Concept Clearance on Enhancing Rigor and Reproducibility of Animal Research by Studying and Managing Environmental Extrinsic Factors

The NIH has long recognized the importance of rigor and reproducibility in biomedical research. The NIH Director convened a working group under the Advisory Committee to the Director (ACD) to prepare recommendations on enhancing rigor, transparency, and translatability in animal research. This ACD Working Group delivered its final report in 2021, which included a recommendation that *"NIH should encourage and support work to better understand, monitor, record, and report important extrinsic factors related to animal care that may affect research results"*. Extrinsic factors can include but are not limited to water quality, temperature, lighting parameters and regimen, movement/vibration, and noises.

Major themes of the ORIP Strategic Plan 2021-2025 are to facilitate development and ensure availability of the highest quality and most useful animal models and related resources for advancement of research on human disease; improve and disseminate the best models for human conditions and diseases that are of interest to multiple NIH Institutes and Centers (ICs); and advance the application of new technologies to support research resources and improve generation, care, preservation, and distribution of animal models. To gauge the status and gaps in rigor and reproducibility of animal studies related to extrinsic factors, ORIP and NIA organized in September 2022 a series of 3 virtual sessions as a workshop in collaboration with several ICs. Topics included extrinsic factors, housing environments, equipment and modern technology. Key factors were highlighted for different animal models, like water quality for aquatic animals, lighting and temperature for rodents, and social structure for large animals. It was also acknowledged that modern equipment is required to manage, measure, and report relevant extrinsic factors critical for the species selected. It was concluded that systematic studies are needed to provide crucial data regarding the impact of environmental extrinsic factors on rigor and reproducibility of animal research.

Based on the recommendations from this workshop, ORIP proposes to initiate a program to support research projects from shared facilities, cores, and resources focused on systematic characterization of the effects of extrinsic factors that affect physiological and behavioral outcomes in experimental conditions using animal models. To align with ORIP's NIH-wide mission, proposed projects must be applicable to two or more NIH ICs and explore multiple body systems or evaluate diseases that impact multiple body systems over the lifespan of the animal model. Proposed projects are expected to support the purchase of modern equipment to manage, measure, and study relevant extrinsic factors in rigor and reproducibility of animal studies.

Examples of suitable projects for the proposed initiative could include studies using appropriate equipment to investigate: 1) application of individual smart tank or cage systems, thus allowing monitoring and management of local environments for animal housing under husbandry and experimental conditions; 2) biological mechanisms affected by a specific extrinsic factor(s) which is mediating physiological responses and contributing to rigor and reproducibility; or 3) development of biomarkers, behavioral changes, and specific physiological parameters in response to extrinsic factors which can be monitored. Proposed initiative outcomes would include key information on critical extrinsic factors related to experimental conditions using animal models which are affecting biologic functions and reproducibility of basic and translational studies; standardized procedures to record, document and report critical extrinsic factors in a standard, reproducible and ready form for computer analyses; and building equipment resources to address gaps in studies of extrinsic factors.

Based on the urgent need to improve preclinical research using animal models, ORIP requests concept clearance from the Council of Councils to support a new initiative for "Enhancing Rigor and Reproducibility of Animal Research by Studying and Managing Environmental Extrinsic Factors."