

In Response to:
NIH Request for Information: Soliciting ideas for new NIH Common Fund programs
Notice Number: [NOT-RM-22-016](#)

By People for the Ethical Treatment of Animals
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1. Transition-to-Translation program

Summary: This proposal would use the NIH Common Fund to create a Transition-to-Translation program, a vehicle for building confidence and competence in reliable and relevant non-animal methods that can best protect human health. This program would make human-relevant research accessible to investigators wishing to switch from animal to non-animal methods, prioritizing support for early-career researchers, but open to all. Built on existing NIH funding mechanisms, this program will help ensure a robust biomedical workforce that is able to compete with a rapidly changing scientific landscape and respond to increasing calls for improved translation of biomedical research findings into human health advancements.

Description: As animal-free research methods continue to expand, increased education and hands-on training will accelerate the transition to these methods. However, in deploying such initiatives, it is important to recognize that barriers can exist to adopting new approaches and technologies, and therefore, efforts to build confidence and provide additional support are needed. Early career researchers wishing to use non-animal methods, such as organs-on-chips or computational modeling, may have not had the training or opportunity to become familiar or adept at using these research tools. At the same time, mid-career investigators may find themselves using animal models they no longer feel to be relevant to their research question, but lacking the time and funding to re-train themselves and their team in non-animal methods, purchase new equipment, and support their students and staff during such a substantial transition.

A new Transition-to-Translation program, supported by the NIH Common Fund, would make animal-free research accessible to investigators wishing to switch from animal to non-animal methods, prioritizing support for early-career researchers, but open to those in all stages of their research career.

There is a need for education and hands-on training in non-animal methods. Students and early career scientists must be provided with opportunities to develop the skills necessary to contribute to the future of their own field, as well as the field of non-animal research, so that the U.S. can compete with international developments and does not fall behind in research advances. However, many study programs lack sufficient courses about animal-free methods. Some supplemental training programs have been developed to begin to fill this gap. For example, in the EU, the European Commission's Joint Research Centre hosts a summer school on non-animal approaches. In Canada, the University of British Columbia has accepted a new undergraduate module offered by the Society for Humane Science on "Non-Animal Methods in Biomedical Science", which focuses on training students in animal-free methods for research and testing. Many online resources by experts in the field also exist, including those offered by PETA Science Consortium International e.V. and the Physicians Committee for Responsible Medicine. The Dutch Transition Programme for Innovation created a series of "helpathons", action-orientated workshops built around a specific question that encourages researchers through a community forum to think creatively and harness the power of coincidence in the discovery of new opportunities with regard to non-animal approaches.

Thus, information about animal-free research and testing is available, but is rarely a component of biomedical education.

The UK's innovation agency, Innovate UK, has recognized that overcoming skepticism about the ability of non-animal methods to model biological processes will help remove a major barrier to the use of these methods. Furthermore, conservatism and inertia obstructing the move away from animal-based methods can be overcome by encouraging scientists "to think beyond their immediate research areas to how their skills, technology and 'know-how' can be leveraged and exploited to accelerate the development and adoption of" advanced non-animal methods. It is vital that such educational initiatives be adopted and given ample financial support from funders such as NIH, to benefit everyone from future scientists to established professionals.

The Transition-to-Translation program would provide early career and established intramural and extramural researchers using animal-based methods with retraining opportunities and encourage them to forge multidisciplinary collaborations to evolve their skills and establish new and innovative ways of asking research questions and methods for answering them.

There are a number of existing funding mechanisms NIH could employ within the Transition-to-Translation program:

- Institutional Training Grants can be provided to trainees at the undergraduate, graduate, and postdoctoral levels to receive training that would allow them to make the transition from animal to non-animal research methods.
- Continuing Education Grants can be offered with the explicit purpose of establishing educational programs to train researchers on available non-animal methodologies.
- The NIH Director's Early Independence Award could prioritize applicants who currently use non-animal, clinically-applicable methods; are making the transition from animal to non-animal methods; or are developing and/or validating non-animal methods.
- The NIH Bench-to-Bedside and Back Program could prioritize pairing basic science researchers using animal models with Intramural Research Program (IRP) clinical researchers. The goal would be to assist those researchers interested in permanently switching from animal-based research to clinical work.
- The NIH Graduate Partnership Program could prioritize those students who are hoping to use non-animal methods in their research but do not have access to those tools at their home institution.
- Program Project Grants or Center Grants can be offered to investigators interested in establishing centers for non-animal methods at their institutions.
- Grant supplements can be offered to investigators who wish to switch to non-animal methods mid-funding.

As the range of animal-free testing methods continues to expand, researchers must keep pace with these pivotal developments. Increased education and training initiatives are urgently required to build confidence and competence in reliable and relevant non-animal methods that can best protect human health. The Transition-to-Translation program would help ensure a robust biomedical workforce that is able to compete with a rapidly-changing scientific landscape and respond to increasing calls for improved translation of biomedical research findings into human health advancements.

