to specify the length as accurately as possible as project feasibility in the timeframe allocated will be a decisive criterion during evaluation. Extensions to this period are possible, but applicants should detail a project plan that is feasible to complete within the originally foreseen period.
- Total Project Cost: Proposed projects should be cost-effective and have clearly justified costs. Requests above the maximum cost specified in the Call brief will be rejected.
- Supporting Institution: Please indicate which Swiss institution(s) will act as the primary research location(s) for the duration of the funding period.
- Proposed Start Date: Indicate when (month / year) the project is set to start. This date will determine the start of finances. All pre-funding requirements must be met by this date. The starting date must be within 12 months of the particular call's closing date.
- Name(s) of Applicants (s) and Primary Organisation: Please list the names of all applicants responsible for the content of the proposal and their affiliated organisation. The CVs of each person listed here should be provided as an attachment to the proposal (for further guidance please consult *Section 5.c*). Project partners from the private sector, who may provide a substantial intellectual contribution to the project, should be listed and their in-kind contributions should be detailed in section 12: Application finances.

## 4.2. Details of lead applicant organisation

Please enter the details of the lead organisation. While collaborations between distinct institutions are encouraged, a single institution must be designated as the *Lead Organisation* and identified here. The lead organisation must be an eligible institution outlined in the section "Eligibility Criteria" above.

## 4.3. Contact details

Please enter the details of the main contact person who will be responsible for communication during the grant evaluation process, ideally the same as for the duration of the project. Any changes to the contact details should be given as early as possible and accepted by the 3RCC.

In the case where there are multiple co-applicants, the lead applicant should be preferentially a member of the *Lead Applicant Organisation* specified in the previous section.

## 4.4. Lay summary for publication *(max. 250 words)*

Please describe the proposed project in simple terms suitable for a lay audience.

**Please note** that the 3RCC publishes abstracts from its funded projects on the 3RCC website to demonstrate the potential impact of its funded research. Applicants are responsible for ensuring that any confidential information, or information that might be considered controversial or sensitive, is not included within this abstract.

## 4.5. Current state of the art and scientific background *(max. 500 words)*

Describe the current state of the art, the scientific background and any competing or other existing strategies for answering your research question. The existing gaps in current scientific knowledge on the project topic should be robustly demonstrated. Include any Intellectual Property Right issues, if relevant. This section should provide sufficient information for the reviewers to understand the key previous studies (and/or technology) which outline the problem that is proposed to be solved in the project.

It is important to highlight the results of any similar previous projects, or alternatively sufficiently demonstrate the uniqueness of the proposed idea. The method of literature search and review should be included in this section. Ultimately, the reviewers should be assured that this project would not be an unnecessary duplication of previous or on-going work.

Specific proposal reviewers are selected based on their knowledge and experience in the field of the proposed study, therefore, unnecessary background information or historical significance can be omitted here.

If critical research publications, especially those authored by applicants, are currently "*in preparation*", or "*in press*", the full pre-press article should be available upon request by the reviewers. Note that this should *not* be attached in the initial submission.

The cited literature references should be included at the end of this section and *does not* contribute to the word limit. No specific formatting is required for the application as far as the original research can be reasonably found by reviewers. If the reference list is exceptionally long, it may instead be included as a separate attachment.

## 4.6. Description of proposed idea and project *(max. 700 words)*

Please provide a structured summary of the scientific and technical basis of the project. Detail the research and development approach to be taken, including the key deliverables (e.g. characterisation, optimisation, validation of proposed methodologies). Describe any potential scientific benefits in terms of e.g. innovation, reliability (e.g. reproducibility, robustness), relevance (e.g., accuracy, mechanistic, complexity, species of interest) and/or animal welfare as compared to existing methodologies. Describe the key scientific and technical challenges of the project and how they will be overcome, including consideration of alternative and risk management strategies.

You are encouraged to include the results from any unpublished preliminary work (e.g. optimisation, pre-validation, pilot work, etc.) in this section if applicable. Note that preliminary work is strictly not a requirement for submission although may add credence to the project's feasibility. Note also that if preliminary work is likely to be key in determining the project's feasibility or demonstrative of overall scientific benefit, we encourage applicants to consider initially submitting a more limited and short-term proposal (e.g. 1 year) for this preliminary work first, and then re-apply for the broader project aims at a later date.

