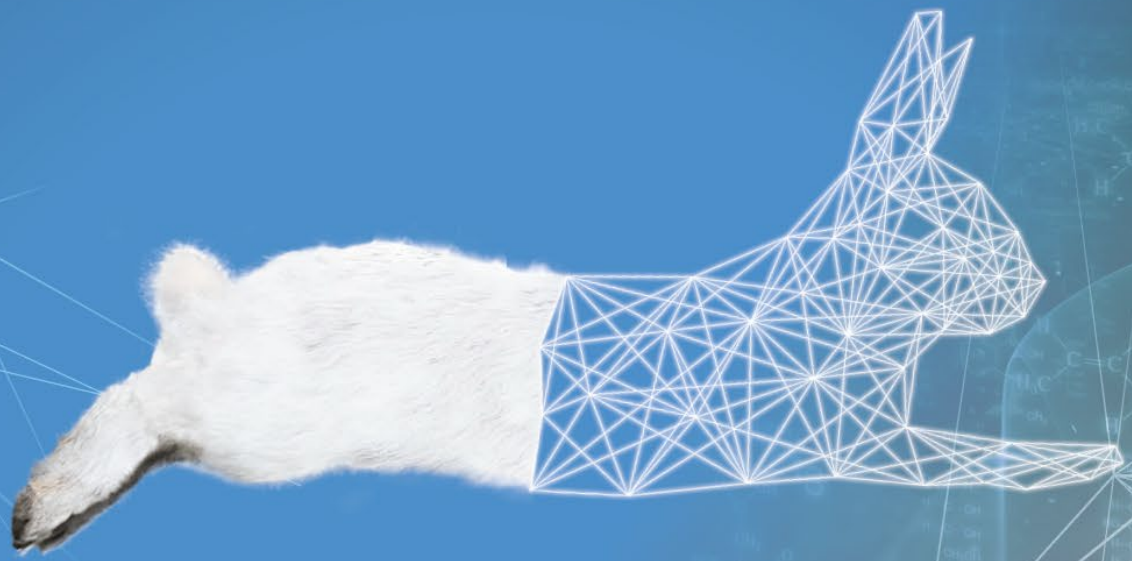
ICCVAM Public Forum

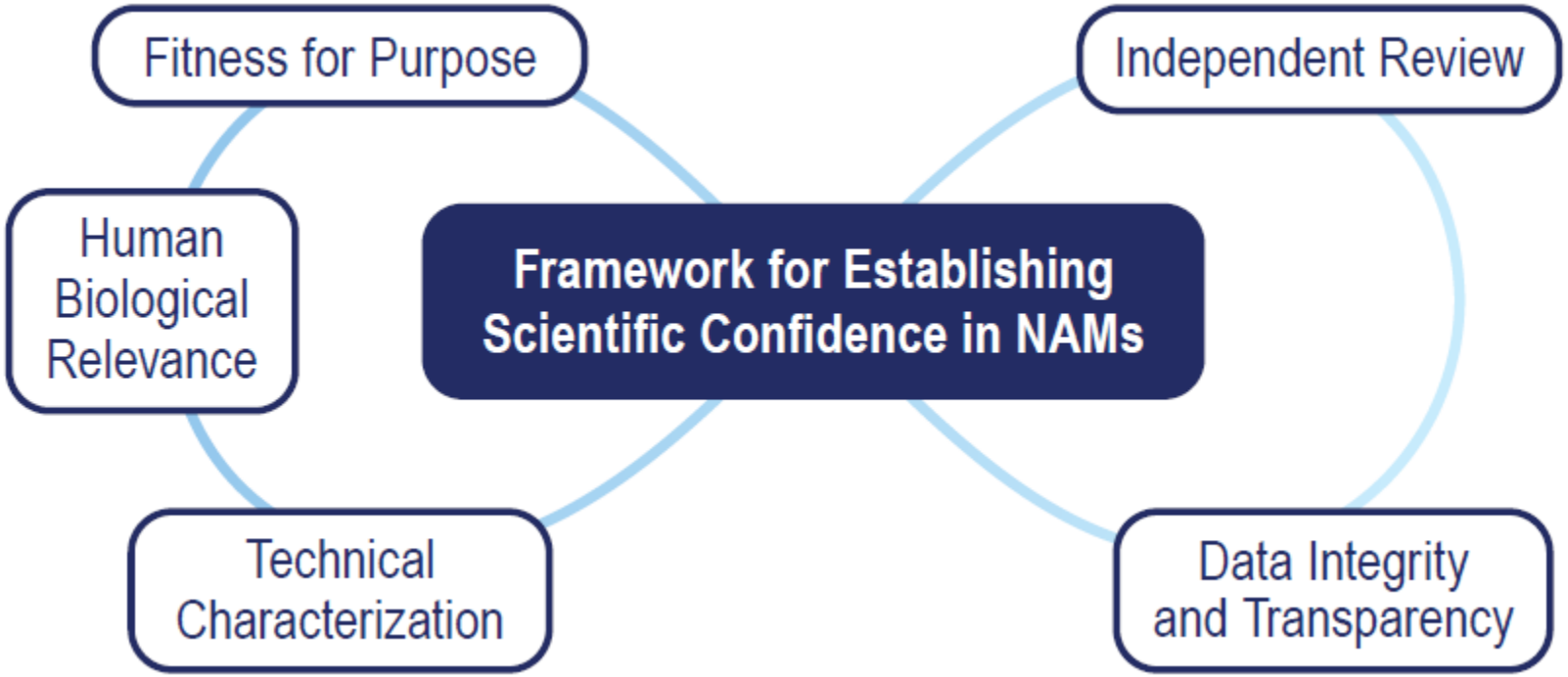
Comments from People for the Ethical Treatment of Animals

