

## Call for research project applications to promote the development and implementation of the three R's

On behalf of the Minister of Food, Agriculture and Fisheries, The Danish 3R-Center calls for applications to promote the development and implementation of the three R's.

**The application deadline is Monday 9<sup>th</sup> October 2023 at 23:59.**

### **Funding**

Grants of up to DKK 500,000 can be applied for, including overhead. Typically, amounts of DKK 100,000-500,000 will be awarded. The total amount available for grants is approximately DKK 1,500,000. Research project grants will be for up to 18 months. The Danish 3R-Center accepts any level of overhead, however not exceeding 44%.

Grants will be made in accordance with the provisions of the Danish Finance Act. Funding is given on the condition that the applicant holds all necessary permits, and that all relevant legislation is complied with at all times.

### **Purpose**

The Danish 3R-Center supports research projects which are expected to lead to the immediate implementation of at least one of the three R's. Applications must therefore be of excellent scientific quality and have a measurable impact on at least one of the three R's.

The Danish 3R-Center was established to promote all three R's. In this context, the three R's are defined as follows:

### *Replacement:*

Methods which replace living higher sentient animals with non-sentient material or human volunteers. Replacement embodies replacement of the tests for experimenting on live animals covered by the Animal Experimentation Act.

Replacement can therefore involve studies using:

1. Isolated cells, tissue or organs
2. Dead vertebrates
3. Invertebrates (excluding cephalopods), plants or microorganisms
4. Synthetic or electronic materials
5. Human volunteers

### *Reduction:*

Reduction refers to a decrease in the number of animals used to obtain a given amount of knowledge with the same precision. The development of animal models which increase the scientific value of each individual animal is also considered as Reduction. The aim of Reduction is not to measure whether an institution or state has used fewer animals in a given time period.

Reduction can be achieved by pre-screening with animal-free models, by using animals with exactly the properties of interest, or by designing more rational experiments.

### *Refinement:*

Refinement refers to any reduction in the severity of stressful procedures which need to be performed on animals. Refinement is achieved when the stress that each animal experiences is reduced. An improvement in animal welfare can be achieved both by improving the experimental procedures and by improving the animal's habitat.

There is some overlap with the principle of Reduction, but Refinement focuses more on experimental technique than on the number of animals. Existing methods can be refined by improving the animals' quality of life, for example by better pain management or housing, or by paying more attention to the different species' needs.

Another important area for Refinement is the use of humane endpoints, which determine criteria for humane killing, the disruption of a trial, or pain management. Refinement will often consist of an endpoint defined as the early symptoms of toxicity or disease, instead of allowing the trial to proceed to the end.

## **Who can apply?**

Researchers affiliated to organizations, institutions or businesses in Denmark.

Researchers with their main affiliation outside Denmark may not be principal applicants but can be included as collaborators.

The minimum formal qualification required is a graduate degree. Applications involving less experienced researchers should normally be made in collaboration with a more experienced colleague.

The Danish 3R-Center sees diversity as a resource and encourages all candidates – regardless of their gender, ethnic origin, and religious or political persuasion – to apply.

## **Processing of applications**

Applications must be submitted to [info@3rcenter.dk](mailto:info@3rcenter.dk).

Files must be converted to PDF and merged so that only a single PDF file containing the application form, reference list and CV is submitted.

Applications may not be altered or added to after deadline Monday 9 October 2023.

All grant applications will be assessed by the Board of the Danish 3R-Center.

The outcome is expected to be communicated to the applicants by the Secretariat of The Danish 3R-Center (The Danish Veterinary and Food Administration) in January 2024.

Contract negotiations with the approved research project and their host organization will shortly thereafter be initiated by The Danish Agricultural Agency. The research projects that receive funding must be launched in 2024, no later than 6 months after the applicant has received notice about funding. However, 1 of February 2024 is the earliest possible starting date.

All applications are treated confidentially under the terms of the Access to Public Administration Files Act.

## **Assessment Criteria**

The Board of The Danish 3R-Center has been approved as a subcommittee of Innovation Fund Denmark. The Board will therefore assess the quality of the research on behalf of Innovation Fund Denmark.

All applications are first evaluated based on the following overall criteria:

- Well-defined research project
- Scientific standard suitable for peer-reviewed publishing

Emphasis will be placed on the following criteria:

- Quality of research/science
- Feasibility

- Relevance
- Potential impact on the three R's
- Current or future importance of the techniques to medical, biological or veterinary research
- Strategy for promoting the proposed research to the scientific community.

It is the intention that all three R's are covered by the grants awarded.

The final funding decision will be taken by the Minister for Food, Agriculture and Fisheries based on recommendations made by the Board of the Danish 3R-Center.

### **How to apply**

Applications must be made using the application form provided. Applications should be written in English and the text must not exceed **five and a half** A4 pages. Empty space on pages due to the format in the application form does not count as text. A reference list of up to **one** A4 page can be attached.

The following issues must be addressed:

#### **1. Project title**

Clear and specific title of the project.

#### **2. Contact person**

Name of the applicant including all relevant contact information. Only one person's name and contact information can be included.

#### **3. Background information (maximum 350 words)**

An outline of existing scientific knowledge in the area and a description of how the project relates to previous and ongoing national and international research.

An explanation should be given for the need for 3R research in this area and how, if successful, the project will benefit medical, veterinary or biological research. If the work has potential application to other research areas, it may also be beneficial to describe this. Sufficient details of other past and current research should be given, to show that the aims are scientifically justified, and to demonstrate that this project will add distinct value to what is already known or is in progress.

Any funding will require that the applicant holds all the necessary permits, and that all relevant legislation is complied with at all times. Please state how all necessary permits will be obtained and how the legislation will be complied with.