**Please note**: If a proposal includes animal experimentation, the attachment on Justification of Animal Use must be completed and included as part of the application. Further guidance can be found in *Section 5: Attachments.*

## 4.7. Three Rs impact assessment *(max. 500 words)*

In this section, please provide a summary of the 3Rs impact of your research.

Please highlight:

1. Which of the 'R' applies to the proposed research
2. Which procedure(s) or parts of procedure(s) are considered
3. How the replacement, refinement and/or reduction would be achieved
4. The likely scale of replacement/reduction in animal use and/or improvement in animal welfare.

It is particularly important to provide metrics around the potential total 3Rs impact. Estimates can be made, for example, by searching literature databases to see how many papers are published each year reporting use of the particular animal model and the typical number of animals used per experiment in the published papers.

We recommend that you consider the following questions:

- **Replacement/Reduction**: How many animals would no longer be used per experiment/procedure/test? How many experiments/procedures/tests of this type are conducted in your laboratory, nationally and internationally? What is the percentage reduction in animal use that could be achieved?

- **Refinement**: What is the evidence that animal suffering will be reduced/animal welfare improved? What objective indicators will be used to assess animal welfare? Is the severity limit for the procedure/protocol likely to be downgraded as a result of the proposed refinement technique? How many animals are likely to benefit per year both nationally and internationally.

Explain the need for research in this area and how, if successful, it will benefit medical, veterinary, biological or other fields of research and/or education. In some instances, it is useful to include letters of support from the research community as a measure of this need. If the work has potential application to other research areas, it also may be beneficial to describe this.

Give sufficient details of other past and current research to show that the aims are scientifically justified, and to show that the proposed model/technique/method will add distinct value to the one

currently used or in development by others. While project feasibility itself should be covered in point 10 of the application form, this section should address the feasibility for the wider scientific, educational, or industrial organisations to implement the transferable aspects of the proposed project, if successful.

What, if any, additional steps will be required before an advance in the 3Rs can be implemented? Describe how the work, if applicable, may be pertinent to industry or regulatory agencies? Which, if any, needs in industry and/or regulatory agencies does the project tackle? If applicable, how might the results have an impact on current regulatory or legislative requirements?

In addition, it is important to describe how the proposed work will impact the 3Rs both locally (i.e. within your own laboratory) and in the wider research community (nationally/internationally).

## 4.8. Methodology & experimental design *(max. 500 words)*

There are a wide range of designs and approaches to experimentation that are appropriate depending on the objectives of the research proposal. In all cases, the 3RCC expects that researchers provide well justified information in their applications concerning the methodology and experimental design and its suitability to answering the research questions posed. Applicants should therefore provide adequate justification for their choice of methodology and experimental design.

A clear definition of the primary and secondary outcome measures should be given. Describe what results need to be obtained to consider the project as successful, and which secondary outcomes are planned that would add valuable knowledge to the field.

If the project involves *in vitro* experimentation, we strongly encourage applicants to consult the international Guidance Document N. 286 on Good *In Vitro* Method Practices (GIVIMP)[1] and the Guidance on Good Cell Culture Practices (GCCP)[2].

In cases where an experimental design is applicable (e.g., animal experimentation, validation study), please provide adequate information concerning for example the bullet points below.

[1] www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=ENV/JM/MONO(2018)19&doclanguage=en

[2] Coecke S, Balls M, Bowe G, Davis J, Gstraunthaler G, Hartung T, Hay R, Merten OW, Price A, Schechtman L, Stacey G, Stokes W. (2005). Guidance on good cell culture practice. a report of the second ECVAM task force on good cell culture practiceAltern. Lab. Anim. (ATLA) 33, 261-287.

