IACUC Newsletter for the Nonaffiliated Member

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In This Issue

New Approach Methodologies (NAMs)

Why are we talking about NAMs in the context of the 3Rs? On page 5, *The Guide* provides these definitions and examples for the 3Rs:

"Replacement refers to methods that avoid using animals. The term includes **absolute** replacements (i.e., replacing animals with inanimate systems such as computer programs) as well as **relative** replacements (i.e., replacing animals such as vertebrates with animals that are lower on the phylogenetic scale).

*Refinement refers to **modifications of husbandry or experimental procedures** to enhance animal well-being and minimize or eliminate pain and distress.*

*Reduction involves strategies for obtaining comparable levels of information from the **use of fewer animals or for maximizing the information obtained from a given number of animals** (without increasing pain or distress) so that in the long run fewer animals are needed to acquire the same scientific information*.

NAMs can be an alternative to any of the 3Rs. The following is extracted from the NIH Policy & Compliance topics section – When Are Alternatives to Animals Used in Research?: Different research questions necessitate the use of different approaches. Some approaches involve animal models; some others do not. While animal models are critical and employed in all fields of biomedical research, NIH encourages researchers to use complementary approaches to ensure rigorous and reproducible studies whenever possible.[1]

Is the IACUC already considering New Approach Methodologies?

Yes! OLAW's Sample for Animal Study Proposal [2] includes questions where NAMs can be provided as alternative methodology. Thus, there is an expectation that NAMs or other alternatives are included in the study proposal. Examples of questions where is appropriate to include NAMs ask about the justification for using animals at all, or considerations for using less invasive, less stressful procedures.

How do the US Government principles relate to NAMs?: [3]

U.S. Government Principle	What the Principle Requires	Examples of NAMs That Support This Principle [5]
Principle II	Procedures involving animals should be designed and performed with due consideration of their relevance to human or animal health, the advancement of knowledge, or the good of society.	**Human cell-based organoids** (e.g., human intestinal or liver organoids) used to study disease mechanisms or drug responses with direct human relevance before animal studies are proposed. **Replacement (partial)** – replaces some exploratory animal studies with human-relevant systems; [6] **Reduction** – narrows animal studies to those needed after human-based data are generated.
Principle III	The animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results. Methods such as mathematical models, computer simulation, and in vitro biological systems should be considered.	**Computational modeling or in silico simulations** used to predict dose ranges or toxicity, followed by **in vitro assays** to refine hypotheses before any animal testing occurs. **Replacement** – when non-animal methods fully answer a question;

Principle IV	Proper use of animals, including the avoidance or minimization of discomfort, distress, and pain when consistent with sound scientific practices, is imperative. Unless the contrary is established, investigators should consider that procedures that cause pain or distress in human beings may cause pain or distress in other animals.	**Reduction** – when modeling and in vitro data reduce animal numbers needed for confirmatory studies. **1. High-throughput in vitro screening assays** used to identify toxic compounds early, preventing animals from being exposed to procedures likely to cause significant pain or distress. **Refinement** – prevents or minimizes painful animal procedures; 2. **Patient-derived tumor organoids** (3D cultures grown from human tumor tissue) used to study tumor growth, drug response, and immune-tumor interactions **in vitro**, before or instead of animal tumor models. **Refinement:** avoids inducing tumor burden and associated distress in animals during early testing

OLAW says the following: Sometimes "NAMs" is used interchangeably with the term "alternatives" in the context of complete replacement of an animal model. However, it is important to remember that NAMs are not the only alternatives in biomedical research. [3]. Indeed, a recent article in Nature highlights that while the use of NAMs—both alone and in combination with animal models—is increasing, significant scientific challenges remain before NAMs can fully replace animal models for studying disease, discovering drugs, testing medical devices, or addressing other hypotheses relevant to human health.[4]

What are the key takeaways for Nonaffiliated [community] members?

- NAMs support the 3Rs (Replacement, Reduction, Refinement)
- Scientific experts choose the research models
- As an IACUC member, I check that:
  -The use of animals is clearly justified [Why are animals used at all]
  - Alternatives have been thoughtfully considered
  - Explanations are understandable to a non-scientist [Lay Summary]
- You are **not expected to recommend specific NAM technologies**—your value is in asking clear, ethical, and public-facing questions.

Resources for You

- U.S. Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training
- Public Health Service Policy on Humane Care and Use of Laboratory Animals
- The Guide for the Care and Use of Laboratory Animals 8th ed.
- USDA Animal Welfare Act and Animal Welfare Regulations
- Guidelines for the Care and Use of Mammals in Neuroscience and Behavioral Research
- Occupational Health and Safety in the Care and Use of Research Animals 1997
- NIH Office of Laboratory Animal Welfare
- United States Department of Agriculture Animal and Plant Health Inspection Service
- AAALAC International
- Guidance on Qualifications of IACUC Nonscientific and Nonaffiliated Members

New Approaches Methodologies (NAMs)

[1] **When Are Alternatives to Animals Used in Research?** https://grants.nih.gov/policy-and-compliance/policy-topics/air/alternatives

[2] OLAW Sample Animal Study Proposal https://olaw.nih.gov/sites/default/files/oacu3040-2.htm#ratanuse
[3] Alternatives and NAMs https://olaw.nih.gov/AlternativesandNAMs#what-are-nams?
[4] The age of animal experiments is waning. Where will science go nexthttps://www.nature.com/articles/d41586-026-00563-3
[5] Roadmap to Reducing Animal Testing in Preclinical Safety Studies- https://www.fda.gov/files/newsroom/published/roadmap_to_reducing_animal_testing_in_preclinical_safety_studies.pdf
[6] Lee CJ, Nam Y, Rim YA, Ju JH. Advanced Animal Replacement Testing Strategies Using Stem Cell and Organoids. Int J Stem Cells. 2025 May 30;18(2):107-125. doi: 10.15283/ijsc24118. Epub 2025 Mar 11. PMID: 40064522; PMCID: PMC12122249.

Would you like more information?

Please contact your IACUC Administration if you would like to recommend topics or activities to enhance and support your role in the IACUC.
Give us your feedback! IACUC Quarterly Newsletter & Nonaffiliated Member Development Survey – Fill out form

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