

Pennsylvania Department of Health Final Performance Summary Report Formula Grants

Overview of the Health Research Project Performance Review Process and Criteria

An applicant that receives a health research grant under Tobacco Settlement Act / Act 77 of 2001, Chapter 9, is subject to a performance review by the Department of Health upon completion of the research project. The performance review is based on requirements specified by Act 77 and criteria developed by the Department in consultation with the Health Research Advisory Committee.

As part of the performance review process, each research project contained in a grant is reviewed by at least three experts who are physicians, scientists or researchers. Reviewers are from the same or similar discipline as the research grant/project under review and are not from Pennsylvania. Reviewers use the applicant's proposed research plan (strategic plan), the annual progress report and final progress reports to conduct the review. A grant that receives an unfavorable performance review by the Department may be subject to a reduction in funding or become ineligible for health research funding in the future. The overall grant evaluation rating is based on the ratings for the individual research projects contained in the grant.

This performance review report contains the outcome of the review for the grant as a whole (outstanding, favorable, or unfavorable), strengths and weaknesses of each research project, as well as recommendations for future improvement.

The following criteria were applied to information submitted by research grant recipients:

- **Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?**
 - Did the project meet the stated objectives?
 - Were the research design and methods adequate in light of the project objectives?
 - Consider these questions about data and empirical results: Were the data developed sufficiently to answer the research questions posed? Were the data developed in line with the original research protocol?
 - If changes were made to the research protocol, was an explanation given, and, if so, is it reasonable?
 - Consider (only for clinical research projects) the extent of laboratory and clinical activities initiated and completed and the number of subjects relative to the target goal.
 - Were sufficient data and information provided to indicate or support the fact that the project met its objectives or made acceptable progress?
 - Were the data and information provided applicable to the project objectives listed in the strategic research plan?

- **Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?**
 - What is the significance of this project for improving health?
 - Consider the value of the research completed towards eventual improvement in health outcomes.
 - Consider any changes in risk factors, services provided, incidence of disease, death from disease, stage of disease at time of diagnosis, or other relevant measures of impact and effectiveness of the research being conducted.
 - Consider any major discoveries, new drugs and new approaches for prevention, diagnosis and treatment, which are attributable to the completed research project.
 - What are the future plans for this research project?

- **Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?**
 - If leveraging of funds were expected, did these materialize?
 - Are the researchers planning to apply for additional funding in the future to continue or expand the research?

- **Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted/filed?**
 - If any of the above listed were expected, did these materialize?
 - Are the researchers planning to submit articles to peer-reviewed publications, file for any licenses, or patents or begin any commercial development opportunities in the future?
 - Consider the number/quality of each.

- **Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?**
 - Were there improvements made to infrastructure?
 - Were any new investigators added or were any researchers brought into the institution to help carry out this research?
 - Were funds used to pay for research performed by pre- or post-doctoral students?

- **Criterion 6 - Did the project lead to collaboration with research partners outside the institution, or new involvement with the community?**
 - Are the researchers planning to begin any collaborations as a result of the research?
 - For clinical research only: consider the number of hospitals and health care professionals involved and the extent of penetration of the studies throughout the region or the Commonwealth.

Overall Evaluation Rating

An overall evaluation rating is assigned to each research project. The rating reflects the overall progress the project attained in meeting the stated goals and objectives. The rating is based on a scale of 1–3, with 1 being the highest. An average rating is obtained from all the reviews (minimum of 3) of each project and is the basis for the determination of the final overall rating for each project as follows:

1.00 – 1.33 = *Outstanding*

1.34 – 2.66 = *Favorable*

2.67 – 3.00 = *Unfavorable*

The grant level rating is an average rating from all projects as above. The numerical rating appears in parentheses for the grant and each project in the ***Overall Grant Performance Review Rating*** section of the report.