- The numbers of samples and interventions needed for statistically acceptable results (alternatively provide a supporting statement from a biostatistician).
- The avoidance of bias (for example blinding of observers assessing outcomes to the group allocation in a randomised design).
- How randomisation will be carried out (if used) or why it is not appropriate if it will not be used.
- How the sample size was determined, for example power calculations (including justification of effect size). If power calculations are not appropriate, please explain why.

**Importantly,** if the project plans to include animal experimentation, applicants must complete the attachment "*Justification of animal use* and include it as part of the application". Further guidance can be found in *Section 5: Attachments.*

## 4.9. Project plan *(max. 250 words)*

The project plan should identify the major packages of work, with well-defined milestones and key deliverables. The key person(s) responsible for each milestone and key deliverable should be indicated. This section should identify the project management processes that you will use to ensure that milestones and key deliverables are achieved in a timely manner.

A Gantt chart should be included indicating the expected deadlines for the milestones and deliverables intended for the duration of the project (see example below).

The emphasis throughout the project plan should be on practicality / feasibility. We are seeking evidence that the project aims can be broken down into scheduled parts and be achieved within a realistic timeframe. In addition, provide details of identified risks and mitigation strategies. These milestones and key deliverables will form a base for the project's progress evaluation.

If applicable the timeline can start prior to the official start of the project (funding start) if key milestones are to be met (e.g. evaluation by the local ethical committee). Certain points can also be included after the end of the project if they are relevant to the broader impact of the study and/or communication and information dissemination of the completed work (e.g. major conferences).

*Example of a basic format Gantt chart:*


## 4.10. Feasibility of the project

Please describe in this section why specifically *you* (co-applicants and associated research group) are in an ideal position to complete the described project.

### a. Scientific/technical team and expertise *(max. 500 words)*

Provide a detailed description of your scientific/technical team, the expertise of each member relevant to this application and the proportion of their time that will be spent on the project. In particular, the expected proportion of the working time of the lead applicant spent on the project should be indicated. The grant will only cover the personnel costs in proportion to the allocated time the researcher is expected to work on the project. In the cases where an experimental design and statistical analysis is required, please indicate whether a dedicated biostatistician is part of the research team, or whether one is available within the host institution.

In the case of collaborative projects, please indicate how the distinct parts of each team may complement and benefit each other.

### b. Infrastructure & equipment *(max. 250 words)*

Provide a detailed description of the appropriateness of the infrastructure and equipment available to address the proposed project.

**Please note** the 3RCC grant does not cover infrastructure costs. Therefore, it is important to identify here all relevant infrastructure and equipment that are available at the institution necessary to complete the project.

### c. Project management *(max. 250 words)*

Include, if applicable the foreseen administration & collaboration plans (e.g. meetings, exchanges).

Discuss the need for ethical authorisations (e.g., animal experimentation, embryonic stem cells, clinical studies, etc.) and specify the identifying number in case the authorisation is already obtained.

## 4.11. Communication & dissemination plan *(max. 500 words)*

In order to generate the highest 3Rs impact, the 3RCC considers a strong communication and dissemination plan to be a key consideration. Please outline how you will communicate and disseminate your research to both scientific and lay audiences to encourage uptake of the 3Rs benefits; this may not be limited to publications and conference attendance and could include e.g. seminars, training, inter and intra-institutional meetings, method transfer between facilities, public forums. This plan should highlight how information will reach a local, national audience as well as international.

What plans, if any, do you have for communicating information about your work to the public? How are these plans supported by the host institution's own policies and facilities for communication with, and education of, the public?

Note that the 3RCC has a policy of open-access publishing (see section 7.b). Where reasonable we encourage the use of pre-prints and archiving of work (e.g. www.biorxiv.org/). If the project involves animal experimentation we strongly encourage applicant to plan to use the ARRIVE guidelines[3].

[3] Available at: www.nc3rs.org.uk/arrive-guidelines

We suggest applicants to plan pre-registration of their project if applicable (e.g. Open Science Framework, https://osf.io/; or www.preclinicaltrials.eu).

## 4.12. Application finances

The total requested project budget should be broken down into individual elements in this section and given a brief justification. We encourage the applicants to keep the project costs as realistic as possible and not simply conform to the *maximum* possible budget.

