Swiss 3R Competence Centre

Swiss 3RCC Application Guidelines for Open Call Project Grants

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1.1 General overview

The Swiss 3R Competence Centre publishes regular calls for funding research projects dedicated to the replacement, reduction or refinement of animal experimentation. Applications will be favoured that have high quality science, that have a crucial impact on the 3Rs and bring benefits as compared to existing methodologies in terms of e.g. reliability, relevance and animal welfare. It is the 3RCC funding program's aim to subsidise projects relating to each of the 3Rs in a balanced manner. Collaborative and multi-centre projects are encouraged.

The 3RCC funding program addresses basic and applied research that supports the development, optimization, application and implementation of new or modified 3Rs approaches, methods and technologies. The maximum duration of projects is 3 years although cost-neutral 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, which are often not supported by traditional sources of 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 specific problems identified as existing gaps relevant to the application and advancement of the 3Rs principle. Topics of the targeted calls will be outlined in detail at the time of publishing each particular call by the 3RCC.

1.2 Eligibility criteria

Lead applicant eligibility

- Lead applicants should be Swiss-based researchers 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 and/or education-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.
    - *Less-experienced* researchers are encouraged to make their applications in collaboration with a more senior colleague.
- Lead applicants who already hold a grant from the Swiss 3RCC, are only able to apply for a new grant within the final 12 months from the ongoing project's end-date. The 12-month maximum period is set at the new application's, first-stage submission deadline. Furthermore, the start-date of the new application must be after the end-date as well as the final report of the ongoing project.
- Lead applicants may only have one project application under consideration by the 3RCC during a call (as the lead applicant). 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 "*Application Finances*" of the project proposal.
- Lead applicants are responsible for finding a host *Research Organisation* / Lead Institution who will act, or is acting as their employer and will manage the administration of the project grant for its full duration.
- Applicants or those financed by the 3RCC project grant may spend up to 6 months at a research institution abroad, yet applicants must indicate this in advance in section "*Project Plan*" of the application. In case such a stay abroad is planned after the grant has been

awarded, the applicant must notify the 3RCC as soon as possible and any required action will be determined by the 3RCC Scientific Advisory Board on a case-by-case basis.

Lead institutional eligibility

The 3RCC funding applies to public and non-profit research institutions including for example:

- Swiss Public 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 research groups. The 3RCC allocates funding only to the "Lead Institution" (see eligibility above). It will be up to the grant managers at the institution to further allocate any funding necessary to co-applicants. Industry partners may participate with in-kind contributions to the project.

In case of any doubt in eligibility, please contact the 3RCC office at funding@swiss3RCC.org.

1.3 Funding scheme

Funding is provided on a yearly basis with 90% of the total budget funding equally distributed for the duration of the project. The remaining 10% is given once the final report is accepted by the 3RCC. Note that in those 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)*
Year 1 *(upon signature)*	30%

Year 2 *(12 months after signature)*	30%
Year 3 *(24 months after signature)*	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 (see the information "final report" in the section "Our expectations for 3RCC granted projects" below).

Infrastructure costs will *not* be covered by this grant and are generally assumed to be in-kind contributions by the host institution.

2 How to apply

Applicants to the Swiss 3RCC Funding Program are required to complete and submit the standardised online application form, which is accessed through the online portal of the 3RCC website. Use the link on the website, or go directly to *funding.swiss3RCC.org* to register for a new account, or login to the portal with your existing details. If you previously had an account as a reviewer, or member of the 3RCC, you should use the same account to submit a new application. All information is saved within the online portal when you log in and out, so you can fill out different parts of the application over time.

The 3RCC Open Call Funding Programme consists of a **two-stage procedure**. In the first stage, applicants are expected to submit a relatively brief outline of their proposed project. This option can be selected on the main page of the online platform under "My Applications". These outlines are then reviewed, and if selected, applicants will be invited to complete a "full application" where they should provide details on the proposed project. These are reviewed and a subset will be selected for funding. The definitive timeline for each open call is provided in the call brief online. The sections "Completing the Outline Application", and "Completing the Full Application" of this document provides guidance on completing both forms. Support is also provided in the individual online-help sections during each step of the application process.

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 content has 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.