May 27, 2022



Gaining confidence in NAMs

Instead of relying on direct comparisons between animal-derived and non-animal data, agencies should ensure that NAMs fulfill their intended purposes and provide technically reliable and human relevant information.



Van der Zalm et al. 2022. A framework for establishing scientific confidence in new approach methodologies. *Submitted*.

Reducing Animal Testing through Alternative Methods (+$5.0 million / 11 FTE)

The FY 2023 Budget includes $5.0 million in new funding to implement a cross-agency New Alternative Methods Program to spur the adoption of new alternative methods for regulatory use that can replace, reduce and refine animal testing (the 3Rs), and improve predictivity of nonclinical testing to streamline the development of FDA-regulated products and bring them to US public and patients more rapidly and more efficiently while assuring they are safe, effective, and that patients can depend on them. The New Alternative Methods Program will be centrally

Except for a few contract research organizations, only NCTR has the infrastructure and expertise in the U.S. to conduct large-scale guideline rodent assays, including developmental and reproductive toxicity studies. NCTR research in support of the Predictive Toxicology Roadmap is essential to providing FDA with the guideline testing required to make an informed transition to alternative testing paradigms. This will be accomplished by implementing a testing strategy where, as possible and in close collaboration with the FDA product centers, animal experimentation and alternative testing methodologies are conducted in parallel. This side-by-

DEPARTMENT of HEALTH and HUMAN SERVICES

Fiscal Year

2023

Food and Drug Administration

Justification of Estimates for Appropriations Committees

Increasing the uptake of NAMs

- Update ICCVAM member agency educational resources
- Incentivize the use of NAMs, such as increased funding, collaborative opportunities, and research exposure
- Increase communication among ICCVAM member agencies and other stakeholders

About the Workshop

The Animal Welfare Act (AWA) regulations require principal investigators to provide Institutional Animal Care and Use Committees (IACUCs) with documentation demonstrating that their activities do not unnecessarily duplicate previous experiments and that alternatives to procedures that may cause more than momentary pain or distress to the animals have been considered (9 C.F.R. § 2.31 (d)(1)(ii-iii)(2022)). An alternative is any method which results in the replacement or

USDA National Agricultural Library
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Animal Welfare Information Center

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Animal Tests

NOTE: This information is provided for historical and other reasons, especially since animal testing is still being done in some cases, and because toxicologists, risk assessors, and others are faced with interpreting the results of new and old studies that used animals.

Animal tests for toxicity have been conducted prior to and in parallel with human clinical investigations as part of the non-clinical laboratory tests of pharmaceuticals. For pesticides and industrial chemicals, human testing is rarely conducted. Years ago, results from animal tests were often the only way to effectively predict toxicity in humans.

Animal tests were developed and used because:

- Chemical exposure can be precisely controlled.
- Environmental conditions can be well-controlled.
- Virtually any type of toxic effect can be evaluated.
- The mechanism by which toxicity occurs can be studied.

Figure 2. Rats have traditionally been used in toxicity studies using animals
(Image Source: iStock Photos, ©)

Standardized Animal Toxicity Tests

Animal methods to evaluate toxicity have been developed for a wide variety of toxic effects. Some procedures for routine safety testing have been standardized. **Standardized animal toxicity** tests have been highly effective in detecting toxicity that may occur in humans. As noted above, concern for animal welfare has resulted in tests that use humane procedures and only as many animals as are needed for statistical reliability.