Overall Grant Performance Review Rating

Grant Rating: Favorable (2.00)

Project Rating:

Project	Title	Average Score
1086701	Acrylic-Bisphosphonate Polymer Mediated Cell Binding to Collagen-Hydroxyapatite Scaffolds	Favorable (2.00)

Project Number: 1086701
Project Title: Acrylic-Bisphosphonate Polymer Mediated Cell Binding to
Collagen-Hydroxyapatite Scaffolds
Investigator: Koepsel, Richard R.

Section A. Project Evaluation Criteria

Criterion 1 - How well did the project meet its stated objectives? If objectives were not completely met, was reasonable progress made?

STRENGTHS AND WEAKNESSES

Reviewer 1:

- The project met several of the stated objectives listed in the strategic research plan but deviated from the proposed objectives as needed to further understand a more 'basic science' objective.
- The research design and methods were adequate to address the major project objectives; however, several of the important subpoints of Aim 1, including "testing the materials for strength, porosity, flexibility and stability," were not met or attempted. In contrast, Aim 2 was sufficiently completed and expanded upon.
- The data obtained from Aim 2 was more than sufficient to meet the stated objectives. As mentioned, the data from Aim 1 was not sufficient to meet the original research plan. However, it appears from the progress reports that Aim 2 was more 'novel;' thus the focus and attention to the successful completion of that aim was of higher priority.
- Changes to the research plan (in particular Aim 1) were not mentioned in the progress reports. It appeared the researcher had an ambitious schedule for completion of these aims, but the active list of researchers on this project should have been able to accomplish both aims in the time given.
- A more comprehensive description of the data obtained would have been helpful in the final report, particularly since much of the preliminary data concerning the concentrations/ optimizations of the fiber-spinning method would have demonstrated the amount of research necessary to meet the early aims.
- The data and information provided were partially applicable to the project objectives listed in the strategic research plan as mentioned above. However, for further grant applications and successful funding opportunities, the emphasis placed on the cell and polymer-binding assays was more vital for success.
- The primary strength was the cell adhesion studies for selective attachment, which were well described.
- The primary weakness was that Aim 1 was incomplete, and there was no comparison to an existing control therapy for translation.

Reviewer 2:

The PI proposed two specific aims for this project. In general, the PI did perform both aims as proposed. However, as part of the strategy for Aim 1, the PI also proposed to evaluate the mechanical properties and the stability of the fibers, both of which were not performed or reported in the progress report. Without characterizing the fibers, other than the scanning electron microscope (SEM) performed to visualize the presence of hydroxyapatite in the fibers, how does the PI know that his fibers are appropriate for its intended application, i.e., scaffold for bone healing? No information was provided in the progress report as to why evaluations of the mechanical properties and stability of the fibers were not performed or reported.

Reviewer 3:

Strengths:

- The project meets most of the stated objectives.
- The research design and methods are adequate.
- The data is sufficient to answer the posed research questions and is in line with the original research protocol.
- Sufficient data and information are provided to support the fact that the project made acceptable progress.
- The data and information are applicable to the projects listed in the strategic research plan.

Weaknesses:

- Several objectives in the strategic research plan were not achieved: 1) the proposed experiment of characterizing the porosity of the fabric scaffolds was not conducted; 2) the proposed experiment of characterizing the degradation of the scaffolds was not conducted; 3) the proposed experiment of binding cells onto fibric scaffolds was not conducted; and, 4) the proposed experiment of culturing mouse osteoblasts within the fabric scaffolds was not conducted.
- Some changes made in the research protocols were not explained clearly.

Criterion 2 - What is the likely beneficial impact of this project? If the likely beneficial impact is small, is it judged reasonable in light of the dollars budgeted?

STRENGTHS AND WEAKNESSES

Reviewer 1:

- The significance of this project for improving health is the use of an intelligent scaffold for repair and regeneration of bone defects. The study makes a significant step toward improvement of scaffold design and has application for current and future bone scaffold therapies.
- The value of this research is significant considering the aging population and incidence of traumatic bone failure as well as military personnel recovering from segmental trauma.
- The current research could be used to augment existing clinical therapies and represents an accelerated translational finding. The PI did not list commercial development of these findings but might consider intellectual property development toward patent application.
- Primary strength: It is a significant clinical target and application.