Resources to support this proposal:

https://joint-research-centre.ec.europa.eu/events/jrc-summer-school-non-animal-approaches-science-3_en

<https://www.forhumanescience.org/influencing-science-culture/university-education>

<https://www.thepsoci.eu/our-work/training>

<https://www.pcrm.org/ethical-science/animal-testing-and-alternatives/nura>

<https://www.tpihelpathon.nl/>

<https://www.ukri.org/wp-content/uploads/2015/11/IUK-071221-RoadmapNonAnimalTech.pdf>.

2. Systematic Review Collaboratory

Summary: This proposal would use the NIH Common Fund to create a Systematic Review Collaboratory (SRC) that would aid in the design and rapid execution of systematic reviews for translational and preclinical research. The SRC would develop and disseminate best practices and training on systematic reviews and provide funding for both intramural and extramural investigators wishing to conduct translational or preclinical systematic reviews. The SRC would work across NIH to perform systematic reviews that would assess the effectiveness of various translational and preclinical research models employed by NIH-supported researchers.

Description: The past two decades have brought to light many obstacles in scientific research, including both the “reproducibility crisis” and failures in the translation of research findings to the clinical setting. Depending on the metrics used, basic and preclinical research fail to lead to human benefit between 90 and 95 percent of the time, representing an enormous inefficiency of resources and a failure to meet the needs of patients and their families in a timely manner. Addressing this crisis requires funding agencies to step back and assess—with great care and accuracy—the sources of these inefficiencies. Systematic reviews (SRs) provide a method for doing this.

According to the Cochrane Library, SRs “identify, appraise and synthesize all the empirical evidence that meets pre-specified eligibility criteria to answer a specific research question. Researchers conducting SRs use explicit, systematic methods that are selected with a view aimed at minimizing bias, to produce more reliable findings to inform decision making.” A new Systematic Review Collaboratory (SRC), supported by the NIH Common Fund, would provide the NIH and other federal funding agencies with clear evidence on which they could reliably base future policy and funding decisions and improve the agency’s return on investment.

The SRC would support the execution of SRs at two levels. First, the SRC would convene or commission an unbiased team to conduct SRs to assess the effectiveness of the preclinical and translational research models—including both animal and non-animal methods—being used by NIH intramural and extramural researchers to provide evidence-based data on whether these models are fit-for-purpose. To assess these characteristics, SRs would include information on past translation of the research model and the return-on-investment received by the public for the results of experiments using such models, as well as the costs of the model, including the harms experienced by animals, where applicable. Examples of such SRs could include examinations of the use of the cecal ligation and puncture mouse models for understanding and treating human sepsis, the use of nonhuman primate models for developing HIV therapeutics, the use of human organs-on-chips for preclinical drug development in specific fields, and many more.

Second, the SRC would develop best practices and training modules to aid U.S. researchers in designing and performing their own SRs and provide funding for them to do so. According to a study on SR training conducted by the Netherlands Organisation for Health Research and Development (ZonMw), coaching researchers to conduct SRs “increased support for the 3Rs,

improved transparency, [increased] awareness of the need for better study quality, [resulted in] greater critical appraisal of the use of animals, and improved knowledge transfer.”

Once resources and teams are in place, the SRC can also be utilized to conduct SRs of clinical and public health research.

NIH already supports the concept that SRs should be used to guide funding decisions. Several U.S. funding entities, including NIH, are members of the Ensuring Value in Research Funders’ Forum (EViR), a collection of the most prominent international funding bodies formed to address waste in clinical and preclinical research. EViR states as its second guiding principle, “Research should only be funded if set in the context of one or more existing systematic reviews of what is already known or an otherwise robust demonstration of a research gap.” It explains, “This is important because new research not set in the context of what is already known leads to unnecessary duplication, studies that cannot change decision making (e.g. will not change the meta analysis), or inappropriate design (e.g. inappropriate outcome measures, incorrect prevalence assumptions, failure to learn from past previous studies).” To apply this principle, EViR says that funders must “[r]outinely assess whether an adequate review has been done and whether the results of that review support the case for further clinical or preclinical research.”

The recommendation to conduct scientific reviews of the efficacy of models is, therefore, already one that the largest funding bodies in the world agree is a necessary principle for guiding valuable research and reducing waste in research funding. Yet, NIH has yet to take concrete steps to implement this principle.

When established, the SRC will create valuable new data on model efficacy that will be accessible to all NIH institutes as well as the larger research community. SRC deliverables will guide funding decisions to improve efficiency and the translatability of NIH-supported research findings into prevention and therapies, helping NIH to realize its goals of protecting and improving health, ensuring a high return on the public’s investment in research, and promoting the highest level of scientific integrity.

Resources to support this proposal:

<https://www.cochrane.org/our-evidence/what-are-systematic-reviews>

<https://www.syrclenetwork/>

<http://www.dcn.ed.ac.uk/camarades/default.htm>

<https://evir.org/our-principles/applying-the-principles/#principle2>

<https://www.elsevier.com/connect/authors-update/why-systematic-reviews-matter>

Menon, et al. 2021: <https://doi.org/10.1371/journal.pone.0260619>

Ritskes-Hoitinga and Pound, 2022: <https://doi.org/10.1177/01410768221093551>

Russell, et al. 2022: <http://dx.doi.org/10.1136/bmjos-2021-100219>