Need for increase in communication – caries example

1995 – publication of the Anticaries Drug Products Monograph

2001 – FDA requests comments on the use of the non-animal IOA model. No response has been issued.

2009 – Procter & Gamble citizen petition (pH cycling model). Petition is open.

2015 – Colgate citizen petition (IOA model). Petition is open.

2020 – grBiosystems citizen petition (pH cycling model). Petition is open.

2021 – Intertek citizen petition (pH cycling model). Petition is open.

Assessing the efficacy of NAMs

The paper "**Animal Metrics: Tracking Contributions of New Approach Methods to Reduced Animal Use**" (*ALTEX* 2022;39(1):95–112) outlines one company's approach to measuring animal use reductions due to NAM use. For each endpoint assessed by a NAM, information is provided on the corresponding *in vivo* test, the number of animals used in that study design, the proportion of equivalent animal savings relative to the *in vivo* study, a rationale to support the value assigned, and the default number of equivalent animal savings by employing the NAM approach.

01

Define what is in scope, starting with the definition of 'animal' (e.g., mammals, vertebrates, animals born during reproductive studies) and applicable studies (e.g., animals used for 'in house' experiments, at contract research organizations, as part of consortia, in funded studies at universities).

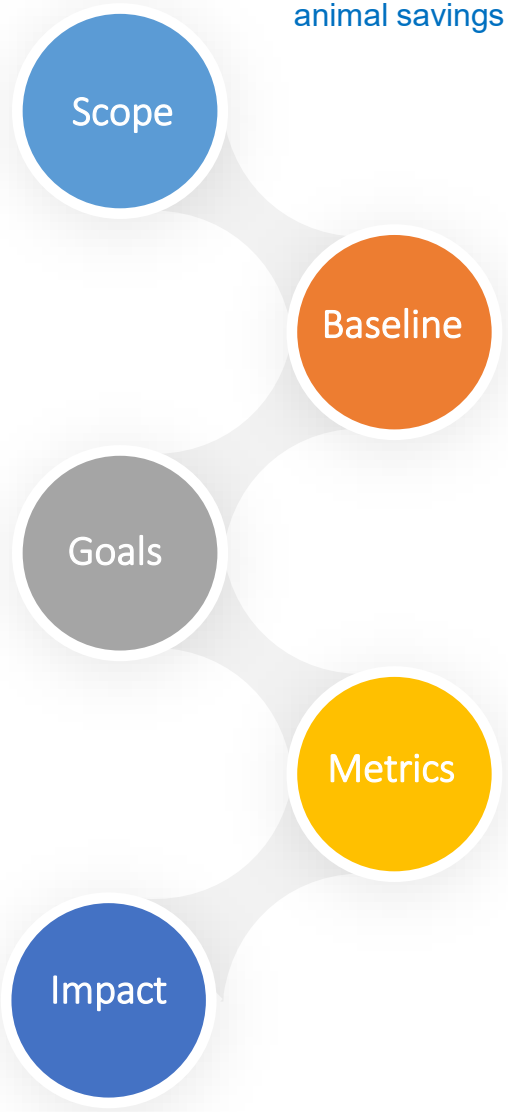
03

Identify goals. These goals will differ among industry, government agencies, and other entities, and they may shift over time, for example, as companies' product portfolios change. Some companies may have a goal of a percentage decrease in animal use. Others adhere to a goal to conduct tests on animals only to comply with regulatory requirements.

05

Measure impact using the absolute number of animal savings due to NAM use or the percent reduction in animal use due to the application of NAMs.

To monitor reduction in animal use and progress implementing NAMs, metrics can be developed to track animal savings based on the utility of NAM data.



02

Establish baseline animal use, including well defined rules for inclusion/exclusion that can ensure consistency in future assessments. Methods used to establish annual animal use numbers may monitor animal orders or animals placed on study in-house.

04

Establish metrics for animal savings from *in silico*, *in chemico*, and *in vitro* methods; study waivers; and intelligent design based on data use and level of certainty. In some cases, a NAM make completely replace animal use, resulting in animal savings equal to all animals used in a study. In other instances, NAM data may partially fulfill information generated by animal-based guideline studies; in which case, the animal equivalent number for the NAM is a subset of the animal-based guideline study.

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