Considerations for Developing Ethical Biomedical Grant Proposals for the National Institutes Of Health

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Introduction

Highly trained medical writers are typically familiar with case studies of scientific misconduct, defined as data fabrication, data falsification, and plagiarism.[1] However, less than 2% of researchers are thought to engage in scientific misconduct.[2] In recognition that avoiding scientific misconduct is only a small part of research ethics, the National Institutes of Health (NIH) released the following statement in 2009: "[R]esponsible conduct of research is defined as the practice of scientific investigation with integrity. It involves the awareness and application of established professional norms and ethical principles in the performance of all activities related to scientific research."[3] This guiding principle can be used to shape every aspect of our work when developing grant proposals.

The ethical codes from the American Grant Writers' Association[4] and the Grant Professionals Association[5] highlight key ethical issues for grant writers, including avoiding conflicts of interest, following confidentiality guidelines, avoiding plagiarism, and accurately representing the prior work and future capabilities of the funding recipient. They also describe the importance of not allowing payment to be contingent on grant success.

This article addresses additional areas in which we commonly see room for improvement for the medical writer regarding research ethics, with a focus on NIH proposals. The NIH supports the work of over 300,000 biomedical scientists through competitive research funding amounting to $41.7 billion in 2020,[6] making the NIH the largest public funder of research worldwide. The NIH received 54,903 research grant proposals in 2019,[7] many of which were written or edited by professional medical writers.

In the last half decade, the NIH has taken concrete action to improve the responsible conduct of research. In late 2015, the NIH released a major change to the application instructions and review criteria for research projects, called "Implementing Rigor and Transparency in NIH & AHRQ Research Grant Applications,"[8] which was updated in 2018.[9] In 2020, the NIH also released an updated Policy for Data Management and Sharing (DMS),[10] which builds upon existing requirements for disseminating research results to the public. These policy statements cover a range of ethical issues in biomedical research, which will be discussed in the next sections. The portions of these policy statements that focus on clinical research design and dissemination of human subjects' research data will not be covered here, as those topics are beyond the scope of this article.

Given that one of the medical writer's responsibilities is to ensure that the text is compliant with the funder's policies, the new NIH policy statements represent important areas in which the medical writer can make a positive impact on ethical conduct in the grant development process.

Research Plan: Enhancing Rigor and Reproducibility

The reviewers will assess 4 elements of rigor.[8,9,11] Below are descriptions of those elements and recommendations to consider.

1. Rigor of the prior research. When justifying the research aims, typically in the Significance section, applicants may be tempted to focus solely on their work and to emphasize only the positive. However, such a narrow focus can give reviewers a biased impression of the state of the field. Therefore, applicants are encouraged to write a more balanced narrative describing the strengths and weaknesses of prior work in light of the whole field and acknowledging competing viewpoints.

Table 1. Considerations for Describing Rigor of the Prior Research

✓ Does the Significance section refer to work performed by other research groups?
✓ Does the Significance section critically appraise the technical and/or intellectual rigor of prior work by the applicant and by others?
✓ Does the Significance section address whether the prior work led to consensus or controversy?

2. Rigor of the proposed work. When describing the current research plans in the Approach section, applicants must justify their experiments in light of the weaknesses in prior work. This justification could be as obvious as clarifying the research milestone that made the present work possible, or it could be more complicated, especially if the proposed work attempts to overcome a controversy. Asserting the rigor of the proposed work also means providing enough detail on the experimental plans and statistical analysis for reviewers to have confidence that the research team can navigate experimental subtleties to arrive at meaningful answers. Consensus guidelines for reporting research results, such as ARRIVE (Animal Research: Reporting of In Vivo Experiments), can clarify how much detail to include in the study design.[12,13]

Table 2. Considerations for Describing Rigor of the Proposed Work

✓ Does the Approach section explain how the current research plans fill any knowledge gaps left by prior work?
✓ Does the Approach section provide sufficient methodological detail to demonstrate that the applicants know the pitfalls in their field and how to avoid them?
✓ Does the Approach section provide a statistical analysis plan, including a power analysis when appropriate?

3. Biological variables. To enhance reproducibility, applicants are expected to justify the experimental design and analysis choices in light of the relevant biological variables that may impact the interpretation of results. The NIH uses a broad definition of biological variables, including intrinsic factors (eg, sex, weight, age, and genetic background) and extrinsic factors (eg, food source and housing conditions for animal studies).[14] In particular, for work with human subjects or vertebrate animals, reviewers will evaluate whether the proposal adequately considers sex as a biological variable, and strong justification is required for experiments using only one sex.[15,16]

Table 3. Considerations for Accounting for Biological Variables

✓ Does the Approach section consider sex as a biological variable in the design and analysis of work with human subjects or vertebrate animals?
✓ Does the Approach section consider additional biological variables, especially those recognized as important in prior research in the field?
✓ Are any proposed analyses based on relevant biological variables sufficiently powered to generate meaningful results?

