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To ensure the best chance of grant success, address rigour and reproducibility in your grant proposal.

THREE QUESTIONS TO ADDRESS RIGOUR IN YOUR PROPOSAL

Addressing weaknesses and limitations in your science will reassure potential funders. **By Jennifer L. Wilson and Crystal M. Botham**

Since 2018, the US National Institutes of Health (NIH) has required that research proposals explicitly describe scientific rigour. They want to know scientists' approaches to ensuring the fidelity of their data, minimizing bias and maximizing new knowledge. The NIH did this to address transparency and reproducibility challenges in research. Other funders have also signalled a long-term commitment to better practices in science. In 2020, for example, the European Commission's Directorate-General for Research and Innovation, the body responsible for the European Union's research and innovation policy, issued guidance to improve research reproducibility. Writing about rigorous choices can be simple. As grant coaches at the Grant Writing Academy at Stanford University in California, we work with scientists who have already thought carefully about the quality of their science and want to address rigour in their grants. Our process focuses on asking simple questions to help them sufficiently justify the rigour in their research proposals.

For example, one recent proposal included a sentence like this: "We will use the stroke mouse model and treat the mice with our novel compound daily, for three weeks."

As grant coaches without specific knowledge of the model, we probed the writer with questions looking for more detail, such as "Why this mouse model?" and "Why daily dosing?" As it turns out, the mouse model and dosing regimen were standard in that laboratory, and the lab had published a study that showed the model was relevant to the stroke outcome of interest.

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Jennifer Wilson and Crystal Botham developed a framework for writing grant proposals.

We pushed the writer to be more specific in their writing, to communicate how their approaches minimize bias due to the choice of model organism: 'We will use the stroke model mouse, a model system we and others have shown to be relevant to understanding stroke outcomes [references], to test the effect of novel therapeutic compounds."

This sentence is more successful because it clearly shows how the writer's choices are adequate for addressing their research question, and how this choice will help them to derive knowledge about the disease condition.

Our three-question framework helps to frame scientific choices when writing research proposals. Our process guides writers to explain their experimental choices, by asking questions that address limitations in their proposal:

1. What are the essential weaknesses or limitations in your science? Every scientific method has limits. Often, these limits are methodological or field-specific.

2. Which methods will you use, or are you already using, to address these limitations? These may be standard methods in your research group, but it's important to highlight them as such for a reviewer.

3. What makes these methods adequate? Justify your choices by confirming how the field has tested or accepted these methods for overcoming limitations.

Revisiting our mouse-model example, one limitation of the approach is whether testing the compounds in the stroke model sufficiently replicated human stroke progression (this addresses question 1). Using the stroke-appropriate mouse model addressed this weakness (and answers question 2), and referencing peer-reviewed publications justified the writer's selection of this model (which answers question 3). The revision justifies the animal model's relevance to the proposed research and references published data that support that statement.

Through our grant coaching, we have found that addressing scientific rigour often requires careful and specific wording: instead of, "We will use our new method to anticipate drug effects," we would guide a writer to "We will calibrate our new method using a landmark dataset, a gold-standard comparison in our field, to benchmark against known effects before anticipating new drug effects." A new method could bias results, but benchmarking the method against a well-regarded dataset of known effects justifies the method's adequacy for understanding effects of a new drug.

"Our framework provides one way to prioritize and address hurdles to reproducible science."

In another scenario, the sentence, "We will assess treatment effects by comparing wound healing of the untreated left leg and treated right leg," needs an introductory clause: "We have previously shown that wound-healing rates are different between individual animals, making it difficult to compare between them [references]. Thus, we will generate two wounds on the same animal and apply treatment to only one wounded area." This explanation helps a reviewer to appreciate the writer's ability to assess the treatment's effect, and to prevent the effect from bias due to differences in wound-healing ability of individual animals.

Addressing rigour in research proposals is often less about changing scientific choices or overall project design, and more about justifying how experimental-design choices address limitations that could prevent the researcher from answering their question or diminish the knowledge they derive from their experiment.

Justifying scientific choices requires deliberate practice to achieve strong, persuasive writing. The grant writer must be aware of and unafraid to share the limitations to their science. The selection of the mouse model is a decision that supports rigour, but someone not familiar with the lab's research, such as a grant reviewer, might not understand this unless the writer specifically justifies it. In the case of the stroke model, the selection of the mouse model is a decision that improves quality, but that might have been taken for granted by the grant writers because everyone in the lab in this example uses this model. Understanding why the lab uses this stroke model would have enabled this writer to better justify their choice to a reviewer who isn't familiar with the lab's best practices.

Often, it's difficult to decide which choices require justification. We recommend examining published work and talks to understand limitations and how they were addressed. It might feel daunting to address all possible limitations to a research approach, so start by investigating journal publication requirements for reproducibility and transparency. Many journals have specific requirements about the reporting of protocols, the use of biological samples, the availability of analysis code and other technical details. Journal requirements are designed to overcome field-specific challenges to reproducibility and transparency. Take note of how others justify their choices – you don't have to go as far as explaining whether an experiment needs a control (almost all good experiments have at least one control), but you will probably need to justify how a particular control is well-suited to your research question.

Gaining this awareness is not an overnight process. Learning the limitations of a scientific field is an ever-evolving process, and assessing how others justify their rigorous decisions will deepen your understanding of how to make them. Our framework provides one way to prioritize and address hurdles to reproducible and transparent science. We encourage writers to have peers outside their research group read their work and use the three-question framework. Often, an outsider can provide a fresh perspective on the choices that a writer has taken for granted or failed to explicitly address.

We feel that developing awareness of rigorous practices during the writing of research proposals will elevate rigorous thinking throughout the research enterprise.

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