- Primary weakness: There was only moderate outreach of the project via one scientific publication, and there are limited further cell studies necessary to prove feasibility for clinical trials.

Reviewer 2:

The likely beneficial impact of this project is the development of a bone scaffold. Significance for this project is high, simply because there is a current lack of solutions for large bone repair. Autograft use is limited in this application due to the inadequate supply, whereas allografts pose the problem of disease transmission. However, given the data in the progress report, the lack of mechanical property and stability evaluations, and the amount of dollars budgeted for this project, the likely beneficial impact is small. Although the PI stated in his report that "what remains is to test the cell binding on the scaffolds synthesized for the project and to test the materials *in vivo*," I am of the opinion that the PI has oversimplified the problem for bone tissue engineering, especially when no mechanical properties or material stability are known.

Reviewer 3:

Strengths:

- The major finding from the project is that polymer can direct binding of cells to specific tissues. It has the potential to result in a method to direct cells to diseased tissues for improving tissue regeneration. It may have some beneficial effects for the treatment of some diseases.
- Although the research project is at the very early stage and the limited data from the current research project is not sufficient to prove its full potential for improving health outcomes, the beneficial impact is reasonable in light of the dollars budgeted

Weaknesses: No detailed future plan was proposed for this research project.

Criterion 3 - Did the project leverage additional funds or were any additional grant applications submitted as a result of this project?

STRENGTHS AND WEAKNESSES

Reviewer 1:

- No additional grant support appears to be mentioned, although the PI clearly states that other funding was used to augment and enhance the research project. No future funding was described, although the supporting researchers listed were identified to continue this research outside the U.S.
- It is a primary strength that significant international connections were created for continuation of project.
- It is a primary weakness that there was no mention of intellectual property protection, further grant support or defined international agreements in place.

Reviewer 2:

The PI had stated that a non-federal source (Government of Kazakhstan) was sought to leverage additional funds. Since no monetary amount was given in the progress report, it was not known if the leverage reported resulted in additional funds for the project or having two visiting students

and a visiting scientist to participate in this project. However, it must be noted that there is co-funding of this research project from the DoD for \$13,000. The PI also stated that he "will be part of the grant submitted in Kazakhstan and will submit a grant using background developed here but on a different topic." It was not clear what he meant by a "different topic." Was it for an application other than for bone tissue engineering, which thus will not be expanding the research performed in this project?

Reviewer 3:

Strengths: The researchers are planning to apply additional funding in the future to expand the research.

Weaknesses: No detailed description was given for how the data and results will be used for applying for additional funding. It is hard to judge the quality of the additional funding application.

Criterion 4 - Did the project result in any peer-reviewed publications, licenses, patents, or commercial development opportunities? Were any of these submitted / filed?

STRENGTHS AND WEAKNESSES

Reviewer 1:

- One peer-reviewed publication is in the creation process with pending review to an international journal. No licenses, patents or further commercial development were listed.
- A primary strength is that one peer-reviewed publication was obtained with limited financial resources.
- A primary weakness is that there was no intellectual property protection generated or pending despite international connections.

Reviewer 2:

The PI reported no manuscripts submitted to journals for publication. The PI also stated that there is no disclosure or intellectual property that resulted from this project.

Reviewer 3:

Strengths: The researchers are in the process of preparing a manuscript based on the results from the project.

Weaknesses: The project did not result in any peer-reviewed publications, licenses, patents, or commercial development opportunities. No manuscript, licenses, or patents were submitted/filed.

Criterion 5 - Did the project enhance the quality and capacity for research at the grantee's institution?

