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CASE AND COMMENTARY: PEER-REVIEWED ARTICLE

How Should Clinician-Researchers Model Regard for Nonhuman Animals Bred for and Used in Human-Centered Science?

Rebecca L. Walker, PhD

Abstract

If we assume that nonhuman animals experience pain or distress, then ethically justifying human-centered research with only nonhuman animals as subjects likely requires that the research's benefits to humans must, at least, outweigh harms suffered by the nonhuman animals. Yet this reasoning does not seem to account well for the ethical view that nonhuman animals are morally valuable in their own right. This commentary on a case considers this ethical tension and discusses how clinician-researchers should navigate it. This commentary also suggests why clinician-researchers' reasoning about the nature and scope of their obligations to nonhuman animals extends beyond governing regulations and federal oversight, which is silent on or ambiguous about nonhuman animals as morally valuable in their own right.

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Case

Dr Q is a clinician-scientist who studies brain tumor growth. The clinical utility of Dr Q's work has grown in importance over the decades, and Dr Q's team has contributed to many improvements in human brain tumor diagnostics.

Over the years, Dr Q's team has responded to many changes required by the Code of Federal Regulations (9 CFR §§1-4.11)¹ and the Health Research Extension Act of 1985,² which augments the Animal Welfare Act of 1966.³ Evolution in social and cultural thought, attitudes, and activism also demand Dr Q's lab staff members' consideration and reconsideration of their roles in creating a market for laboratory animal cultivation and in using live mice in human-centered research. Dr Q seeks advice from Dr A, a veterinarian member of their organization's Institutional Animal Care and Use Committee (IACUC), to more carefully consider the team's short- and long-term efforts to minimize suffering among the live mice needed to carry out Dr Q's protocols.

Dr Q mentions to Dr A, "I'd like to model thinking carefully about whether and when our efforts to minimize our animals' pain and suffering is enough to meet our obligations to

the animals we use for human clinical science applications. I suspect that orienting ourselves to these questions and concerns will be key to the future of our lab and work."

Dr A considers how to respond, how to continue the exchange of ideas, and how to advise Dr Q.

Commentary

Dr Q is interested in "thinking carefully" about the broader moral question of when the lab's efforts sufficiently meet its obligations to nonhuman animals. This query calls for more than a regulatory approach, since it asks basic moral questions that are typically not addressed within nonhuman animal research oversight. A take-home message from this commentary is thus the importance of using moral reasoning to address complex ethical issues in laboratory practices. Because oversight is also integral to the conduct of ethical animal research, I additionally consider how US nonhuman animal research oversight relates to some of the points raised from the perspective of moral reasoning. After all, the researcher in this case consults with a veterinarian member of the IACUC, and it is the job of the IACUC to oversee application of the regulatory structure, not necessarily to address broader moral concerns.

Identifying common biases is key to this endeavor. Regardless of their purposes or origin stories, mice are individual creatures with their own subjective welfare, which is undermined by pain and distress, and whose value is independent of their usefulness. Thus, when we are asked to "model" regard for nonhuman animals bred for and used in human-centered science, we must distinguish between what we owe these creatures themselves and how we might support their interests only for the sake of some other important purpose.⁴

To illustrate, we might treat nonhuman animals well in research merely because doing so is good for the science-healthy animals lead to better data.⁵ Or we might treat nonhuman animals well in research merely because this "models" care that mentees should learn to perform or helps to curb public "attitudes ... and activism" about nonhuman animal use. All of these reasons for treating the mice well in these studies, important as they are, are consistent with the idea that the mice themselves have no independent value. Thus, if it turns out that nonhuman animal welfare is not consistent with the goals of a particular protocol, then there remains no independent reason to support animal welfare. Or if it turns out that the public doesn't care about nonhuman animal welfare or that students can learn to perform good animal care in other ways than direct modeling of such care, then again there is no independent reason for supporting the welfare of the nonhuman animals in question. For these reasons, if we want to take seriously what the case refers to as "our obligations to the animals," then we must assume from the outset that the nonhuman animals themselves matter, morally speaking-meaning that our obligations are directly to them and not merely to further some other goal.6

Justifying the Research

The idea that mice have some value independent of their purpose-bred status has implications for how we should think about what does or does not justify their use. By using the term *human-centered science*, the case seems to refer to animal research that, like most research of its kind, aims at human health or human welfare benefit. For such research, the only moral justification available, once we assume that animals themselves are morally valuable—and once we also agree that they are harmed by the

research—is that the human benefit outweighs, in some morally appropriate sense, the animal harm.⁷

Are nonhuman animals in this case harmed? The case study focuses on tumor growth, an area of nonhuman animal research in which pain and distress are expected.⁸ The researcher, moreover, is wondering if efforts to "minimize" these harms are sufficient, which indicates that they are present in the research. Looking beyond the specifics of the studies in question, mice are typically killed at the end of experiments,⁹ and, even if they are not killed, they must live their entire lives in vivarium confinement. Such confinement includes restricting the types of food, space, and cohabitants available to the mice and subjecting them to the prescribed lighting and temperature settings of the human-controlled space.^{9,10} There is reasonable debate regarding whether and how mice are harmed through being killed or living in vivariums; however, it is important to recognize these potential sources of nonhuman animal harm as well as those imposed by the study protocol itself.

