

# **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 (2.09)

**Project Rating:**

<b>Project</b>	<b>Title</b>	<b>Average Score</b>
0862301	Analysis of Ulnar Collateral Ligament Reconstruction	Favorable (2.00)
0862303	A High Fidelity Rat Model of Pulmonary Arterial Hypertension	Favorable (2.00)
0862304	Myofibroblast Inhibition in Dupuytren's Contracture	Unfavorable (2.67)
0862305	Flooring Renovation of the ASRI Rodent Animal Facility Research Infrastructure	Favorable (1.67)

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**Project Number:** 0862301  
**Project Title:** Analysis of Ulnar Collateral Ligament Reconstruction  
**Investigator:** DeMeo, Patrick J

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## ***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 showed excellence in meeting the objective of determining in situ strains in the mUCL. Great detail was given in recognizing the complexity of the task, and a novel, clever interpretation was used.

The second part of the first objective, the measurement of the force transmission, was addressed by the research. Unfortunately, not enough detail was given to ascertain how appropriate this work was. Better documentation of the 6-DOF robot and how the specimen is mounted is needed. It was troubling that the authors seem to imply a scalar difference of the forces applied by the robot is appropriate to determine the forces on the ligament in what is surely a lever-like system. If a 3D or even a 2D mechanical model (i.e., a free body diagram) was used, that should be presented. Alternatively, the problem could be approached from an elastic energy perspective to estimate the forces. Unfortunately, any depth to how the force was determined was lacking.

Although a more full explanation of the set up is needed, the change from the MTS to a 6 DOF robot was reasonable.

The second objective was originally worded vaguely, but it was disappointing that the work was so disjointed from the first half of the study. It was expected, as proposed, the FE validation would be of the data (or a subset of data) presented under Objective 1. The FE modeling was done of separate components. Three models were presented. The first was validated with strain gauges, although the subject of the FE model was not the same as the cadaver used in the mechanical test. The second and third models had no validation.

The second and third FE models described loads, but there is no presentation of the time changes in these loads. Were these static/quasi-static tests? The use of LS-dyna and the project seem to argue against it, but the methods and results lead this reviewer to suspect that is the case. The second model mentions that "a displacement was applied to the tendon ends to simulate a moment of 14 Nm," which needs an explanation of how it was done.

The big shift in method from FE model 2 to 3 is curious. Was there a reason for the change? Much of the confidence gained from the validation of the first model is lost by this. Also, while it is appreciated that the research studies done to gain confidence in the element types/sizes used and domain limits, etc., for the third model, they aren't very reportable. A sentence or two is really all you need here. It read like "filler."

Overall, the FE modeling as proposed was ambitious, especially for the resources given, but what was delivered seems quite unfocused generally in relation to the proposed project. The FE research presented may give insight into how stresses may increase with different methods, which is useful. The conclusions are viewed with skepticism largely because the forces applied are not clear, nor established as what might be seen in situ.

In summary, the data collected in the first half of the first objective (determining in situ strains) is what should be emphasized; objectives were met. The force determination, I cannot tell if it did from the information given, but the presentation gives me great concern. For the second objective (the modeling), the progress was significant but not outstanding and not well focused on the overall study.

Reviewer 2:

Objective 1:

Determine the in situ strains and force transmission characteristics of the medial ulnar collateral ligament.

Because the investigators focused on in situ strain and force in the ligament, this task is achievable.

Specific Aim 1:

Use an elbow simulator creating physiologic conditions in a cadaveric elbow to quantify strains using small optical markers.

Strength:

Specific Aim 1 of Objective 1 was mostly achieved in that optical strain data was obtained using an elbow simulator with cadaver specimens.

Weaknesses:

Whether or not the testing conditions with the simulator were physiological, is clearly debatable. The simulator is capable of actuating five different muscle-tendon units, but only one was used to activate the brachioradialis to simulate elbow flexion. No other flexors or antagonists were included in the simulation.

Another shortcoming is the lack of measurement of the true resting length of the ligaments. While this was inferred from test results and observations of slack portions of the ligament, the ligaments were never removed to measure a true stress-free resting length. All the results should be rephrased as relative elongation measurements. Thus, the investigators fell somewhat short of fully completing Specific Aim 1 of Objective 1.

#### Specific Aim 2:

Materials testing of bone-ligament-bone constructs in a specially designed fixture that replicates the kinematics of the elbow.

#### Strength:

Specific Aim 2 of Objective 1 was to perform materials testing, later described as tensile testing. Though this aim was not accomplished, a surrogate test was used in its place.

#### Weaknesses:

The intent of this aim was never completely and clearly described, but both places in the Strategic Plan imply that the ligaments will be tested in tension to failure to characterize their load/elongation behavior, such that the strains from the “physiologic” experiment could have been used to determine ligament forces. However, the test actually performed was an in situ test with passive motion in a robotic simulator. While this test did provide forces in the ligament during passive motion, it did not provide any information about active motion. That is, the robotic test did not replicate the kinematics of the elbow simulator, so the ligament forces during active motion could not be determined. It is not clear why the investigators chose the passive force analysis over the original strategy; the investigators fell short of completing Specific Aim 2 of Objective 1.

#### Objective 2:

Complete a mathematical model of the elbow and ligaments and use the data from Objective 1 to validate the mathematical models.

#### Strengths:

Objective 2 in the Strategic Plan implied a full model of the elbow with humerus, ulna and radius, and all relevant ligaments - at least the figure used in the Strategic Plan implied that, as does the basic objective, which includes ligaments. Also, the goal was to validate the model data within 10% of the experimental ligament data.

