No need to duplicate prior pilots

We agree with Jones' contention that the federal funding agency (presumably the National Institutes of Health [NIH]) had already

evaluated the reproducibility of her research during the peer review process. The NIH has been aware of the concerns regarding the issue of reproducibility¹. Indeed, its

webpage states, "the NIH is committed to promoting rigorous and transparent research in all areas of science supported by a variety of grant programs. Grant application instructions and the criteria by which reviewers are asked to evaluate the scientific merit of the application include the expectation for full transparency in proposing and reporting experimental details so that grant reviewers may assess the proposed research and others may reproduce and extend the findings."² We can therefore conclude that this facet of the PI's research had been thoroughly vetted before the grant was awarded.

However, peer review does not preclude an IACUC member from raising the issue of reproducibility as a concern. As opined by the reviewer of Jones' protocol, an IACUC member's responsibilities may include assessment of the reproducibility of a study as a means to assure the committee that animals are not being inappropriately used. *The Guide for the Care and Use of Laboratory Animals* states: "While the responsibility for scientific merit review normally lies outside the IACUC, the committee members should evaluate scientific elements of the protocol as they relate to the welfare and use of the animals."³

Although the grant was awarded, it is possible that discrepancies exist between the methods described in the grant proposal and the animal use protocol. The IACUC is performing its due diligence by ensuring that the issues of reproducibility and grant congruency are effectively addressed at the protocol level before further studies are approved⁴. To this end, a pilot study can be very valuable in validating the reproducibility of a technique, and an IACUC is certainly authorized to require that one be performed. However, since pilot studies have already been performed by the PI and assessed by the committee in this circumstance, we agree with Jones' contention that duplicating those studies would neither be informative nor a responsible use of animals. We suggest that Jones include the results of the previous pilot studies in the animal use protocol to proactively address this concern.

While we cannot comment on the quality of peer review for the journals in which Jones has published, if those journals do in fact limit detail in the Materials and Methods section, it is possible that the manuscript might not provide sufficient

A WORD FROM USDA AND OLAW

In response to the issues posed in this scenario, the U.S. Department of Agriculture Animal and Plant Health Inspection Service (USDA-APHIS) and the National Institutes of Health Office of Laboratory Animal Welfare (NIH-OLAW) provide the following clarifications.

In this scenario, the IACUC is deciding whether a pilot study is indicated to validate the reproducibility of a researcher's established methods because of concerns raised in publications about the techniques.

USDA-APHIS response

The Animal Welfare Act regulations require an IACUC to review an animal study proposal to ensure it meets the requirements that the work avoids or minimizes pain/distress, and contains a written assurance that the activity does not unnecessarily duplicate previous experiments^{1,2}. In addition, the regulations require a proposed activity to include a rationale for the numbers of animals to be used³. In this scenario, the IACUC is deciding whether a pilot study is indicated to validate reproducibility. The investigator however relayed that her work had been peer reviewed for Federal funding, and that pilot studies were already performed as requested by the IACUC three years ago, hence to do so again would be a waste of time and animals.

The Animal Welfare Act regulations do not give the IACUC the authority to prescribe methods or set standards of design, performance, or conduct of research⁴; however the IACUC has the authority to request additional information that supports the written assurance that the work is not unnecessarily duplicative, and the investigator's rationale for the appropriateness of the numbers of animals to be used. The IACUC also has the authority to invite consultants to assist in reviewing the protocol⁵ before deciding whether to approve, require modifications to approve, or withhold approval for the proposed activity⁶.

NIH-OLAW response

As noted by other reviewers, the PHS Policy and the Guide expect the IACUC

to consider whether the research design is sound^{7,8}. Besides further pilot studies, OLAW agrees with the other reviewers that the IACUC has better options to reconcile the reproducibility concerns. The IACUC may choose to 1) ask the researcher to include the outcome of the pilot studies in the renewal protocol, 2) increase post-approval monitoring of the study to confirm consistency in the application of the techniques in question, or 3) request that the researcher provide more details of how she internally validates her techniques. Regarding NIH grant applications proposing the use of animals, it is the institution's responsibility, not the IACUC's, to ensure congruency between the application and the IACUC protocols^{9,10}. Institutions have flexibility in which program carries out this responsibility. □

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Published online: 27 January 2020

<https://doi.org/10.1038/s41684-019-0464-x>

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