AO VET News

How to Choose the Right Animal Model and Make Appropriate Decisions in Preclinical Research

AO VET GUEST BLOG POST WRITTEN BY STEPHAN ZEITER AND CAROLINE CONSTANT

Non-reproducibility is a major killer of research value in preclinical studies. According to the most recently published estimate (2015), it wastes 28 billion US dollars annually in the US alone. Of that amount, inappropriate study designs account for almost 28%[1] of the problem. That means poor study design choices cost American research funders 7.8 billion dollars annually. And as the study design depends heavily on the animal model used, the choice of that model is crucial.

In an AO PEER webinar, researchers Stephan Zeiter and Caroline Constant from the AO Research Institute Davos explained some key principles of optimizing the value of preclinical research. This article accompanies and summarizes that webinar's main points.

How to Choose the Most Suitable Animal Model

The Starting Point

The starting point to decide upon your model is not the animals you have access to, the model you are familiar with, or the available budget. The priority is to formulate a well-chosen research question. But what makes a research question suitable? It must be answerable, relevant, focused, and precise. The more precise your research question is, the higher the chance of selecting an appropriate animal model to answer it. This will be the base for the hypothesis and study aim.

However, researchers must resist the urge to save resources by using one study to answer multiple questions. This can end up diluting the first question. Ideally, a study has one main question to answer and one hypothesis to test.

Is an Animal Model Absolutely Necessary?

Before planning a project involving animals, every researcher should remember the first of Russel and Burch's three Rs of principles of animal research (i.e., replace, reduce, refine):[2] Replace animal experiments whenever possible. Every possible alternative must be explored. If cell culture experiments or a bioreactor are appropriate methods to answer your question, these methods must be prioritized over animal experiments. Also, if someone else has already done what you want to do, a thorough literature review will avoid using more animals to answer the same research question.

Determine your Primary Outcome

Once the research question and hypothesis are in place, and no alternative methods to animal experiments are suitable, a primary outcome must be chosen. This should be chosen to allow the research to answer the research question and prove or disprove the hypothesis. Further, the primary outcome will be used to determine the sample size. Additional outcome measures can be defined as secondary outcomes of the study.

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Assessing the parameters that best answer the research question requires appropriate methods. For example, if the research question deals with bone healing, the possibility of observing bones as they heal includes CT imaging, mechanical testing, or histology. The researcher's choice will depend on which method will be most useful in relation to the research question. Secondary outcomes may require other methods.

Choosing the Preclinical Model: Animal Species and Strain

Once your primary outcome measure is selected, choosing the preclinical model that will allow you to answer your research question best. The optimal animal model (species and breed/ strain/ stock) is the one that will yield the necessary type and range of data to answer the research question, using the smallest sample size possible and considering the associated costs.

To summarize, the research question determines the primary outcome measure. And the combination determines the choice of animal model and strain. As with many decisions affecting research projects, the optimal animal model is the one that enables the research team to answer the research question both thoroughly and reproducibly.

How to Increase Scientific Rigor

Control Groups

Controls must be included in animal studies. Negative and positive control groups should be considered. Depending on the research question, the type of controls may vary: for example, within-subjects designs involve testing the same subjects before and after an intervention. Other study designs use control groups for comparison with the experimental group. In the case of a vaccine study, for example, the experimental group would receive the vaccine being tested; a positive control group would receive another vaccine (possibly the current gold standard) with a predictable rate of success; and a negative control group would receive injections containing no active ingredient.

Randomization and Blinding

Research has shown that randomization and blinding have a major impact on the number of false positive outcomes from preclinical studies involving animals… The AO VET Guest Blog post continues on the AO VET Web site. Access the complete blog post here.

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