- Applications should be completed within the online submission portal found on the 3RCC website [insert direct portal link].
    - External attachments (e.g. PDF or image files) should be uploaded at the relevant points in the online application and will *not* be accepted in any other form.
- Failure to complete mandatory fields on the application form and to submit all required attachments are likely to result in the rejection of the application. In case of minor omissions or errors, the application could be returned to you with a new deadline.
- Text word limits are indicated for each section and cannot be exceeded.
- The entirety of the application must be written in English.
- The use of acronyms should be kept to a minimum and described in their full-form when first used.

Resubmissions

- Resubmissions of the same, or similar, project are only accepted when **directly invited** to do so by the 3RCC Scientific Advisory Board.
    - The invitation for future resubmission will be sent to the applicant at the time the applicant receives the notification that their application has been rejected.
    - The applicant may be invited to resubmit their application with a similar topic at the **Outline Application stage**, or be invited to bypass this stage entirely and submit the project directly as a **Full Application**.
    - For invited resubmissions, an additional section of the application is required in which the applicant should detail the **major changes** to the application.

- Applications which have not been explicitly invited for resubmission must **wait until at least one further Open Call has passed** prior to submitting a similar project.
    - Note that even if the resubmission is after this initial embargo period, we expect the applicants to **acknowledge the resubmission** and complete an additional section detailing the major changes from the previous submission.
    - Any application submission by the same applicants, that is deemed too similar to a previously uninvited application within the year embargo period will be **immediately rejected** by the 3RCC Directorate.
    - If you are unsure about whether your application is too similar to a previous application, you should **contact the 3RCC Directorate** directly for a brief evaluation.
        - As a general guide, an application would likely be considered as a resubmission if there is a major overlap in the title or keywords used to describe the project.
- Our resubmissions policy is part of a suite of demand management measures, to help 0alleviate pressure on all involved with our peer review process.

3 Completing the Outline Application

Note that the Outline Application is the first-stage of the funding process. Its content will determine whether you are invited for the Full Application stage. However, the 3RCC understands that some of the content may change in the meantime, and so we allow for the applicant to adjust the content for the second-stage. We nevertheless urge you, the applicant, to provide the most accurate estimates possible here.

3.1 Basic overview

- **Project Title**: Please provide the title for your project. This should be both descriptive and concise.
- **Lead Applicant Details:** Information in this section is imported directly from the "My Details" page of the applicant. These details can be changed at any time by editing the information there.

- **Co-applicants**: Please list the names of all applicants responsible for the content of the proposal. Project partners from the private sector, who may provide a substantial intellectual contribution to the project, should be included as co-applicants.
    - **Important**: all the co-applicants of the project will receive an email to register and login to the portal to approve (or reject) their participation in the project submission. All co-applicants must indicate their approval prior to submission. Therefore, if this approval cannot be guaranteed prior to the deadline (e.g. holidays), we suggest removing them as co-applicants at this stage, and adding them in at a later date.
- **Indicate which of the 3Rs your project most closely target**. For information on the definitions of each R that the 3RCC uses, please visit our website (https://swiss3rcc.org/2018/05/02/what-are-the-3-r/)
- **Keywords:** include up to 10 keywords that are most relevant to your project proposal. Words that appear in the title of the proposal should *not* be duplicated here.
- **Scientific area**: please select from the drop-down list which scientific field(s) your proposal most closely corresponds to. The available options are:
    - *Nervous system | Immune System | Oncology / cancer | Cardiovascular system | Multisystemic studies | Pharmacokinetics & pharmacodynamics | Blood system | Reproductive / urogenital systems | Endocrine system | Musculoskeletal system | Gastrointestinal system (including liver) | Respiratory system | Sensory organs (skin, eyes, ears) | Infectious disorders | Antibodies (e.g. production, resistance profiling) | Humane education (mannequins, simulators, virtual models, etc.) | Ethology / animal behaviour | Wildlife ecology & ecotoxicology | Animal farming.*
    - *If a scientific field covers the scope of the project, that is not mentioned above, simply indicate "other" in the classifications list.*
- **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. While extensions to this period are possible, applicants should detail a project plan that is feasible to complete within the originally foreseen 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 expected starting dates are indicated in each Call brief. Project starting times outside the indicated period are acceptable but should be justified in the proposal.

