

Request for Information (RFI):
Effects of Extrinsic Environmental Factors on Animal Research: Rigor and Reproducibility
Notice Number: [NOT-OD-17-011](#)

EXECUTIVE SUMMARY

The Office of Research Infrastructure Programs (ORIP) issued this RFI to learn from the broad biomedical research community about: a) the current knowledge concerning the effects of extrinsic environmental factors on experiments using animals, b) general practices regarding collecting data on environmental factors and reporting them in publications, and c) to receive recommendations to improve documentation and the reporting of extrinsic environmental factors in the future.

A total of 14 responses came from the biomedical research community, offering perspectives from stakeholders with diverse professional backgrounds - academia, veterinary medicine, professional and advocacy organizations. They commented on several types of animals, including non-human primates, rodents, other mammals such as dogs, pigs, and rabbits, aquatic animals, amphibians, and insects. Most responses mentioned the impact of extrinsic environmental factors on rodents.

All responses indicated that there is a significant deficit in our knowledge of how the environmental factors may impact results of experiments involving animals. Without this knowledge and mitigation of environmental factors, it is impossible to ensure repeatability among experimental outcomes.

The effects of the extrinsic environmental factors are complex and involve multi-level interactions that affect physiology and behavior through various, often undetermined, biological mechanisms. Responses listed a variety of factors of potential significance, such as noise, vibration, relative humidity, temperature, light cycle, bedding, type of caging, quality of drinking water, diet, quarantine practices, husbandry, and maintenance procedures. The level of influence of any of these factors varies with the particular animal species. Depending on the species, responders identified the most pressing issues that need standardization or further studies; for example, diet for Zebrafish and flies, or noise for rodents.

Overall, underreporting of environmental conditions in metadata associated with experimental data is a compelling issue. Responders agreed that environmental parameters must be monitored and recorded to augment experimental data, making them more valuable for future use.

However, practices vary among facilities and even if the parameters are monitored, they may not be recorded. Metadata associated with extrinsic environmental factors are rarely shared with researchers and are seldom reported.

Since extrinsic factors are a large and mostly unacknowledged source of experimental variability, the impact of these factors should be systematically studied. The responders recommended that the NIH initially focus on the extrinsic factors which have the largest impact on research outcomes for key animal models of human diseases (rodents, zebrafish, and flies) in areas such as development, endocrinology, reproduction, neurobiology, and pharmacology.

Research that promotes rigor and reproducibility requires thorough documentation of extrinsic environmental variables in experimental protocols and publications. The responses suggest the NIH can provide support and guidance as outlined below:

- developing species- or research field-specific templates that would assist the process of collating relevant extrinsic variables;
- organizing workshops or sponsoring lectures at scientific research meetings;
- supporting free online webinars and web-based courses;
- raising awareness by publishing editorials in the professional press; and
- working together with journal publishers on implementing detailed reporting of extrinsic factors in research publications.