Direct Costs are costs that are specific to the project, including:

- **Personnel costs** for all those contributing to the project (broken down by individual): include the level of education / training, as well as the foreseen percentage involvement in the project (e.g., % of full time employment)
- **Consumable costs:** materials specific to the project
- **Equipment costs**: specialised equipment should be made available by the host institution, however certain exception* may be made if adequately justified and if the equipment foreseen is specific and core to the scope of the project
- **Animal costs**: animals, animal facility costs, cage, etc.
- **Travel and meeting costs**: conference registration, accommodation, sustenance, etc.
- **Publications and communication**: open access publishing

**Indirect Costs** (e.g. infrastructure, learning resources, specialised software, overhead) is expected to be covered by the host institution. The 3RCC will not cover these expenses.

**Please note** that infrastructure that is deemed necessary to successfully complete should be provided either by the host institution or by a third party.

In this section below the project budget: "Funding from other public and private bodies that may contribute to the delivery of this project", refer, where necessary, to the resources provided as in-kind contribution from the host institution(s) or additional funding sources regarding e.g. infrastructure or other costs. Necessary infrastructure and any other significant costs, which are provided by the host institution, should be indicated in this section.

*Any *exceptional* costs over CHF 20'000.- (e.g. specialised equipment that are core to the scope of the project) will need to be approved by the 3RCC Scientific Advisory Board and the details about these costs should be included in the cover letter. As a general rule, these costs are only considered when the host institution or additional funding source contributes at least 50% of the total cost.

### 4.13. Declaration

All applicants must tick the box and agree to the declaration of the application.

# 5 Attachments

## 5.1. Data Management Plan (DMP)

The Swiss 3RCC has adopted the data management policy of the Swiss National Science Foundation (SNF). All applications, which will generate or re-use data, are required to attach their own Data Management Plan (DMP) as part of the submission. The DMP should comply with the SNF's Policy on Research Data Sharing: www.snf.ch/en/theSNSF/research-policies/open_research_data/pages/data-management-plan-dmp-guidelines-for-researchers.aspx.

The DMP should demonstrate how the applicant will meet, or already meets their responsibilities for research data quality, sharing and security. It should refer to any institutional and study data policies, systems and procedures and be regularly reviewed throughout the research cycle. The DMP is reviewed by peer reviewers. The length of the DMP should be no longer than a page.

The DMP form comprises four sections: (1) data collection and documentation, (2) ethics, legal and security issues, (3) data storage and preservation, and (4) data sharing and reuse.

## 5.2. Letters of support

A letter of support is required from the responsible person at each of the participating institutions. The letters of support must bear the official letterhead of the host institution and an original signature of the head of the institution or head of the research group (scanned). The confirmation has to state clearly that the necessary infrastructure is available for the duration of the project. The letter should mention the project title, names of the co-applicants at that particular institution, as well as the expected start and end dates of the project. Letters should be no more than one page.

## 5.3. CVs

Please only provide CVs for the lead applicant and co-applicants. CVs should not exceed two pages, and include a list of the most relevant publications.

The CVs should only include information relevant to the application. Unnecessary personal data (e.g. home address, date of birth, personal phone numbers and emails) should *not* be included.

While no explicit format is required, we encourage applicants to follow the guidelines provided by the Swiss National Science Foundation[4].

## 5.4. Cover letter

The inclusion of a cover letter is not compulsory but if the applicant wishes to supply one with their application, they are welcome to do so. It should be no longer than one page. It must not be used to cover anything that should be included within the application form or other required attachments. Any exceptions to the rules in the guideline, such as exceptional costs should be included here, as well as the names of any conflicted experts that you request not to be used as reviewers (where applicable). For conflicted experts, please include the name and institution of the person to be excluded and the reason why they should not be approached.

**Please note** that cover letters will not be sent to peer reviewers and will only be made available to the 3RCC directorate. Any confidential or other information you do not wish the peer reviewers to see should therefore be included within the cover letter.