#### Weaknesses:

The investigators did not compare the model to the Objective 1 data at all, because the intact ligament was never included in the models. None of the models developed included more than one bone. Rather, the models focused on failure modes of reconstruction by avulsion fractures through the tunnels drilled for the reconstruction. Also, while there were a number of parametric studies related to the models, there was not much validation.

#### Strengths:

The investigators did include convergence studies of the finite element models, so even though they may not be fully validated, they at least give an accurate numerical approximation for the given geometry, material properties and boundary conditions. The actual validation focused on relating experimental strain measures to strains calculated in finite element models.

#### Weaknesses:

Relevant to the validation, the investigators only give a single comparison from a single condition and a single strain gauge to support the validation. For that anatomic condition, site,

and strain gauge, the maximum principal strain is said to “closely match,” while the minimum principal strain has substantial error. Only a bar graph is given, no tabular data, and the investigators do not indicate if the maximum principal strain is within the 10% criteria. The visual on the bar graph is inconclusive, though it appears to be close. But this is just one measure at one site. What about all the others?

The investigators indicated twice the shortcoming of trying to validate a model against an experiment with a different specimen. Once they indicated they would create a specimen-specific model (a model of a bone actually used in experimental validation testing), but it was apparently never accomplished. It must be concluded that the finite element model of the human elbow was only partially completed and that the model was not validated. The investigators fell far short of completing Objective 2.

The writing of the grant-related documents is not very clear or consistent. Important details like material properties used or the types of finite elements used in the models are not given until the Final Report. Even the data that is presented is often not presented clearly and is not explained well. Interpretation and/or further analysis of the data is hindered by poor labeling of graphs, figures, etc., and the limited amount of data that is provided. There are inconsistencies such as the June 2010 report indicating eight male specimens were used for ligament strain testing and the Final Report indicating that seven male and three female specimens were used for ligament strain testing. Similarly, the Strategic Plan indicates 1.5 mm markers will be sutured to the ligament; an interim report stated 0.8 mm spherical markers were glued to the ligament; and the Final Report states that 1.0 mm markers were glued to the ligaments. Likely, many of these variations are due to changing technique or simply errors/differences in reporting. But if the technique keeps changing, can all the data be used together? And if the report has inaccuracies, were the research methods performed carefully?

#### Reviewer 3:

There are two specific aims for this project. The first is to quantify ulnar collateral ligament (UCL) strain in vitro using a cadaver model. To achieve this goal the applicant laid out two goals: (1) to develop a robotic system for UCL testing, and (2) characterization of the force associated with the strains of the entire ligament. The second specific aim was to develop a finite element model of the bone to assess fracture potential resulting from stress concentrations resulting from the drill holes needed to perform a UCL soft-tissue reconstruction.

The investigators completely met the first goal by developing a mechanical elbow simulator. They completed mechanical testing on ten cadaver specimens. Moreover, they were able to adapt to a new research opportunity by incorporating a six degree-of-freedom robot into their testing paradigm. They originally meant to use a single-axis test system. However, their actual testing was more innovative than the approach initially proposed. They used the principle of super position to estimate forces from trials with and without the ligament. This is a well-established method developed by Dr. Savio Woo at the University of Pittsburgh. It has been extensively used in the soft-tissue biomechanics arena.

The investigators also were successful in achieving their second specific aim. The second aim sought to assess the possibility of bony fracture resulting from the reconstruction. Their approach

was to use a finite element model to predict the maximum stresses in the bone post-reconstruction. The investigators used Mimics to segment the humerus from CT data. The results were used as the basis for generating a finite element mesh for analysis. Reasonable material properties were applied to the elements, and the bone was assumed to be a linearly elastic isotropic material. They added holes to simulate the bone tunnels required for a UCL reconstruction. A similar model of the ulna was also created. The model converged, and the investigators were able to make numerical predictions of bone stresses and strains. Often FEA models are developed but not validated. The investigators went the extra mile to validate their model using a cadaver model. Strain gauges were used to measure surface strains, and they compared favorably to model predictions. The model was used to analyze the effect of hole separation on von Mises stress. They also performed extensive sensitivity analyses.

Overall, the investigators did an outstanding job of meeting their objectives and achieving their specific aims. They accomplished a substantial amount of work during the project period and collected significant data. The research methods were appropriate and well-executed.

***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 work done on determining strains is significant in any type of research into this joint. It is hoped that this data will be used for future work to interpret it fully. The dissemination of this part of the work is important.

A validated model of the full elbow, including soft tissue, of both intact and surgical interventions, would be huge. The presented work is a step toward this, but there is still a tremendous amount to be done.

The models presented, if the applied forces can be justified as critical, are important for these techniques, and possibly other techniques. As it is, however, there is not enough information (directions, locations, justification that these forces are the ones out of many that matter).

#### Reviewer 2:

##### Strengths:

There are two primary areas where this research may have a beneficial impact. First, the experimental work under Objective 1, while clearly hindered by some shortcomings, appears to provide guidance to clinicians with regard to elbow flexion angles for ulnar medial collateral ligament reconstruction. This appears to be clinically significant, as it differs from current practice. I expect that there will eventually be a published paper that will help provide guidance in this area. However, it would also be useful (and possibly necessary to convince clinicians) to perform the reconstruction on cadavers and document the strain profiles of the reconstructions.

Second, the finite element models appear to provide some indication of the best placement for reconstruction tunnels to minimize bone stresses.

