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Collaborative studies and animal reuse

Toby Pfeiffer, PhD, was well known for her contributions to the field of learned helplessness and its relationship to prisoner-of-war captivity stress in humans. She used squirrel monkeys for much of her research, subjecting them to mild but frequent electrical shocks, such as 0.75 milliamps for 30 s, repeated 20 times in 1 hour. She justified her methodology to the IACUC by noting that she had subjected herself to the same shock intensity and duration and had felt only moderate pain. She said that the monkeys also appeared to have experienced only moderate discomfort, as evidenced by the shifting of their position and related evasive movements, but no vocalizations or other indicators of severe pain. Furthermore, she presented data showing that cortisol levels in shocked monkeys were only slightly higher than those in unshocked control monkeys. These statements were typically included in all of Pfeiffer's protocol applications. Her studies included behavioral tests followed by euthanasia and subsequent brain structural and biochemical analyses.

Pfeiffer's most recent protocol submission was somewhat different. She planned

to use a modified animal shock protocol (fewer repetitions) and then carry out her behavioral testing. Instead of euthanizing the monkeys, however, she proposed sending them to a nearby colleague who would carry out multiple physiological samplings (metabolomics) with equipment available only in his laboratory. As part of his work he would reshock the animals, using the same methodology used by Pfeiffer. Pfeiffer's protocol went into great detail about the science behind both studies, the methods of transporting the animals, the means of accounting for shipping and other stressors, the need for approval by the receiving university's IACUC and many other details. Initially, this seemed somewhat reasonable to the IACUC, but after a discussion with Pfeiffer, the committee became firm in its contention that the two studies were independent and could be done with two groups of squirrel monkeys, not just Pfeiffer's. The committee decided that it was inappropriate to subject the animals a second time to the inescapable electrical shocks. In other words, the IACUC concluded that the reuse of the animals was

more of a convenience and cost savings than a required extension of Pfeiffer's research. Approval of the study was withheld.

Pfeiffer responded to the committee's action with three related arguments. The first was that the IACUC was essentially forcing the use of twice as many squirrel monkeys because her colleague would now have to purchase the same number of animals that she already had. The second argument was that the learned helplessness, not the shocks, was the real source of animal distress and would not be induced in this study. Her final argument was that there is no federal regulation against subjecting an animal to repeated mild (or even severe) pain or distress in the same or in unrelated experiments. In her proposed protocol, Pfeiffer argued, there was only moderate and transient pain, and she disagreed with the IACUC that the studies were unrelated.

Should the IACUC reconsider its decision and allow the animals to be sent to Pfeiffer's colleague, based on the arguments she presented?

RESPONSE

One study, two institutions

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Learned helplessness is an animal model of human depression. The subject gives up trying to escape a noxious situation and learns that any action on his part is fruitless¹. The NRC *Guidelines for the Care and Use of Animals in Neuroscience and Behavioral Research* state, "In all those behavioral tests of depression, proposed procedures for monitoring, recordkeeping, and humane intervention should be described in the associated animal-use protocol and approved by the IACUC"². Pfeiffer seems to have satisfactorily assured the IACUC that

her original protocol was in compliance with these guidelines.

Metabolomics is defined by the National Institutes of Health (NIH) as a science whose goal is "to identify, measure, and interpret the complex time condition-dependent concentration, activity, or flux of metabolites in cells, tissues, and other biosamples, such as blood, urine, and saliva" (<http://grants1.nih.gov/grants/guide/rfa-files/RFA-RM-06-010.html>). The NIH issued Requests for Applications for grants supporting metabolomic studies in this and recent years in a roadmap initiative to encourage the use of innovative technologies in metabolomics.

Pfeiffer can justify the use of her colleague's equipment to get metabolomics data as a continuation of her own studies of learned helplessness, but that doesn't seem to be all that's going on here. There are many unanswered

questions for the IACUC to ask. We see no reason to purchase additional monkeys. It is part of the IACUC's duty to keep animal numbers to the minimum statistically required. We do, however, feel that more information is needed to explain the changes to the original protocol Pfeiffer suggests. Will she still be euthanizing the animals and doing the brain analysis after her colleague obtains his data? Why is she reducing the number of shocks? Her argument falls down, in my opinion, when she states that these animals will not be in a state of learned helplessness when they are sent out. Can she still compare the data with that from her previous protocols? And if they are not inducing learned helplessness, then is she perhaps using the animals in this protocol to get control data for studies in the future? From the information given, we cannot tell. The notes given suggest that