From a moral reasoning point of view, then, the use of mice in studies like those of Dr Q could only be justifiable if it leads to human benefit that is greater than the harms they experience. To say that the use of mice could only be justified in this way is not to say that it necessarily can be justified in this way. For example, if mice have rights not to be used in these ways, these rights would preclude their use even if the balance of benefit and harm would support their use.¹¹ Let us stick nevertheless with the idea that such use could only be justified if the human benefits outweigh the nonhuman animal harms. The case states that the clinical utility of the work in question "has grown in importance," which indicates that this research has a generally promising trajectory. From the point of view of justifying animal protocols, however, the question is whether each study gives a reasonable trajectory of benefit and whether this benefit is greater in some morally suitable sense than the harms caused to the animals.¹² As a moral justification for an individual study, then, it is not enough that the research program in general is beneficial for humans. Dr Q's research team should ensure that each one of its studies is assessed for the potential value of the research in comparison with nonhuman animal harms that cannot be alleviated, including pain and distress experienced in the study, any potential environmental stressors, and death.

If we suppose that a study can be justified by being, overall, more beneficial for humans than harmful for the nonhuman animals involved, it might still be the case that some kinds of harms to nonhuman animals are out of bounds, morally speaking, because the levels of pain and distress are too great. This is an evolving area of consideration in nonhuman animal research, but ethically it seems right that there are some harms that are wrong to inflict on other sentient beings even if the benefits could be significant. Thus, Dr Q should consider establishing parameters on the types of tumor-related harms studied in the lab. Doing so not only is a matter of humane end points, but also rules out types of studies in which the burden of nonhuman animal harm is too great to be conscionable.

Ethics and Oversight

How does the US oversight regime, as reflected in IACUC standards for animal care and use, relate to these points gained through moral reasoning? On the specific question of if animals have independent moral value, US oversight does not take a definitive stance,¹³ although it does appeal to obligations to uphold animal welfare for all who work in animal science.⁹ Regarding the obligation to balance harms to animals against

specific benefits of a protocol, US regulations are ambiguous about how or if IACUCs are to balance benefits and harms,¹⁴ unless unrelieved pain and distress are necessary to meet scientific goals.⁹ Finally, there is no established upper limit to animal pain and distress, with researchers relying instead on scientific justification, searches for alternatives, and refinements to any research methods that cause unrelieved nonhuman animal pain and distress.¹⁵ Given that US oversight does not dictate an approach to some of these important moral issues under consideration, it stands to reason that the regulatory structure itself will not guide Dr Q on how to meet a sufficient standard in fulfilling moral obligations to the animals. At the same time, meeting regulatory obligations is itself a necessary (though not sufficient) condition for the conduct of ethically sound research. In other words, ethical research must at minimum meet regulatory standards, but meeting such standards does not guarantee that a project is ethically sound.

Beyond justifying Dr Q's research, crucial ethical considerations arise during the research itself. For example, researcher obligations of care for these dependent nonhuman animals require more than merely monitoring overt signs of health and welfare and following minimal housing standards dictated by oversight regimes. Instead, teams should be aiming to support the highest level of species-specific animal flourishing possible for the animals in their care.¹⁶ For example, the study team should consider how housing, food, vivarium space, and cohabitation can be implemented to best support mice as mice. Furthermore, in managing tumor burden for these animals, the team may be able to better support their animal subjects by thinking creatively about analgesic interventions.¹⁷ Finally, it is important in this case that Dr Q is concerned about the use of nonhuman animals and is looking for outside advice from Dr A. Taking this step shows character traits important for being a practically wise researcher.

Conducting nonhuman animal research in an ethical manner requires much effort and thought. Being motivated by compliance with regulations and public concern for nonhuman animals are both important ways to spur ethically better practices. However, the willingness to look beyond regulatory requirements and public perception to engage questions of broader moral justification and deeper ethical practice is an important feature of the practically wise researcher. The researcher in this case wants to meet ethical obligations to the nonhuman animals themselves and that requires taking a moral reasoning approach.

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Rebecca L. Walker, PhD is a professor of social medicine and a professor of philosophy at the University of North Carolina at Chapel Hill. Dr Walker earned a PhD in philosophy from Stanford University and was a postdoctoral fellow in bioethics and health policy at Johns Hopkins University. Her journal publications and edited volumes span topics in animal and human research ethics, genomic ethics, health justice, and respect for autonomy.

Editor's Note

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