[4] www.snf.ch/en/funding/documents-downloads/Pages/guidelines-cv-research-output-list.aspx

## 5.5. Letters of recommendation

Letters of recommendations can be included in the proposal, but are not required. Only information that directly relates to the project's feasibility should be included and should ideally come from external researchers within the same general field of study. Information on the applicant's personal characteristics will be disregarded.

## 5.6. Guideline to Attachment "Justification of animal use (if applicable)"

Only information that is not already contained in the main application form should be included in this section. In cases where there may be a risk of duplicated information, please refer to precise section/statement in the main application form rather than re-word information already expressed. This attachment should be completed also in the case of an existing accepted license.

### 5.6.1. Have you already applied for an animal authorization?

Indicate whether there is already an accepted license in place at the host institution that covers all elements of the proposed project. If there is, indicate the license number, and in that case, several answers in this section can be directly copied and/or expanded upon from the original license document. Note that initial funding will only be released at the time that the appropriate license is accepted and in-place.

### 5.6.2. Does the proposed research involve the use of species protected by the Animal Welfare Ordinance (art. 1 , art.112 OPAn, TSchV 445.1)?

Please indicate if the proposed project involves the use of:

- Vertebrates (e.g., mouse, rats, etc.)
- Decapods (*Reptantia*) and cephalopods (*Cephalopoda*)
- Mammals, birds and reptiles in the last third of the gestation period prior to birth or hatching
- Larva stages of fish and amphibians that take in food *ad libitum.*

### 5.6.3. Please provide the reason(s) for selecting the proposed animal species

Justify in the case of mammals, why invertebrates or lower vertebrates cannot be used in the project. The use of animals of the same sex, need to be justified. Do the model reproduce the situation found in human patients? Is the selection of the chosen model evidence-based? Is there a possibility to compare results obtained from other groups? Are experiments in other species not

possible because their biology is either too different from that of the human or they have not been studied in sufficient detail?

### 5.6.4. Does the proposed research include procedures to be carried out on animals described in the Animal Welfare Ordinance (OPAn, TSchV 445.1)?

Add procedure names (non-exhaustive) as for example, behavioural studies, anaesthesia, surgery, substance administration, blood sampling, euthanasia, etc.

### 5.6.5. What is the degree of severity (DG) of the procedures?

Please refer to the Technical Information on Animal experimentation from the Food Safety and Veterinary Federal Office (FSVO) "Severity degrees 1.04"[5]

### 5.6.6. Please provide details of any DG2 or DG3 procedures (no more than 1 page) and a flowchart of the experimental procedures foreseen in the animal.

Include here any information that was not already given in section 8 of the main application and that will nonetheless apply to your experiment. If all relevant information is given in section 8 of the application, simply indicate so in this section.

### 5.6.7. Please provide the reason(s) for choosing the selected model or method and describe its peculiarities and/or advantages.

Indicate the peculiarities and/or advantages with regard to the scientific objectives of the project. Restrictions arising for the animals must be described and compared to other possible methods. Please describe the relevance of the animal model and reproducibility. To what extent is it possible to generalise or extrapolate to other animal species or humans? Provide a description of the various experimental models that could be used to answer to the scientific objective of the proposal with their pros and cons.

### 5.6.8. For genetically modified or mutant animals: Please provide a breeding scheme to obtain the experimental animals. Do the animals show any burdened phenotype *(Chapter 1 art. 2k&l; Chapter 6, section 3 OPAn/TschV)*?

[5] Available at: www.blv.admin.ch/blv/en/home/tiere/tierversuche/forschende.html

Under this section, please provide the breeding plan to obtain the number of experimental animals needed. Furthermore, if your animals show a clinical pathological phenotype which necessitates a M-form for announcing the constraint observed in the animal line(s)[6], please provide:

- The animal facility address where the animals will be bred if different from the lead institution.
- Description of the line and the measures to be taken which reduce constraint and interruption criteria.
- Provide the weighing of interest (constraint versus benefit) for this clinical pathological phenotype model.
- Provide potential welfare conditions requested by the authorities, if applicable, and how you will ensure them.

## 5.6.9. Besides the main scope of the study describe any existing 3R experimental methods that could be used (e.g., refinement methodologies, *in vitro* methods, computational modelling, etc.)