STRENGTHS AND WEAKNESSES

Reviewer 1:

- While no improvements were made to the infrastructure, the project did allow for a significant number of international and student opportunities to be made over the course of the study. Several new investigators were invited to the institution from Kazakhstan, and the research may continue in their home country with governmental support.
- Visiting scientist/students were listed as having 50% effort.
- It is a primary strength that there was significant student and post-doctoral involvement.
- Primary weakness: None

Reviewer 2:

Since no new instruments were made available and no publications, patents or disclosures resulted from this project, the only visible enhancement to the capacity for research at the grantee's institution is the ability to continue collaborating with the PI's fellow scientist from Kazakhstan.

Reviewer 3:

Strengths: Some new investigators were brought into the institution to help carry out the research.

Criterion 6 - Did the project lead to collaboration with research partners outside of the institution or new involvement with the community?

STRENGTHS AND WEAKNESSES

Reviewer 1:

- The research directly contributed to an international collaboration.
- Significant potential for continued collaboration and international exchange is a primary strength.
- Primary weakness: None

Reviewer 2:

This project did lead to collaborations for the PI with his fellow scientists from Kazakhstan. The PI stated that he "will be part of the grant submitted in Kazakhstan and will submit a grant using background developed here but on a different topic." It was not clear what he meant by a "different topic." Was it for an application other than for bone tissue engineering, which thus will not be expanding the research performed in this project?

Reviewer 3:

Strengths: The researchers are planning for collaborations with research partners outside of the institution.

Section B. Recommendations

SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

1. It is apparent that the funds and time necessary for the aims of the strategic plan (proposed) were not sufficient. In particular, it was noted that the first aim (characterization of the material) was not completed. Consider revising or limiting the number of time-intensive aims to match the scope/funding of the project. The completed work was certainly proportional to the time and funding provided. This research could easily be scaled to an R01 mechanism or equivalent.
2. Consider coordination of research with commercial aims. Even if the PI has no interest in the commercialization aspects, the institution may wish to create an agreement with the PI and visiting scholars for further development and protection of the research. Note that these agreements should be in place before the research is submitted for peer-reviewed publication.
3. During the annual progress report, the deviation from the original aims could have been reported. In particular, the move from a 'material characterization' study to the more polymer/scaffold binding study emphasis of the second aim was perfectly valid, but not well described. In addition, the last statement, "what remains is to test the cell binding on the scaffolds synthesized for the project to test the materials *in vivo*," needs much greater description. Are these studies planned for your laboratory? Are they intended for the visiting scientists to continue?

Reviewer 2:

1. Given what was stated in the research strategy, the PI should have evaluated the fibers for material properties and stability. Knowing these two parameters is critical in order to ensure that the project has any clinical significance.
2. There is a lack of publications. I understand the budget limitation, but the funding obtained from this project plus the co-funding from DoD should have allowed the PI to obtain critically needed data to produce at least one manuscript for publication.
3. There is no disclosure as a result of the work performed. It is recommended that the PI talk to his technology office to determine if there is intellectual property that needs to be protected as a result of this work.

Reviewer 3:

1. No peer-reviewed publications resulted from the project. The researchers should communicate their results to the scientific community.

2. No license or patent was submitted/filed. It will be helpful for the researchers to look into the potential of protecting the intellectual property and commercialization of the technology.
3. Several objectives in the strategic research plan were not achieved. It will be helpful to give some explanations.
4. Some changes made in the research protocols were not explained clearly. It will be helpful to provide some detailed justifications.
5. No detailed future plan was proposed for this research project. It will be helpful to provide some details for how the researchers will use the data/results from the current project to continue/expand the research.

Generic Recommendations for the Institution

Reviewer 1:

The involvement of international pre-doctoral students and visiting scientist were exceptionally strong in this research; however, no agreements for commercialization or protection of intellectual property are listed in this research summary. In addition, the funds were limited and are reflected in the accomplishment of the aims in this study. Future reviews should focus on correctly matching the percent of time and dollar contributions to the research with the projected aims/effort. The success of this research appeared to rely, in some part, on funding and effort from other sources.

Reviewer 3:

In general, the researchers have met their research goals and made acceptable progress.