- **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 not be accepted. The maximum total cost is indicative of the budget required for the complete duration of the project, regardless of the actual duration proposed.

- **Do you expect to have equipment costs over 20'000.-?**

    - Note that the 3RCC Open Call funding programme generally does not provide funding for equipment costs over 20'000.- CHF. These items are generally considered to be the responsibility of the hosting institution. Only in exceptional cases where an equipment is specific and essential to the project an exception might be made if adequately justified and approved by the 3RCC Scientific Advisory Board. As a general rule these costs are only considered when the host institution or additional funding source contributes at least 50% of the total exceptional equipment costs.

    - If there is a clear expectation that the costs of a specific equipment that is essential to complete the project will be over 20'000.- an additional section will be made available. In this section, the application should provide details on the equipment itself, why it is core to the scope of the project, what additional funding sources are available to contribute to at least 50% of the total costs of the equipment and why this is unlikely to be obtained through other means than the project proposal.

3.2 Project Proposal Outline

Please provide a brief description of the project including:

- the background and motivation for the project;
- the primary and secondary outcomes; an overview of the methodology (and, if applicable, the experimental design) to be employed;
- what are the expected benefits of the project compared to the state-of-the-art in terms of innovation, reliability (e.g. reproducibility, robustness), relevance (e.g. accuracy, mechanistic, complexity, species of interest) and animal welfare;
- the feasibility of the project;
- how the results are planned to be used/promoted to the wider scientific community or public;
- end-user involvement (when applicable), and
- regulator or regulatory office involved (when applicable)

3.3 Expected impact on the 3Rs

Please outline the potential 3Rs benefits arising from the successful completion of the project. Where possible, be specific about the number of animals that would be affected, the degree of severity, etc.

Furthermore, applicants should outline the 3Rs impact of the project in terms of the scientific area(s) covered and the local or wider impact.

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4 Completing the Full Application

4.1 Basic Overview

As far as possible, the required information for the full application will be automatically imported from the *Outline Application* and *My Details* of the online platform. The applicant is however free to change the information found here in case of changes since the submission of the *outline*.

Please note that as this information was used as the basis of the invitation to submit a full application. Therefore, in case of changes that may have impacted that decision, please contact the 3RCC directorate for clarification (funding@swiss3RCC.org, or use the online portal).

4.2 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.

4.3 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 or (educational) learning objectives. The existing gaps in current scientific knowledge on the project topic should be robustly demonstrated. 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.

Furthermore, if applicable, applicants must disclose any existing or potential future Intellectual Property Rights (IPR) issues, and discuss how the methodology implied will be made available to all taking into account any IPR issues.

It is important to highlight the results of any similar previous projects, and/or sufficiently demonstrate the uniqueness of the proposed idea. The method of literature search and review should also 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.

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 in the specific section of the online application "references". No specific reference formatting is required for the application as long as reviewers are able to find the original research articles.

4.4 Description of proposed idea and project (max. 700 words)

In this section you have the opportunity to describe the project proposal in detail. Specify the approach you are taking and the concrete objectives that you aim to achieve in the period of funding; include specific references to the issues and knowledge gaps identified in the previous section. Describe any potential scientific or educational benefits in terms of e.g. innovation, reliability (e.g. reproducibility, robustness), relevance (e.g., accuracy, mechanistic, complexity, species of interest, translational value) and/or animal welfare as compared to existing methodologies. Be sure to indicate which of the aims are key to the project, and which can be considered more secondary. Describe the studies / experiments / assessments that are planned and how each plays a role in achieving those aims.

A realistic perspective should be taken which adequately recognises and assesses the risks involved in the approaches proposed; if possible describe alternatives that could be implemented to manage those risks. Include any key scientific, educational and/or technical challenges of the project, and how they would be overcome.

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 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.

You may attach any figures or illustrations that help to understand the project details in the field below this section. The attachment should be used as visual aids to the content already described and should not be used as a space to include any additional information.

4.5 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 most closely 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 institution? What is the percentage reduction in animal use that could be achieved, nationally and internationally?

- **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 applications 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.

What, if any, additional steps after successful completion of the proposal (e.g. validation study, implementation activities), 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? Describe potential activities, after the project is successful, that are required to accomplish this.