If these are common injuries in baseball athletes, there may be some hope of funding by Major League Baseball, but it is not clear what level of funding is available.

**Weaknesses:**

It must be realized that the models are not validated, so enthusiasm for the results must be either corroborated somehow or tempered with that limitation.

While the investigators indicate their intention to seek further funding for this research, that will clearly be difficult. It is unclear how much further these projects will go. Also, the investigators do not state the prevalence of these injuries, nor do I know them, but I assume that these affect a small portion of the population. Thus, it may be difficult to build the significance for NIH funding.

**Reviewer 3:**

Although the investigators did a great job of meeting their goals, it is unclear how their results will have a wide impact. Epidemiologically, there are few UCL injuries that require this kind of repair. While every baseball fan knows about the Tommy John surgery (UCL repair), there are comparatively few throwers in the population and few other occupations that impose large biomechanical stresses on the UCL. Considered in the context of knee replacement surgery (500,000 procedures performed per year in the United States), UCL repair is an uncommon procedure.

Compared to non-orthopaedic health conditions like diabetes and cardiovascular disease, UCL repair seems even less significant in the big picture of American public health. Thus, the weakness identified here is the lack of public health significance of the research problem selected. However, within the limited field of elbow surgery, these results will help guide surgeons in deciding where to place the drill holes when performing an MCL repair.

***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:**

Approximately \$32.5k was brought in from two external private foundations. The authors plan to submit grants in the future and have identified sponsors.

**Reviewer 2:**

**Strengths:**

The investigators did apply for funding on two different NIH grants during the grant period. The investigators indicate they will submit grant applications to the NIH and Major League Baseball in the near future.

**Weaknesses:**

Neither of the grants applied for during this grant period appears to be directly related to this study. Both grants were to private organizations and not for major federal funding.

Reviewer 3:

The investigators did secure two additional grants of small-to-modest size to support their elbow research. These appear to be from a foundation and industry. No federal funding was secured, although the report indicated intent to submit two NIH applications. There are also plans to submit a grant to Major League Baseball.

***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:

No peer-reviewed publications were submitted but two are planned that seem appropriate. The first appears novel and original, and the second is solid.

Two abstracts for conferences have been submitted and accepted. Both conferences are very good and appropriate for this work.

Reviewer 2:

Strengths:

This project resulted in four research conference presentations and will likely result in at least one peer-reviewed research article in the future.

Weaknesses:

No manuscripts have yet been submitted for peer-reviewed publication.

Reviewer 3:

No publications were listed in the report. No patents or inventions were listed.

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

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

The experience in using FE modeling that was gained should serve them well.

Reviewer 2:

Strengths:

The funding for this project appears to have at least partially supported one undergraduate, one master's level student, three pre-doctoral students, and one post-doctoral student.

Weakness:

While the investigators indicate improvement to research infrastructure, these statements are vague and non-specific.

Reviewer 3:

Allegheny-Singer Research Institute has been working on developing the capability to perform biomechanical studies of elbow biomechanics. This project has helped that institute move that work along. As such, it has helped build the capacity for research at that institution.

***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 report emphasized collaboration with the University of Pittsburgh and the use of the robot, but one of the principal investigators (Miller) was already associated there.

Reviewer 2:

Strength:

The project led to collaboration with the University of Pittsburgh.

Weakness:

It is not clear whether that collaboration will continue or if other collaborations on this project are planned for the future.

Reviewer 3:

The project did lead to collaboration with the University of Pittsburgh. That collaboration appeared to be related to the use of the robot in Specific Aim 1. The collaboration between Allegheny-Singer Research Institute and the University of Pittsburgh is particularly encouraging because the two hospital systems are competitors on the clinical side. Cross-town collaborations like this can be beneficial to both sets of investigators.

***Section B. Recommendations***

***SPECIFIC WEAKNESSES AND RECOMMENDATIONS***

Reviewer 1:

1. The strain data in Specific Aim1 is good and promising, but it seems quite disconnected from the work done in Specific Aim 2. I was excited and hoping we'd get a modeled simulation of ligament strains over a range of motion as well as forces to compare to the experimental work. (I envisioned plots of the experimental work with FE simulated curves with which to contrast.)

It is a bit ambitious for the funding, but as presented, it seems like the approach for Aim 2 went in a different direction. It would be beneficial to see a simple FE model of two bones and a ligament, simulated over a range of motion with contact at the joint.

2. The lack of models presented for the relationship between the force applied by the robot and the forces in layers of the ligament, is a large weakness. It can not be assumed that the force applied to the arm at a lever is constant at the far end.