4. Authentication. Research performed with reagents that are unreliable or mislabeled can lack reproducibility. Thus, applicants must briefly describe the plan for validating key biological and chemical resources, such as cell lines, antibodies, specialty chemicals, and transgenic animals.[17] The goal is to describe the methods used to validate reagents, including validation performed by commercial sources.

Table 4. Considerations for Describing Authentication of Reagents and Key Resources

✓ Is there a separate Authentication Plan for Key Biological and/or Chemical Resources?
✓ Does the Authentication Plan contain information about reagents and resources and not preliminary data or methods?
✓ Does the Authentication Plan sufficiently detail how and at what frequency key resources will be authenticated?

Data Management and Sharing Plan: Storing and Disseminating Biomedical Research Data

Because science advances through building on past findings, sharing data is a best practice that positively benefits applicants, their fields, and funding agencies. Additionally, because the NIH uses public funds, there is an additional ethical duty to share research findings with the public.

The current NIH Data Sharing Policy[18] went into effect in 2003 and remains in effect until January 2023. Under the 2003 policy, all investigator-initiated applications seeking >$500,000 in direct costs per year, or as specified in the individual Funding Opportunity Announcement (FOA), are required to include a plan for the sharing of final research data or a justification for why data sharing is not possible (eg, privacy concerns, third-party agreements, and national security issues). This policy was extended in 2014 by the Genomic Data Sharing policy, which establishes expectations for the broad and responsible sharing of genomic research data.[19] Beginning in 2023, all NIH applications must include a DMS Plan and adhere to the updated NIH policy[10] and supplemental information,[15,20,21] including abiding by FAIR (Findable, Accessible, Interoperable, and Reusable) data principles.[22] Because the 2023 policy includes all of the elements of the 2003 policy and expands upon several key concepts, we will focus on the ethical considerations for writing a DMS Plan that complies with the newer guidance.

DMS plans will be evaluated for compliance in the following areas[20]:

1. Data type, common data standards, and repository selection. Applicants are expected to describe what types of data and accompanying metadata will be preserved and shared and what common data standards will be applied to the shared data and metadata, if applicable. Decisions on what to preserve and share should be based on justifiable ethical, legal, and technical considerations. Applicants are strongly encouraged to use existing data repositories, especially those that follow FAIR principles. The NIH does not always require deposition into an NIH-supported repository, so it can be appropriate to consider third-party repositories.

Table 5. Considerations for Describing Data Types, Common Data Standards, and Repository Selection

✓ Does the DMS Plan briefly summarize the types of data and associated metadata to be preserved and shared?
✓ Does the DMS Plan indicate what common data standards will be applied to the data and metadata? If no applicable common data standards exist, is that noted in the Plan?
✓ Does the DMS Plan identify appropriate NIH-supported or third-party data repository archive(s)?
✓ Does the DMS Plan indicate if the selected archive(s) is limited to certain data types? If required by the FOA, does the DMS Plan affirm the use of a designated NIH-supported repository?

2. Timelines and plans for data preservation, access, and sharing. Data and metadata should be preserved, at a minimum, in accordance with all applicable guidance (eg, data repository policies, specific award requirements, and journal policies). Final research data and metadata should be accessible no later than the time of publication or the end of the performance period, whichever is earlier, unless there are justifiable exceptions explained in the DMS Plan.

Table 6. Considerations for Describing Data Preservation, Access, and Sharing

✓ Does the DMS Plan conform to FAIR principles for the identification, access, and reuse of shared data and metadata? Does the DMS Plan indicate how shared data and metadata will be findable and identifiable?
✓ Does the DMS Plan affirm an acceptable timeline for sharing data and metadata?
✓ If specialized tools are needed to access or manipulate shared scientific data and metadata to support reuse or replication, will these tools be available as long as the data are shared? How can these tools be accessed?

3. Limitations on access, reuse, and distribution. Certain types of data and metadata may be confidential, sensitive, or proprietary. The NIH expects data and associated metadata to be shared to the maximum extent allowable. Any limitations or controls on their access, reuse, and distribution must be justified on ethical, policy-based, or legal grounds.

Table 7. Considerations for Describing Limitations on Access, Reuse, and Distribution

✓ If the data and/or metadata are confidential, sensitive, or proprietary, has a reasonable justification for exclusion from sharing been provided in the DMS Plan?
✓ Are there any restrictions on how data can be accessed, reused, or distributed, for example, only with explicit approval?
✓ If there are no limitations, has that been indicated?

In addition to the above considerations, the NIH will also expect a statement on how the DMS Plan will be managed and monitored and by whom.

Conclusions

Recent world events have underscored the ethical justification to ensure biomedical research is conducted in a rigorous manner and that the fruits of research are shared with the larger scientific community and the public. For example, the coronavirus disease 2019 (COVID-19) pandemic has demonstrated what the scientific community can quickly achieve when rigorous methods are applied and when high-quality data are disseminated widely and rapidly. We have focused on a subset of ethical considerations to guide the development of biomedical research grant applications for the NIH; however, the underlying ethical ethos of ensuring scientific rigor and the timely sharing of scientific data can guide the development of proposals for all funding agencies.

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