*According to art. 137 para. 2 and 3 OPAn/TSchV) (no more than 1 page).*

Are alternative methods available to further replace, reduce or refine the experiments? Please provide in this section a literature research (i.e. keywords, number of hits, important publications) on the replacement (i.e. *in vitro* methods), reduction or refinement options (*in vivo* methods). Include as well personal experience if applicable. Finally, please describe if any measures are foreseen regarding the fate of the used animals such as e.g., rehoming, sharing of organs and tissues through the AniMatch platform (www.swiss.animatch.eu) or others.

## 5.6.10. Please include a weighing of interests (harm vs. benefit) evaluation: assess the anticipated information or results in relation to the stress caused to the animals *(art. 3 and 19 para. 4 TSchG).*

In this paragraph, a balance according to ethical considerations between the expected gain of knowledge and the constraint caused to the animal (e.g. pain, suffering or injury) should be provided. For this part to be correctly completed, please consult the document "Weighing of interests for proposed animal experiments"[7]. Applicants may also consult Pound and Nicol (2018)[8].

[6] https://www.blv.admin.ch/blv/en/home/tiere/tierversuche/forschende.html under forms for genetically modified lines or mutants with an impaired phenotype

[7] Guidance for applicants SWISS ACADEMIES COMMUNICATIONS, VOL. 12, NO 3, 2017. Available at: www.akademien-schweiz.ch/en/index/Portrait/Kommissionen-AG/Kommission-fuer-Tierversuchsethik.html

[8] https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193758

# 6. Assessment procedures

## 6.1. Project grant assessment procedure

Every submission must pass an initial screening procedure conducted by the 3RCC directorate. This step comprises of administrative checks on application completeness. In case of minor omissions, the directorate may contact the applicant seeking further information. In the case of larger omissions, the proposal is rejected at this stage. The 3RCC directorate will also perform a preliminary check on the suitability of the proposal to the aims and mission statement of the open call. Furthermore, it will perform preliminary sorting of the received proposals according to the scientific expertise required for their evaluation.

All suitable submissions are then assessed by the Scientific Advisory Board of the 3RCC as well as selected external referees.

The following criteria are taken into consideration when making the funding decisions:

- Potential impact on the 3Rs
- Quality of the science
- Benefit of the proposal as compared to current methodologies in terms of reliability (e.g., reproducibility, robustness), relevance (e.g. accuracy, mechanistic, complexity, species of interest) and/or animal welfare
- Strategy for promoting the proposed research and 3Rs outcomes within the scientific community
- Expertise and track record of the team
- Feasibility of the project
- Chance of successful implementation in the broader scientific community
- Clear justification for the required budget
- Previous funding history with the 3RCC (if applicable)
- Feedback will be provided for each application. However, the level of detail will depend on how far the project has been evaluated by the 3RCC and external reviewers. The 3RCC aims to be as transparent as possible with this process.

## 6.2. Requirements for members of the Scientific Advisory Board and external reviewers.

The 3RCC Scientific Advisory Board is composed of scientists that:

- Are internationally knowledgeable scientists involved with the 3Rs;
- Have expertise covering different aspects of the 3Rs including e.g. *in vivo, in vitro* and non-animal 3R alternatives;
- Represent (as much as possible) industry, academia, welfare, regulatory agencies;
- Have a view on future technologies/principles, quality concerns, influence in scientific community/scientific journals;
- At least a few, have knowledge of the Swiss national funding schemes;

Members of the 3RCC Scientific Advisory Board are required to declare any private, professional or commercial interests that might, or that might be perceived to have potential conflict(s) with specific project applications. Interests are declared under the following categories:

- Personal remuneration (employment, consultancies, directorships, honoraria etc.)
- Research support
- Registrable shareholdings and financial interests in companies
- Intellectual property
- Public statements and positions
- Interests of immediate family members
- Any other relevant information (e.g., major collaborations)

Identification of a potential conflict of interest will preclude their evaluation of specific grant proposals where such conflict may exist.