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).

4.6 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 information 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 and indicate whether these are already standard in the field, or novel approaches.

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 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].

For in *vivo* projects, we recommend using the Experimental Design Assistant, developed by the NC3R, and freely available for use[3], as well as the PREPARE guidelines[4]. 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.

- The numbers of samples and interventions needed for statistically acceptable results (alternatively provide a supporting statement from a biostatistician).
    - Include information on how the sample size was determined: for example power calculations (including justification of effect size). If power calculations are not appropriate, please explain why.
- The avoidance of bias (for example blinding of the experimenters when collecting data, as well as those analysing the outcomes).
- How randomisation will be carried out (if used) or why it is not appropriate if it will not be used.

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[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.

[3] https://www.nc3rs.org.uk/experimental-design-assistant-eda

[4] https://journals.sagepub.com/doi/full/10.1177/0023677217724823

4.7 Preregistration

In this section you should indicate whether you plan to preregister your project in an openly accessible platform. While the 3RCC recognises that this will not always be applicable or possible, we suggest applicants plan to preregister their project whenever possible: for example, Open Science Framework, https://osf.io/; https://www.animalstudyregistry.org; www.preclinicaltrials.eu.

4.8 Project plan (max. 250 words)

The project plan should identify the major work packages, with well-defined milestones. Whenever possible indicate the key person(s) responsible for each milestone. This section should also identify the project management processes that you will use to ensure that milestones 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 achieved within a realistic timeframe. These milestones and will form a base for the project's progress evaluation.

If applicable this timeline can start prior to the official start of the project (i.e. 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:

4.9 Feasibility of the project

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

4.9.1 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.

You are required to upload the CV of the lead applicant in PDF format. You may also upload the CVs of any of the other co-applicants if this information will add to the feasibility of the project (in cases where this information was not already described in the section above).

4.9.2 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. It is therefore important to identify all relevant infrastructure and equipment that are available at the institution necessary to complete the project in this section.

4.9.3 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.).

4.10 Communication & dissemination plan (max. 500 words)

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/education outcomes 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 applicants to use the ARRIVE guidelines[1].

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

4.11 Justification of Animal Use

Please note that this section is subject to changes prior to the final date of submission for the full applications. In early 2020, the authorisation licensing procedure for animal experimentation (*form A*) will be updated. This section will then be updated accordingly so that applicants can re-use the information here for upcoming licenses, or vice-versa.

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 section must be completed even in the case of an existing accepted license.

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.

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.*

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?

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. 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"[1]

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.

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.

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)?

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)[2], 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.

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) .

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.

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"[3]. Applicants may also consult Pound and Nicol (2018)[4].

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[1] Available at: www.blv.admin.ch/blv/en/home/tiere/tierversuche/forschende.html
[2] https://www.blv.admin.ch/blv/en/home/tiere/tierversuche/forschende.html under forms for genetically modified lines or mutants with an impaired phenotype
[3] 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
[4] https://journals.plos.org/plosone/article?id=10.1371/journal.pone.0193758

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**: any specialised equipment over CHF 20'000.- should be made available by the host institution. Only in exceptional cases where an equipment is specific and essential to the project an exception* might be made if adequately justified.
- **Animal costs**: animals, animal facility costs, cage, etc.
- **Travel and meeting costs**: conference registration, accommodation, sustenance, etc.
- **Publications and communication**: open access publishing, data management

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

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 during the process of reviewing the Outline Application. In cases where the equipment cost was not yet foreseen at the time of submitting the Outline Application. As a general rule, these costs are only considered when the host institution or additional funding source contributes at least 50% of the total exceptional equipment costs. In cases where the equipment cost was not yet foreseen at the time of submitting the Outline Application, the request will generally be rejected, however the applicant should contact the 3RCC to discuss the issue on a case-by-case basis.

4.13 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 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. 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.

4.14 Suggested reviewers

In this section you will be able to both suggest reviewers that you recommend review your application and those that you wish to exclude from the process. The 3RCC commits to not sending your application to those reviewers you wish to exclude.

4.15 Declaration

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

5 Additional Information

Please note that these items are only applicable at the Full Application stage of the submission.