### Reviewer 2:

1. With regard to the elbow flexion simulation, the use of a single muscle does not appear very physiological. The investigators should perform simulations with additional muscles actuated, including antagonists. Even if these simulations are not exactly physiological, they will allow a determination of the sensitivity of ligament strains on the muscle activation pattern. These additional tests would provide corrections and/or improve confidence in the current findings.
2. If ligament specimens are still available from the physiological strain testing and ligament force testing, these ligaments should be analyzed for stress-free resting length. Using true stress-free lengths (and subsection lengths) will allow the elongation measurements to be converted to actual strain measurements. This could be done with physical measurements (calipers, as proposed) or with optical measurements with a calibration frame in the images. This would provide information about regional strain in the ligaments and should improve the confidence in the interpretation of the physiological strain measurements.
3. With regard to ligament force testing, there are two possible improvements that could be made. One improvement would be to match robotic simulator kinematics to those of the elbow simulator. In this case, the in situ forces would then be known for an in situ active elbow flexion, instead of the current passive elbow flexion. The second improvement approach would be to do the actual bone-ligament-bone tension testing. This would allow strains from the active elbow flexion simulator to be used to calculate the corresponding ligament forces. Either approach would provide more useful and relevant data.
4. The validation of the ligament reconstruction finite element models should be improved. First of all, the validation experiments should be performed on the same specimen used to construct the finite element model. The model loading conditions are not provided in detail, but were apparently to replicate multiple muscle forces. The main point, besides a specimen-specific validation, is that the loading conditions in the experiment precisely match those in the model. Also, the registration of the strain gauge locations, with model locations/data, is important so that the data will properly correspond; then clear quantitative comparisons can be made to determine if the model meets the 10% validation criteria. The measures to be validated should be clearly stated, as many investigators tend not to perform clear and thorough quantitative validations. Also, thorough quantitative validation of a model is generally difficult to achieve.
5. The investigators should submit a manuscript on the in situ ligament strain data from the elbow simulator. Based on this strain data, once clearly summarized, they should submit grant proposals to continue this work and provide more definitive data on research questions.

### Reviewer 3:

1. As the investigators continue to use their elbow simulator to study biomechanics of pathology and treatment, they may want to consider expanding their scope to include conditions that affect more people. For example, epicondylitis affects both athletes and workers. Focusing on conditions of working populations makes this kind of research more relevant to large populations of people.

***Generic Recommendations for Allegheny-Singer Research Institute***

Reviewer 2:

Overall, the objectives of this study were too ambitious, and not enough preliminary work had been done to establish clear procedures. Thus, the procedures appear to have continuously developed during the study. This, however, is typical for the early stages of research, when obtaining preliminary data. The investigators clearly worked hard to make as much progress as possible during the study period.

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**Project Number:** 0862303  
**Project Title:** A High Fidelity Rat Model of Pulmonary Arterial Hypertension  
**Investigator:** Passineau, Michael J.

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### ***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:

##### Major strength:

The principal investigator (PI) successfully met the stated objectives, which were to deploy a rat model of pulmonary arterial hypertension (PAH) at the McGinnis Cardiovascular Institute (CVI).

Both Aims 1 and 2 were successfully completed. The objective of Aim 1 was to learn the PAH rat model from Dr. White at the University of Rochester. The objective of Aim 2 was to validate the implementation of the PAH model at CVI by comparing data collected to the published findings of Dr. White.

Minor changes were made to the research protocol in the form of altered endpoint analyses. The changes were well documented and justified by the PI. The changes (i.e., Micro-CT 3D angiography) are state-of-the-art methods and improved the endpoint analysis of the pulmonary tissue.

##### Weaknesses:

The resulting PAH model data (i.e., echocardiography functional analysis and pressure measurements) were not included in the Final Report. Confirmation of data by White, et al. was not presented with explicit data. The PI did not give any reference data to validate the successful duplication of the model.

##### Comments for future success:

The PI shows evidence that the model was successfully implemented and validated at CVI. To increase the competitiveness for extramural funding, evidence of full implementation of the model by a peer-reviewed publication is highly recommended. Note that a publication using the PAH model was not a “stated objective” of the project.

The PI should also incorporate the use of pressure-volume conductance catheterization in future studies. Pressure-volume catheterization is the “gold standard” for cardiac functional analysis and can be used to evaluate right ventricular function. The PI mentioned this as a possibility in the year one Progress Report, and this methodology would be a great addition to future studies.

Be aware that the original application stated that ultrasound would be used to measure pulmonary artery (PA) pressure, which is not possible by that technique. Technically, PA pressure can be estimated by ultrasound, which should be confirmed by invasive endpoint measures.

Reviewer 2:

Strengths:

The project achieved its immediate objectives, namely of introducing the pneumectomy-monocrotaline model of severe pulmonary hypertension at Allegheny University. Based on the data provided, it appears that the rats developed pulmonary hypertension.

Weaknesses:

The number of experiments to implement/develop the model is relatively low, which limits the ability of the research group to improve the survival and full characterization of the experimental model. There were no data on pulmonary hemodynamics, which is a key parameter in the model. Furthermore, emphasis on microCT was not justified as this is not a gold standard to define the angiopathy, but rather histology as outlined in the original application. No further experiments were performed to advance the goals outlined in the original application including gene expression profiling, transgene interventions, etc.

Reviewer 3:

The objective of this funded proposal has been to duplicate a rat model of PH established by J. White, et al.

The investigators have not performed the surgical procedures required for the establishment of a robust, reproducible model of PH often enough (i.e. their collective experience with the procedures and the model is still insufficient). The change of the plan from hemodynamic measurements to imaging of the lung has been ill-advised—the data are not quantitative. There are also no documented quantitative data addressing RV performance and function. There is also a lack of histological assessment—lack of progress.

***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:

Major strength:

The establishment of this animal model of PAH and CVI will increase the competitiveness of the PI and other researchers at the institute for extramural funding from NIH and other agencies. The topic of this research is highly significant and relevant to human disease. Studies utilizing this newly established PAH model may identify key mechanisms responsible for pulmonary hypertension. The PI has ongoing collaborations with consultants associated with this project and plans to continue this research by securing extramural funding.

Reviewer 2:

Strengths:

The incorporation of experimental research in pulmonary hypertension at the Allegheny-Singer Research Institute is a worthy endeavor, as it builds on a strong clinical program. The approach, reliant on the development of a suitable animal model, is justified as it allows for development of expertise in models of pulmonary hypertension. Although there are no immediate benefits for patients with pulmonary hypertension with this project, this particular developmental step may, in the long run, generate useful insights into the disease.