# 7. Our expectations for 3RCC granted projects

## 7.1. Terms and conditions

The applicant(s) undertake(s) to:

- Use the grant received for the purposes of the approved research project and to present the 3RCC with regular reports (as defined in section "c" below) and communication with the 3RCC when applicable;
- Request the 3RCC approval before any changes are made to the conditions under which the grant was approved, i.e. in the case of technical modifications, alterations to the research schedule or changes in the budget, or changes to personnel (including lead applicants);
- Inform the 3RCC directorate in good time if any funds allotted are not likely to be needed;
- Submit a final report including results to the 3RCC directorate at the latest 3 months after the project has been completed;
- Inform the 3RCC directorate of any patent applied for in relation to work carried out as part of the research project funded by 3RCC.

## 7.2. Publications and open access publishing

The 3RCC has an open access policy for publications funded by the grant. This policy aims to disseminate the funded research to the widest possible community; not only to promote the scientific outputs, but also to ensure the highest level of utilisation and awareness of 3Rs methods. Holders of the 3RCC research grants are expected to disseminate their results by publishing in appropriate scientific journals.

Any publications that are related to the project should be reported to the 3RCC.

While not mandatory, grant holders are highly encouraged to share any conference posters or presentations with the 3RCC; we can in turn promote the work and we can help ensure it has the widest possible impact in the scientific community.

## 7.3. Reporting requirements and evaluation

All reports should be prepared in English, unless for specific cases where this may be requested differently by the 3RCC.

### Final report

All projects must submit a final report to the 3RCC within 3 months of the end-date of the project. The final report should explicitly reflect the project goals, plans, and milestones and deliverables of the original application. It should make clear whether the primary (and secondary) objectives(s) were ultimately met according to the original plan, and outline the most important findings. This must also include a final accounting of the funds used, with specific reference to the original project budget. Furthermore, it should highlight the particular challenges (both foreseen and unforeseen), that the project faced, and whether they were overcome (also if not, why not). The final report should be seen as a way that researchers can share results from preliminary or pilot aspects of the projects that were not suitable for peer-reviewed publication. Final reports should be no more than six pages.

The remaining 10% of the project funds are released upon 3RCC approval of the final report. Note that the 3RCC may ask for clarifications or additional material before accepting the final report.

### Mid-term progress report

For projects over 18 months in total duration, a single *mid-term* progress report is required at the halfway mark of the project (typically at the 18th month of the 3-year project). The report will be evaluated by the 3RCC.

The mid-term report should be focused around the original project plan, with specific reference to the progress of the milestones and project schedule. The report should make clear whether the original plan is on schedule and give a brief outline of intermittent results (if possible). Project delays or setbacks should be explained and justified in detail for evaluation.

**Important to note** that continued funding of the project is dependent on the acceptance of the mid-term progress report. Acceptance of the mid-term progress report is not dependent on the specific results of the ongoing project, but rather on a determination of the ongoing *feasibility* of the project. Therefore, if the project plan is considerably delayed, the 3RCC will review the justifications, and determine whether the overall project goals are still acceptable in the time remaining, or whether new goals should be set given a justifiable deviation in the project course.

The 3RCC might ask for specific milestone deadlines to be met within a short time frame from the submission of the mid-term report for further consideration. For example, a milestone should be met at the 2-year mark of a 3-year project before yearly funding is awarded.

Projects under 18 months of duration do not need to submit a mid-term progress report and are assessed on the final report only.

### After funding period

The 3RCC expects to be informed about any publications that have come either directly or indirectly from the funding of the project. There is no time cap on this from the end of the project funding.

Given the importance of the funding to highlight issues around the 3Rs in a general way, and the difficulty in assessing the impact of the project in the immediate aftermath of funding, the 3RCC may contact previously funded applicants to enquire about the long-term impact their work has had in the years after project funding.

## 8. Acknowledgements

We acknowledge the various organisations that contributed to both the application form and the guidelines in both intention and phrasing: the Swiss National Science Foundation (SNF), the Swiss 3R Foundation, and the National Centre for the Replacement, Refinement and Reduction of Animals in Research (NC3R).