

Jerald Silverman, DVM, Column Coordinator

## IACUC evaluation and external scientific review

Dr. John Smith, a distinguished investigator at Great Eastern University, had spent his career searching for a treatment for hearing loss. After 20 years of research, he developed a drug that could potentially improve auditory function after damage to the inner ear. The drug was administered by injection into the middle ear with the use of a fine needle inserted through the eardrum.

Smith submitted a protocol to the IACUC describing a small study on cats in which he would treat one group of animals with the drug and another with saline to determine whether the drug prevented the changes in the anatomy of the inner ear that normally occur with aging. After a discussion, the IACUC asked Smith to modify his experimental design such that each animal would act as its own control by injecting the drug into one ear and saline into the other. This design would reduce the number of animals required by 50%. To avoid controversy and lost time, Smith accepted the opinion of the IACUC and

carried out the experiment subsequent to protocol approval.

The result of the initial study was quite promising, and Smith submitted a grant application to the National Institutes of Health (NIH) to fund a more complete examination of the effectiveness of his new drug. He proposed the same experimental design suggested by the IACUC, with each animal serving as its own control. The NIH reviewers were impressed by Smith's preliminary data but were seriously concerned about each animal serving as its own control. Because the drug was lipophilic, they argued that it was likely that some of the drug would be absorbed into the bloodstream and would indirectly affect the untreated ear. Still, the grant application received a very good score, but not quite good enough to be funded. Smith revised his grant according to the suggestions of the NIH reviewers and received an exceptional score when the application was reconsidered.

During the 'just-in-time' period, Smith submitted to the IACUC the protocol that

related to his grant. Once again, the IACUC indicated he could eliminate 50% of the animals he proposed to use by using each animal as its own control. Smith stated in his communications to the IACUC that the design of the study was demanded by the NIH scientific review group that considered the grant and whose membership included leading experts in the field. He said that the review group raised a significant scientific concern about the experimental design stipulated by the IACUC in its effort to reduce animal usage. Smith received the same reply to all the arguments he made: "The IACUC has no obligation to consider the opinions of peer review panels, including NIH review groups, during its deliberations."

Should Smith persevere, arguing that good science, not reduction of animal numbers, should prevail? Or should Smith capitulate to the wishes of the IACUC? Do you think that the IACUC should consider the opinions of an external review panel during its deliberations?

### RESPONSE

#### Study section's opinion matters

Bill J. Yates, PhD &  
Joseph Newsome, DVM, DACLAM

IACUCs must consider the *US Government Principles for the Utilization and Care of Vertebrate Animals Used in Testing, Research, and Training*<sup>1</sup> when reviewing and approving protocols. Principle III states that "the animals selected for a procedure should be of an appropriate species and quality and the minimum number required to obtain valid results." In this case, the principal investigator provided the IACUC an opinion from an impartial expert body (an NIH Scientific Review Group (SRG)) indicating that it violated the principles that it was

attempting to uphold, by demanding the use of a number of animals and an experimental design that may not produce valid results.

Section 2.31 of the Animal Welfare Act and Regulations<sup>2</sup> stipulates that an IACUC has limited authority to dictate the experimental design of studies: "Except as specifically authorized by law or these regulations, nothing in this part shall be deemed to permit the Committee or IACUC to prescribe methods or set standards for the design, performance, or conduct of actual research or experimentation by a research facility." Moreover, the Public Health Service (PHS) recognizes that SRGs should have a key role in determining how NIH-funded research, including that using animals, is carried out. The Office of Laboratory Animal Welfare's Frequently Asked Question D-12 about the *PHS Policy on Humane Care and Use of Laboratory Animals*<sup>3</sup> (PHS Policy) specifies that "the primary focus of the SRG

is scientific merit and the primary focus of the IACUC is animal welfare." This view was recently reiterated in NIH Notice NOT-OD-10-027 (ref. 4).

An IACUC is not compelled to consider the opinions of SRGs. But because the membership of SRGs includes leading scientific experts, grant reviews can provide valuable information to an IACUC, particularly with regards to how a study should be carried out in such a way as to generate valid results. Neither the Animal Welfare Act and Regulations nor the *PHS Policy*<sup>5</sup> instructs an IACUC not to consider the opinions of consultants, including grant reviews conducted by SRGs. Item 9:4 of *The IACUC Handbook*<sup>6</sup> encourages IACUCs to solicit opinions from consultants, particularly if an investigator appeals an IACUC decision.

When making complicated decisions, an IACUC should consider all available sources