Weaknesses:

The project would have benefited from a more comprehensive design, involving a range of needed expertise, including physiology, pathology, pharmacology, molecular biology, etc. The aggregate of this expertise would have allowed for the needed interactions in order to move forward with state of the art interrogation of the model. Furthermore, the project would have also benefited from the elaboration of feasible methodological or mechanistic hypotheses. The program should have also included the development of alternative models, including transgenic mice and other rat models, aimed at specific experimental questions. It is clear that no single model accurately reflects the complex pathogenesis of the disease; focus on a particular model may detract from a more comprehensive approach towards the elucidation of the pathogenesis of the disease.

Reviewer 3:

This model of PH, if established as a highly reproducible model of severe PH & RH dysfunction, is of benefit for further in-depth preclinical studies. New drugs can be evaluated.

***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:

Strength:

The PI listed two research grants related to the project that were funded during the CURE funding period. They were: A Gilead Sciences Research Scholars Program and an Entelligence Young Investigators Award for a total of ~\$200,000. Also, the PI plans to submit an NIH R01 application which will utilize the PAH model established at CVI as a result of this funding.

Reviewer 2:

Strengths: None.

Weaknesses:

Given the limited scope of the goals of the proposal, no additional funds have been obtained or actively pursued. The plan to submit an R01 application is not detailed, and no new investigator training and development has been initiated with this project.

Reviewer 3:

No additional funds have been raised.

***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:

Weaknesses:

No publications were submitted during the course of the funding period. However, the PI states that the projects funded through the Gilead Sciences Research Scholars Program and the Entelligence Young Investigators Award will lead to peer-reviewed publications. As mentioned above, producing a peer-reviewed publication using the PAH model is highly recommended for evidence of full implementation at CVI.

Reviewer 2:

Weakness:

The project had a limited scope, which translated in no publications or potential projects leading to publications in the immediate period after the funding ends.

Reviewer 3:

No publications by the group have materialized—the number of animals studied is still too small and the data set is at present poor. This is not enough progress.

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

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

Major strength:

The PI shows evidence that the model was successfully implemented and validated at CVI. The ability to utilize this model in future studies will increase the competitiveness for extramural funding.

Reviewer 2:

Strengths:

The project led to training in the specific model of pulmonary hypertension, with the ability to transfer the knowledge base to the institution.

Weaknesses:

Given the limited scope of the proposal, particularly of funding, there were no resources or plans to bring outside investigators. The project does not list any trainee who might have benefited from the project.

Reviewer 3:

The project, once completed, is likely to enhance the local research capacity and environment.

***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:

Major strength:

The project has led to the collaboration between the PI and Dr. White utilizing the PAH model. The PI is using the Micro-CT 3D angiography technique to perform tissue analysis as part of their collaborative study.

Reviewer 2:

Strength:

It is apparent that the investigative team has implemented a collaborative interaction with Dr. R. James White at the University of Rochester.

Reviewer 3:

The project has been started as a collaborative effort with the University of Rochester, but tight and timely collaboration may be lacking.

### ***Section B. Recommendations***

#### ***SPECIFIC WEAKNESSES AND RECOMMENDATIONS***

Reviewer 1:

1. The PI should publish a study utilizing the PAH model to demonstrate that the model is fully established at CVI. This will increase the competitiveness for future extramural funding in the area of pulmonary hypertension by the PI and other researchers at the CVI.

Reviewer 2:

Recommendations:

1. To expand the scope of the project, to include the development of specific methodological and/or experimental hypotheses, and test as the model is developed.
2. To incorporate the development of a multidisciplinary research group aimed at utilizing this model and other pertinent models in pulmonary hypertension research.
3. To develop an organized training program for technicians and research fellows to expand the scope of research in this model and in pulmonary hypertension. An extension of this recommendation would include the creation of a pulmonary hypertension modeling core to serve as a "hub" for a research program in pulmonary hypertension.
4. To prioritize the characterization of the experimental model based on accepted endpoints, namely pulmonary catheterization and pulmonary vascular histology. The development of accessory tools, such as microCT, should be not prioritized at the expense of these standard methods.

5. To develop a specific plan of development of models of pulmonary hypertension into competitive grant applications.

Reviewer 3:

1. The grantees must use more animals and establish routine hemodynamic measurements.
2. Lung and heart histology are essential and none have been provided.
3. Overall quantitative data—with the exception of data reflecting survival of the rats—are needed.

***Generic Recommendations for Allegheny-Singer Research Institute***

Reviewer 3:

Due to the lack of progress, I would recommend to reset milestones and discontinue funding if no publishable data are forthcoming.

***ADDITIONAL COMMENTS***

Reviewer 3:

There is yet to be a robust model or published data. The incomplete tool kit does not promise definitive data or future studies.

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**Project Number:** 0862304  
**Project Title:** Myofibroblast Inhibition in Dupuytren's Contracture  
**Investigator:** Satish, Latha

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### ***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:

This project did not meet the stated objectives. Essentially, none of the work proposed in Specific Aim 1 was carried out. For instance, Specific Aim 1 suggests a quantitative approach beginning with measurement of cAMP levels in fibroblasts versus myofibroblasts. However, such studies were not performed; therefore, no evidence is forthcoming regarding the central question of whether cAMP levels are different in fibroblasts and myofibroblasts. Single experiments with one concentration of forskolin show some effect on TGF $\beta$  stimulated, but there are no controls and the overall quality of the data collected is not convincing. Finally, one experiment on cell contraction of collagen matrices is shown, but no work on cell proliferation or cell migration as proposed.