5.1 Letter of support

A letter of support is required from the responsible person at each of the participating institutions. This letter should generally come from the head of the institution or vice president of research. Applicants are invited to contact the 3RCC Executive Board member from their respective universities for any further clarifications needed[1]. For example, for the University of Zürich lead applicants must submit a letter of support from the Vice President of Research[2].

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 and

are submitted as an attachment on the online platform.

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[1] List of the 3RCC Executive Board members:
https://swiss3rcc.org/wp-content/uploads/2019/02/3RCC-Executive-Board_2019.pdf

[2] To receive this letter in due time, lead applicants from the University of Zürich are invited to follow the procedure described here asap: https://www.research.uzh.ch/en/funding/researchers/3rcc.html

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5.2 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.

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.

5.3 Letters of recommendation

Letters of recommendation 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.

6 Assessment procedures

6.1 Project grant assessment procedure

6.1.1 Outline Application

The online submission system has a series of checks for most of the information entered, however the 3RCC directorate will nevertheless perform an additional screening of the *Outline Proposal*. This step ensures application completeness. In case of minor omissions, the directorate may contact the applicant seeking further information and temporarily re-open the application. 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.

The members of the 3RCC Scientific Advisory Board (SAB), will perform the evaluation of the first-stage Outline Proposals and select the Outline Proposals to be invited for a full-application submission. Each submission will be reviewed by at least two SAB members based on the scientific area and on the "R" which corresponds best to the proposal. In special cases where the scientific topic of the outline is deemed to be outside the expertise of members of the SAB, external scientific reviewers may be invited to review the Outline Application to inform the decision of the SAB members assigned to the application. The final decisions to invite a submitted Outline Proposal for a full-application submission will then be made together with all evaluating SAB members.

6.1.2 Full Application

Evaluation of the full applications using a two-step procedure. As soon as the applications are received the 3RCC Directorate will begin the search for potential external reviewers. External reviewers are generally found by one of three approaches: using the title and keywords (provided by the applicants) in an online database search (e.g. PubMed) for relevant publications; examining the reference list in the application itself for eligible reviewers; or searching through a 3RCC internal database of external reviewers that is constantly being revised from previous funding calls and research networks.

External reviewers must complete a structure evaluation form in the same online portal as the original submission. The 3RCC aims to obtain a minimum of 2 external reviews per application, with a maximum of 5 external reviews. A minimum of 10 reviewers will be initially contacted to ensure that a sufficiently broad base of experts in the field are given the opportunity to evaluate the application. Each incoming review is screened by the 3RCC directorate and the assigned SAB members for both overall quality of the review, and appropriateness of the commentary. In cases where a review is lacking, additional external reviews will be sought.

Based on the mean scores from the external evaluations, a sub-selection of applications will be further reviewed by the assigned SAB member. In most cases, this will be the same SAB member who had previously seen, and subsequently invited, the outline application. The two SAB members are then required to submit their evaluation. Note that at this stage, the SAB member will have access to the external evaluations provided. Once all SAB members have completed their individual reviews, the SAB will meet in-person. During this meeting, each application is presented, discussed, and given a final ranking. This ranking is then submitted to the 3RCC Strategic Board for a final decision on funding based on the recommendations of the SAB and on the amount of funds available.

See the 3RCC website for the 3RCC's criteria for external reviewers and definitions of conflicts of interest.

6.2 Assessment Criteria

The following criteria are taken into consideration when making 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
- Feasibility of the project
- Strategy for promoting the proposed research/education strategy and 3Rs outcomes within the scientific community and chance of successful implementation in the broader scientific community
- Expertise and track record of the team
- Clear justification for the required budget
- Previous funding history with the 3RCC (if applicable)
- If applicable, the scientific value for the proposed use of animals (note that ethical considerations are handled separately by the local ethical committees)

Feedback will be provided for each application.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 in our efforts to support research related to the 3Rs.

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.

In addition to these general points, individual contracts are written for each project selected for funding that may contain additional stipulations.

7.2 Publications and open access

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 then 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.

7.3.1 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.

7.3.2 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.

7.3.3 After funding

The 3RCC expects to be informed about any publications where the 3RCC funding is cited in the acknowledgement or funding sections of a manuscript. In general, we will leave this decision up to the reasonable determination of the authors. There is no predefined 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).