

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
0863501	Genomics of Pregnancy-Related Complications	Favorable (2.00)

Project Number: 0863501
Project Title: Genomics of Pregnancy-Related Complications
Investigator: Carey, David

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 has two aims, including: 1) recruitment and collection of biospecimens from 1000 patients, and 2) genetic (DNA) analysis of the samples.

The investigators exceeded the first aim and did not complete the second one due to insufficient genetic materials collected from the cohort.

However, they did three paired control versus preeclampsia miRNA array studies and found over 50 miRNAs were differentially regulated in preeclampsia. This information is useful and important, although it is not within the scope of Aim 2.

Reviewer 2:

The proposal itself is well-written with reasonable aims that were accomplished during the time period of this proposal and will likely lead to a possible R01/R21 grant in the future from NIH. In Aim1, the investigators recruited a cohort of patients seen for obstetric care at the Geisinger Medical Center and obtained biological specimens, including DNA and RNA from mother and baby. During the time period of this study, they obtained approximately 100 subjects of which 59 specimens were from women with preeclampsia. Using the MyCode database, the investigators were also able to obtain additional DNA from 259 PE subjects and 1500 controls. In Aim 2, the investigators conducted pilot studies from the material collected and performed a microRNA expression analysis using three controls and 3PE subjects and found, not surprisingly, a number of altered microRNAs. Interestingly, miR191 and miR598 were increased in preeclampsia and miR101 and miR223 were decreased in PE. These studies have profound significance in not only understanding the pathogenesis of preeclampsia, but potentially in the development of novel diagnostic and therapeutic strategies for patients with preeclampsia.

Reviewer 3:

Aim 1: The investigators found creative patient recruitment options and exceeded their recruitment goals. However, the investigators should have been concerned with and taken steps to evaluate bias in the recruitment and population selection process depending on the specific hypotheses to be tested and the desired generalizability of the results.

Aim 2: The number of subjects was insufficient to conduct single-nucleotide polymorphism (SNP) analyses as proposed, but investigators found other creative alternatives for piloting genomics analyses. These were analyses of microRNA in placental tissue of preeclamptic and control babies.

Fulfillment of the objectives dealing with preterm labor was not discussed in adequate detail in the progress reports to evaluate whether they were met or not.

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 merit of this project is providing a tissue bank for material-fetal medicine research. Considering the dollar amount provided and the samples collected, it should be viewed as successful. However, it is not clear how these samples (bank) will be used in the future and what the investigators' future plans are regarding these .

Reviewer 2:

Unbiased genetic approaches are likely to yield novel diagnostic/therapeutic targets for preeclampsia. For example, the miR101 and miR223 alterations would not have been predicted without using a whole genome microRNA chip.

The investigators' plans include continuing recruitment and exome sequencing of family trios.

The microRNA data are being documented for a publication.

Reviewer 3:

The significance of this project is tempered by the small and selected population size. As such, findings are suggestive only and not confirmatory on their own. Large effect sizes may be discoverable, but not small ones. This field of study is still far from identifying a major genetic susceptibility risk factor. However, the results may provide more evidence for understanding preeclampsia and preterm labor.

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:

Institutional funds were used for this project, although the total dollar amount is not stated in the report.

The investigators will apply for NIH or March of Dimes funding in the future.

Reviewer 2:

Researchers plan to submit for federal funding based on the preliminary data generated.

Reviewer 3:

The investigators indicate that funds from Geisinger Clinical Research Fund will be used to continue the project. No grants have been sought.

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:

There have been no publications at this point. However, they are working on the miRNA data for publication.

Reviewer 2:

Data from the microRNA studies may generate a peer-reviewed publication.

Reviewer 3:

Investigators are planning to submit articles once data analyses have been completed, but so far none have been submitted.

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

STRENGTHS AND WEAKNESSES

Reviewer 1:

There was no evidence of infrastructure improvement. Maternal-Fetal Medicine (MFM) fellows were trained with this project. A full-time research technician was paid. However, it is not clear whether the MFM fellows were paid based on their efforts.

Reviewer 2:

Genomic research will likely yield unbiased and novel targets that may have both diagnostic and therapeutic uses. The investigators are focusing their efforts on a complex problem, and these funds provided an infrastructure for the investigators to build on and apply for federal funds. Two MFM fellows and one staff scientist served as collaborators.

Reviewer 3:

Funds have been used for students, and the project has resulted in improved communications and interest in research in the obstetrics clinic.

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:

None.

Reviewer 2:

There were none outlined except for Geisinger Medical Center.

Reviewer 3:

A research fellow who worked on the project was recruited into a position at the Geisinger Clinic.

Section B. Recommendations

SPECIFIC WEAKNESSES AND RECOMMENDATIONS

Reviewer 1:

The investigators have developed a useful tissue bank for perinatal research. However, a clear research focus needs to be developed using these materials.

Reviewer 2:

1. The investigators need to focus on extreme phenotypes when evaluating genetics. In this regard, focusing on early onset preeclampsia would have been ideal, as these subjects have the greatest morbidity.
2. Ethnicity and race were not discussed in the application. If the subjects were predominantly white or black, that would have significantly affected the genetic studies.
3. No plan is provided with regards to follow-up of the microRNA work. Are they planning to do validation and functional studies?
4. The plans for preterm labor were not clearly outlined in the proposal.

Reviewer 3:

1. The investigators should consider adding epidemiologic support to the project to determine the accuracy and completeness of the electronic medical record data, the denominator from which findings can be generalizable, and the nature of bias in study population selection, including those emerging from high-risk referral patterns into the obstetrics facility, from retrospective recruitment (parity effects), from differential follow up, etc.
2. If a sufficient number of study subjects continues to hamper the conduct of single-nucleotide polymorphism (SNP) analyses in this project, the investigators should continue to look at

novel approaches (e.g., trios), different tissue types (e.g., placenta, amniotic, vaginal), lab analyses (e.g., comprehensive sequencing, proteomics) and other hypotheses to test.

3. The investigators should consider that the strengths of the Geisinger Clinic setting for research may be in the depth of laboratory analysis, breadth of exploration, and in its patients' long-term stability, not so much in its being population-based, and revise their research goals appropriately.