##### Reviewer 2:

1. The project meet only some of the stated objectives.
2. The project did not:
  - a. measure cAMP levels or overexpress AC6 as proposed in Specific Aim 1a
  - b. examine  $\alpha$ -SMA organization by immunostaining or percent cells expressing  $\alpha$ -SMA
  - c. measure proliferation in response to changes in cAMP
  - d. look at the effect of specific PKA pharmacologic agents
  - e. contraction as measured by cell traction force microscopy
3. A key result was opposite of the hypothesis, and was not discussed: Hypothesis stimulation of cAMP/PKA pathway in DD would blunt fibrosis. The PI found increased expression of AC6 in DD diseased and in diseased palmar fascia fibroblasts as compared to control (CT) fibroblasts. This suggests cAMP/PKA pathway activated more in DD fibroblasts than in CT fibroblasts – opposite of the hypothesis.
4. Activating cAMP/PKA pathway had no effect on TGF- $\beta$ 1 increased expression of collagens - inconsistent with the hypothesis.
5. The PI only examined fibroblasts from DD cords and not from nodules. The cords were composed of primarily of residual fibroblasts; nodules of myofibroblasts. Others have reported cells cultured from nodules more myofibroblastic than cords. It is a major flaw to only examine fibroblasts from cords.

6. Overall, the project made minimal progress and has minimal data for submission of an R21 grant.

Reviewer 3:

The strength of this section is that a lot of preliminary control experiments were performed to determine the baseline behavior of the cell cultures. These include the assessment of alpha smooth muscle actin, collagen I, fibronectin, MMP1, TIMP1, and CTGF. The weakness is that very little novel research directly related to the specific aims was performed; these novel data include the adenylyl cyclase-6 presence, and forskolin-induced reduction of alpha-sma. Another weakness is that the grantee developed novel data on forskolin effects on fibronectin and CTGF (not part of the specific aims) rather than providing data on cAMP, the primary emphasis of the specific aims.

*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:

Little beneficial impact is expected.

Reviewer 2:

Results obtained from this project have been previously reported for fibroblasts from other tissues. Not surprisingly, there are similar results for DD fibroblasts. There are no new ideas proposed as to how altering cAMP/PKA levels may be having effect on fibroblast-myofibroblast differentiation.

Plans include the submission of an R21 grant application. No other future plans were discussed in the Final Report.

Reviewer 3:

The strength of the impact is that the goal is to provide a non-surgical treatment for Dupuytren's contracture; this would lower the healthcare burden for a certain population of primarily elderly individuals. Another strength is that the grantee plans to apply for NIH R21 funding in the future. A weakness related to this is that the grantee did not identify any specific "request for proposal" or NIH granting agency that would accept a proposal based on this research.

The primary weakness is that the afflicted population is rather small, and the disease is not life-threatening.

***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 funds were leveraged. The PI states that he is planning to submit an NIH grant.

Reviewer 2:

The PI plans on submitting an R21 grant application.

Reviewer 3:

The only identified strength is that the grantee plans to submit an NIH R21 grant at some time in the future, but has not provided any other details. One weakness of funding leverage is that no other funds or funded projects were identified that could have collaborated ( e.g., summer student support through NSF grants or state grants, if available).

***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:

No publications have materialized. The PI states that he is preparing a manuscript for the *Journal of Hand Surgery*.

Reviewer 2:

The PI plans to submit results to the *Journal of Hand Surgery*; it is unclear as to what they plan to submit.

Reviewer 3:

One strength of this section is that the data accumulated will be submitted for publication to the *Journal of Hand Surgery*, the targeted audience for this subject. The major weakness is that most of the provided data simply characterize cell lines with already-recognized benchmarks for Dupuytren's disease and derived cells. For example, it is well known that myofibroblasts express alpha smooth muscle actin and produce collagen.

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

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

Two undergraduate students worked on this project.

Reviewer 2:

1. Two undergraduate students were supported for the summer.
2. There are new ideas for expanding to animals; however, it is unclear as to what this means.

Reviewer 3:

This is where the most outstanding strength of the project in its current state lies, and that is the generation of multiple cell lines of Dupuytren's diseased cells and their non-diseased counterparts, the carpal tunnel release cells. This will provide future capacity to do research on many levels, including molecular, cellular, and tissue biology (this was not identified as a strength by the grantee). Another obvious strength is that students were involved in the research. Continued student support would enable the grantee to apply for funding from NIH through the R15 AREA grants, or through the National Science Foundation's Research Experience for Undergraduates (REU). The only possible weakness identified is the lack of collaboration outside the University of Pittsburgh pathologist listed.

***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 PI has initiated collaboration with Dr. LaFramboise at the University of Pittsburgh.

Reviewer 2:

A new collaboration with an investigator at the University of Pittsburgh was stated.

Reviewer 3:

The primary strength of this criterion is that a pathologist from the University of Pittsburgh is now a collaborator. Other collaborations were not identified.

***Section B. Recommendations***

***SPECIFIC WEAKNESSES AND RECOMMENDATIONS***

Reviewer 1:

1. Quantitative experiments on cAMP levels should be carried out as proposed in the application. Use of forskolin to increase cAMP levels should be quantified.
2. Experiments should be carried out in parallel with the control and involved fibroblasts. All RT-PCR experiments should be accompanied by parallel western blotting as was proposed in the application. Reproducibility of results from experiment to experiment should be analyzed.
3. Contraction, migration and proliferation experiments should be carried out as proposed in the application.

