

ACLAM Position Statement on Reproducibility

Although characterized by observation and experimentation, advances in science greatly depend upon peer-based communication and evaluation to ensure that new information is analyzed, verified, and confirmed. Ideally, published studies should include methodological and procedural descriptions, environmental conditions and meta-information, which should be readily accessible and provided in sufficient detail to enable a knowledgeable and capable researcher to replicate experiments and achieve equivalent results. However, many published reports lack these basic elements or omit essential information. As a result, attempts to repeat the studies conducted in other independent laboratories or animal facilities may result in different and often contradictory outcomes. Consequently, a public and scientific crisis of confidence in the veracity and reliability of scientific discoveries, including but not limited to biomedical research, is occurring. Numerous reports have identified multiple causes of lack of reproducibility, including faulty experimental design, inconsistent technique, missing or incomplete descriptions of experimental details, and a lack of insistence by funding agencies and peer-reviewed journals on well-established criteria for conduct and publication of good science (1,2). When laboratory animals are involved, the ethical stakes are heightened. Experimental results that cannot be replicated and result in the use of additional animal subjects violate Russell and Burch's Principles of the replacement of animals, reduction to the lowest numbers of animals needed, and inclusion of refinements for improved animal use practices (3). Veterinarians, scientists, Institutional Animal Care and Use Committees (IACUC), Institutional Officials and others engaged in the care and use of laboratory animals must work together to ensure the generation of reliable research data and avoid wasteful animal experimentation.

Humane laboratory animal care, including consistent, efficient and effective practices in husbandry, staff and investigator training, careful technique development and validation, and both preventive and clinical veterinary medicine, can enhance data reproducibility by providing scientists with quality animals and providing those animals with appropriate food, water, bedding, caging, and environmental and social conditions. Although all of these parameters have been emphasized for decades as critical determinants of high quality research and continue to be highlighted in the *Guide for the Care and Use of Laboratory Animals* (4), it is of utmost importance, with respect to reproducibility, that scientists include comprehensive descriptions of details of animal care and husbandry in their manuscripts and supplementary materials. No detail of this sort should be deemed too small for sharing. For example, macaques with origins from different Asian countries may differ in their disease profiles after simian immunodeficiency virus inoculation (5). Similarly, the interplay between ambient temperature, cage ventilation rates, diet, and environmental enrichment materials can impact mouse metabolism in important ways (6). Regardless of species, thorough documentation of animal's genetic make-up, dates of birth or arrival, sex, pathogen exclusion lists and documentation of infectious disease outbreaks, cage sanitation processes, environmental enrichments in housing quarters, and any other particulars will, in turn, assist other scientists in using the same

husbandry conditions or identifying differences that may influence experimental outcomes.

Experimental reproducibility is impacted by differences in laboratory animal use and institutional oversight. For example, IACUC reviewers should assess whether the number of animals requested in protocols will satisfy statistical power needs in accordance with Russell and Burch's original guidance on reduction (7). Animal studies should be designed in the spirit of the ARRIVE (Animals in Research: Reporting *In Vivo* Experiments) guidelines, thus encouraging the reporting of more detailed methodologies that will greatly aid other laboratories in their attempts to recreate the same model systems (8).

Another critical influence on reproducibility, and one that is gaining both scientific and administrative attention, is the role of the microbiome in data variability and study outcomes. Encouraging investigation and increased understanding and acknowledgement of the interaction between microorganisms and the whole animal is necessary to further analyze the impact of this variable on the outcomes of modern biomedical research.

In conclusion, it is incumbent on laboratory animal veterinarians and the scientific community to define elements of study design that affect experimental reproducibility. Scientific progress relies on rigor and reproducibility, particularly for advances made possible by comparative medical research with animals.

References

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