#### **4. Non-technical summary in Danish (maximum 250 words)**

A short summary in layman's language, i.e. with minimal use of technical terms and with concise sentences.

#### **5. Aim of the research project (maximum 100 words)**

The overall aim of the project should be described.

The main aims and objectives of the proposal should be listed, in order of priority.

An indication must be given as to which of the 3Rs the application will address.

#### **6. Hypothesis**

The underlying scientific hypothesis/hypotheses should be described.

#### **7. Which R does the application primarily address?**

It must be stated which R the application primarily addresses. However, a research project may in rare cases concern two or even three R's to exactly the same extent. In that case, more than one R may be specified. For further inspiration, see the Danish 3R-Center's statement paper on replacement:

<https://en.3rcenter.dk/the-3rs/the-concept-of-replacement/>

#### **8. Materials and methods (maximum 350 words)**

A description and the rationale behind the materials and methods to be used must be given.

Any ethical considerations concerning the use of human participants, animal research objects, primary cells or tissues, or genetic and biological risks must be discussed.

Details must be provided of any procedures of severe or moderate severity, including how the procedure is to be undertaken, the adverse effects experienced by the animals, and the measures to be taken to minimize any pain, suffering, distress, or lasting harm. Any animal experiments must be described in as many details as possible. Details should include information on animal care, housing and husbandry, refinements to procedures, and any welfare assessments that will be carried out.

Details must be given of the experimental approaches, study designs, and techniques which will be used. It is not necessary to describe each experiment, but sufficient detail must be given to demonstrate how and

why the research is likely to be competitive in its field, and that it has been carefully planned to provide useful and reliable results. Details of experimental design must be given, including:

- Calculation of sample size for the cells or animals per study, in a power evaluation if possible.
- How the experimental design will minimize the number of animals to be used.
- What measures will be used to reduce bias in experimental design (e.g. blinded assessment of results).
- How experimental outcomes will be assessed and analysed.

Those parts of the application or plans that are particularly original or unique should be highlighted.

## **9. Timetable**

A detailed, graphically presented work plan should be provided, preferably as a Gantt chart displaying milestones and progress to be made.

## **10. Relevance, perspective and potential impact on the three Rs (maximum 400 words)**

The impact of the research on the 3Rs must be described. This should take the form of a detailed description of the impact, highlighting the key points. The application should clearly state which of the 3Rs the proposal contributes to.

An exact description of how the research will directly replace, reduce, and/or refine the use of animals in research or testing must be given. It is important to include measures of impact (see below) and to describe how the proposal will have an impact on the three R's within the research community. An application that does not include measures of impact will not be considered.

The description must include:

- Which of the three R's the proposal will advance.
- How the Replacement, Refinement and/or Reduction would be achieved.
- The likely scale of Replacement/Reduction in animal use and/or improvement in animal welfare, both locally and in the wider scientific community.

It is particularly important to provide calculations concerning the potential impact on the 3Rs, including any intermediate results likely to be achieved. Estimates can be made by, for example, searching literature databases to see how many papers are published each year reporting use of animal models and the typical number of animals used per experiment in the published papers.

The following questions are **important to consider**:

Replacement/Reduction:

An estimate should be made of how many animals will no longer be required per experiment/procedure/test. An estimate should also be made of how many laboratories/companies worldwide who conduct these tests. Likewise, the percentage reduction in animal use that could be achieved should be estimated.

Refinement:

The following questions should be addressed:

- What are the evidence that animal suffering will be reduced, and/or 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 locally and in the wider scientific community?

Relevance and perspective:

A description should be given of the relevance and perspective of the research project in relation to the expected outcome, including how this is relevant and can be implemented. Relevant questions include:

- Does the proposed model/technique have scientific advantages over traditional ones?
- Is the proposed research likely to generate commercially exploitable results?
- Does the research group or the host institution have experience in taking forward the commercial exploitation of research in this area? Any such plan must be realistic and credible and, if applicable, appropriate industrial links should be given.

Those who will benefit from the research should be described, as well as details of academic or industrial collaborators. The areas of research on which the work could have an impact, any clinical translation potential, as well as the general benefits to science should also be discussed.

## **11. Collaborators**

All those involved in the project should be mentioned (name and title) and their role(s) described.

For each person a CV (maximum 1 page) and a list of the 10 most relevant publications/patents during the last 5 years should be attached.

## **12. Dissemination plan**

In order to generate the highest impact on the three R's, the Danish 3R-Center will place emphasis on a robust plan for communication and dissemination of the results. An outline should be given of how the research will be communicated and disseminated to encourage use of the 3R benefits, not just limited to publications and conference attendance.

Plans, if any, for communicating information about the work to the public should also be described. This should include a description of how such plans are supported by the host institution's own policies and facilities for communication with, and education of, the general public.

The communication plan should include, among other things, participation in the annual conference organised by the 3R-Center, oral/poster presentations at conferences, as well as scientific and non-scientific publications. A list of peer-reviewed publications or plans for such should also be provided. Close collaboration with the 3R-Center regarding publication of project results on the 3R-Center website and in non-scientific media is expected. Expenses for Open Access publication are to be covered by the hosting organisation/institution/company.

For projects selected for funding, the following applies:

- An **English version** of the Danish non-technical summary from the application form (a maximum of 250 words) in layman's language – i.e. with minimal use of technical terms and with concise sentences suitable for publication on the 3R-Center website – must be submitted to the Danish 3R-Center. The Center must receive the English summary within a week after the applicant has received notice about funding.

## **13. Budget**

Please provide a budget in which you specify all expenses including salary (scientific and technical personnel), equipment, and overhead.

## **14. Project start**

Write the project start date (day, month, year).

## **15. Project termination**

Write the date when the project is finished (day, month, year).