Reviewer 2:

1. The PI proposed to do a number of experiments that were critical to address hypotheses that were not done, most importantly to measure levels of cAMP. The second was to overexpress AC6. Neither were done.
2. The PI found increased expression of AC6 in DD cord fibroblasts and uninvolved palmar fascia compared with carpal tunnel control fibroblasts. Anticipated AC6 would have been decreased in DD cord and PF fibroblasts. The opposite result was found. The PI needs to address this finding. This needs to be compared with measured levels of cAMP.
3. The PI only examined DD fibroblasts from cord tissue and not from nodule tissue. As the PI described in the Background section, differences have been found between these two cells and nodule cells appear to be more myofibroblastic. The PI needs to obtain and examine DD nodule fibroblasts.
4. For the most part, the specific aims proposed have already been done on other types of fibroblasts, like cardiac and lung. Little new with regard to fibroblast-myofibroblast differentiation, will be discovered with these specific aims. The PI needs to design specific aims that will test underlying mechanisms by which changes in cAMP levels can alter fibroblast-myofibroblast differentiation. Such findings may provide new therapeutic interventions for DD disease.

Reviewer 3:

1. The grantee did not adhere to the specific aims as written: performance of preliminary data points (Figures 1, 2, 3, and 10 from question #17, Final Progress Report). It is recommended that the grantee recognize when preliminary data are needed, and include in the first aim. An alternate recommendation would be to perform these experiments ahead of time. A third recommendation would be to have done one preliminary experiment at a time followed by a specific aim. For example, assay the alpha-smooth muscle actin in the cells; then follow up by testing the effect of forskolin and related aims. Only after completing the next preliminary experiment, move on to TGF-beta preliminary experiments, etc. This weakness may be related to the lack of anticipated work load.
2. The grantee did not adhere to the specific aims: inclusion of outside experiments (Figures 6B and 7 from question #17, Final Progress Report). In addition to the preliminary experiments performed, the grantee produced data on fibronectin and CTGF, not included in the specific aims as written. The recommendation is that the grantee periodically read the grant proposal and ask whether the aims are being met. One way of doing this is to have a chart, PowerPoint slide, or worksheet of the specific aims and required experiments listed; then, every time there is a lab meeting (or set a weekly alarm), produce the document and determine what experiments have been done and what have yet to be done. This weakness may also be related to the lack of following instructions on question #17.
3. Weakness:  
The grantee did not adhere to the instructions provided for question #17, Progress in Achieving Goals, Objectives, and Aims, in the Final Progress Report. As written, the material for question #17 read as a rough-draft manuscript for a journal article, not a progress

report for a grant. It is difficult to determine why most of the work expected was not done because no information is given in this regard.

**Recommendation:**

Provide information to enable the reviewer to make a qualified recommendation. There is no page limit for question #17. The grantee could simply cut and paste the specific aims from the text of the proposal and answer the questions whether the aims had been met, and if not, why they were not met.

**4. Weakness:**

The grantee's expectation of the amount of work to be done apparently exceeded the ability to do the work. A conservative estimate lists 30 discrete units of experimental methodology, each requiring multiple cell lines and replicate experiments. For example, in Specific Aim 1 the grantee stated that adenylate cyclase activity would be measured by RT-PCR; this was considered an experimental unit. The grantee was able to complete one of these units (the adenylyl cyclase RT-PCR), and partially performed four other units (forskolin effect on basal alpha-sma; forskolin effect on TGF-b treatment; RT-PCR for Col1A1; RT-PCR for Col3A1), leaving the other 25 or so units unreported (most of Specific Aim 1A, more than half of Specific Aim 1B, half of Specific Aim 2A, all of Specific Aim 2B). Without provided details of why the work was not performed, the reviewer assumes that too much work was promised.

**5. Weakness:**

There was lack of progress toward external funding leverage.

**Recommendation:**

Become aware of grant opportunities. There is probably a grant helper on your campus who could help find grants that would be appropriate for this research. For example, the grantee listed an R21 but no details were provided. This study would likely be appropriate for the National Institute of Aging, or the NIGMS. The team members on study sections are posted at the NIH website, so the grantee can find the best fit for this study by finding study section members whose work focuses on scars, fibroses, wound healing or aging. In addition, since students were employed on this study, the grantee is taking advantage of a research aspect that is a primary component of grants from the National Science Foundation (REUs) and the NIH AREA Grants (R15).

***Generic Recommendations for Allegheny-Singer Research Institute***

**Reviewer 3:**

If the institute provides grant writing or grantee support, there should be a method for providing advice on how much work can be done in a grant proposal. In addition, personnel support (especially for students) can be sought for the grantee perhaps through a grant writing office at the institute.

## ***ADDITIONAL COMMENTS***

### Reviewer 2:

1. The project did not meet most of the stated goals.
2. The project only used fibroblasts from DD cord and none from DD nodule.
3. The project obtained results opposite of the hypothesis and did not discuss results - increased expression of AC6 observed in DD cord fibroblasts and uninvolved palmar fascia fibroblasts compared with carpel tunnel fibroblasts.
4. The investigator did not measure cAMP levels which was one of the major goals and would help to resolve the above issue.
5. The results were already demonstrated for other types of fibroblasts. There was no proposal to understand the mechanism by which altering cAMP levels could alter fibroblast-myofibroblast differentiation.

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**Project Number:** 0862305  
**Project Title:** Flooring Renovation of the ASRI Rodent Animal Facility Research  
Infrastructure  
**Investigator:** DeFranc, Leslie P.

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## ***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:

New flooring was installed. The project director, Ms. DeFranc, has a bachelor of science degree in biology and is a laboratory animal technician, but does not appear to have the expertise or experience needed to select the optimal material for this project. No mention was made of a qualified engineer or materials expert needed for this project. No data are provided to justify selection of the product used or evaluation of its service after installation. It is said that bids were solicited for this renovation project, but no details were provided on which competing products/installation companies were considered or the dollar value of their bids. It is known that the project involved 600 sq. ft. of floor. The project cost was \$72,000, which computes to \$120/sq. ft.

#### Reviewer 2:

The project met the stated objectives – floor renovation in the ASRI Rodent Animal Facility. This was Research Infrastructure Project 5 and was allocated \$71,962.62 to renovate 600 sq. ft. of hallway, animal rooms and work rooms floors. No specific data were to be generated. There was slight modification to the proposed research Strategic Plan provided with these documents in that the floor was installed in August 2009, instead of January - June 2009 as indicated in the Strategic Plan.

#### Reviewer 3:

This was an infrastructure project that met all objectives including time lines.

***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 offered to justify this project is that a 20 year old floor in the experimental animal resource facility needed replacement. The facility currently serves two investigators. The general topic of research of the two investigators is given, but no details are provided on

peer-reviewed funding of these projects or any measure of productivity of these investigators; therefore, it is not possible to assess the value of research that this facility supports.

Reviewer 2:

Improvement of research infrastructure ensures continuity of research programs and competitiveness in attracting funding. The research also maintains compliance with regulatory requirements as to protection of labor from health hazards and maintenance of appropriate care and use environments for laboratory animals.

Reviewer 3:

This was a significant infrastructure project that was needed for continued accreditation to be able to do animal research. This was completed successfully and at reasonable costs.

***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:

There was no attempt to leverage grant funding for this facility maintenance project. The statement given is that grant funding for maintenance frees funding to further research, which as indicated above, cannot be assessed based on the information provided. It is doubtful that after observing the deteriorating floor for two decades that there was not some opportunity for institutional funding or generation of maintenance funding through charge backs to facility users or indirect costs, if the projects are funded. It should be considered poor management if there is not a program in place for animal facility maintenance without dependence on grant funding.

Reviewer 2:

No additional funds were leveraged except for the improved potential to attract competitive research funding. In addition, as indicated in the Strategic Plan, "operational efficiency opportunities are maximized by reducing repetitive repair and reducing daily maintenance. The cost savings from floor repair and labor can then be reallocated to other laboratory needs." In addition, downtime from repair activities on the old flooring is eliminated, which also is a cost savings that may qualify as 'leveraged funds.'

Reviewer 3:

Direct leveraging of funds was not expected.

***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:

No details are provided on peer-reviewed publications or any other measure of research quality of projects supported by this facility improvement grant.

No data are provided to assess the success of the finished floor renovation.

Reviewer 2:

No peer-reviewed publications are expected for this funding, except for the continuity in research activities in the improved facilities that certainly will lead to additional publications over the life time of the facility.

Reviewer 3:

This was an infrastructure project that supports animal research and was not expected to result in direct publications or other opportunities.

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

***STRENGTHS AND WEAKNESSES***

Reviewer 1:

This was an infrastructure improvement project.  
No new investigators were mentioned.  
No funding was used for research or support of students.

Reviewer 2:

This was an infrastructure improvement project. As such, it contributes to maintaining the competitiveness of the institution in attracting research funding and collaborations, protect investigators, technicians, students and support personnel from potential hazards due to old and inadequate flooring (maintenance difficulties, microbiologic hazards, 'slip and slide' hazards) and maintains compliance with regulatory requirements.

Reviewer 3:

This was an infrastructure project that upgraded animal housing flooring. No additional funds were used.

***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:

No external interaction was mentioned.

Reviewer 2:

Improved facilities bring about collaborations.

Reviewer 3:

This was an infrastructure project that did not add additional resources but would allow continued ongoing research.

## ***Section B. Recommendations***

### ***SPECIFIC WEAKNESSES AND RECOMMENDATIONS***

#### Reviewer 1:

1. This institution should provide a funding mechanism for routine maintenance of its animal resource without dependence on extramural funding. Planning for projects of this magnitude should be supported by qualified engineering or materials expertise.
2. The only justification given for this project was that regulatory agencies require a sound floor. While this may be true, the emphasis is misplaced. Unless the projects served by the facility are equal to the investment, the need to satisfy regulatory standards is moot.
3. It is incumbent on the institution to justify the cost of this project based on the need of investigators and research projects served by the facility. Some reasonable assessment of the finished product should be included in the project planning and followed after completion of the project. It is stated that the new flooring is expected to serve for only 5-10 years. Considering the range of flooring materials available and the high cost of the material/application used in this product, a service life of only 5-10 years is a serious flaw in planning and product selection.

#### Reviewer 2:

1. No necessary improvements are identified from the progress reports.

#### Reviewer 3:

None.

### ***ADDITIONAL COMMENTS***

#### Reviewer 1:

Based on the project description provided, the fundamental flaws in this project start with planning and end with assessing the finished project. No information is provided about engineering or materials expert advice in selecting the product used. No information is provided about competing products/vendors considered. No information is provided about cost assessment. No details are provided about the quality of research served by this project. No information is provided about the assessment of the finished floor.