

Response Form for the Final Performance Review Report*

1. Name of Grantee: University of Pittsburgh
2. Year of Grant: 2008 Non-Formula Grant
3. Project Title: Center of Excellence in Prevention and Control of Antibiotic Resistant Bacterial Infections
4. Principal Investigator: Lee H. Harrison, MD

A. Briefly describe your plans to address each specific weakness and recommendation in Section B of the Final Performance Review Report using the following format.

Reviewer Comment on Specific Weakness and Recommendation (*Copy and paste from the Final Performance Review Report the reviewers' comments listed under "Section B. Recommendations, Specific Weaknesses and Recommendations*):

Response (*Describe your plan to address each specific weakness and recommendation in ongoing or future research funded by the Health Research Program*):

Note: Below we list each comment in Section B of the Final Performance Review Report and provide our response in **bold**.

Reviewer 1:

1. Future proposals should provide specific justification for the novel aspects of each aim that will advance the field.

We agree and strive to do this with all of our grant applications.

2. Unsuccessful aims should be sufficiently investigated to provide an explanation for the lack of success.

We agree. However, with the end of the funding of our Center we did not have sufficient resources to pursue this.

Reviewer 2:

None.

No response needed.

Reviewer 3:

Continue to seek publication of any unpublished results, particularly for the MRSA studies which are currently represented only by the economic analyses in the literature.

We would ideally like to pursue additional publications. However, because our MRSA studies were completed at the end of the funding period, our MRSA personnel left to pursue other employment opportunities before publications could be completed.

* Please note that for grants ending on or after July 1, 2007, grantees' Performance Review Reports, Response Forms, and Final Progress Reports *will be made publicly available on the CURE Program's Web site.*

Reviewer 4:

1. Overall the studies outlined in the MRSA section were limited in scope and in their novelty.

No response required.

2. Further studies characterizing the utility of screening for acinetobacter would be useful.

We agree.

Reviewer 5:

1. One sub-aim was not initiated due to lack of time and personnel. However, this was likely to be a low yield study due to the low prevalence of *C. difficile* in the long-term care facility. As the investigators have no doubt concluded, *C. difficile* studies, at least in this particular facility's long term population are not likely to be fruitful. It is not clear how generalizable this is, however. It may be useful to look at other centers and also to look at antibiotic use patterns to correlate with *C. difficile* prevalence.

We agree with these comments.

2. Several original aims were changed or substituted and there was good rationale for this. With regard to the *C. difficile* studies, there is a lot of work now regarding changes in the colonic microbiome that may be very important with regard to preventing *C. difficile* colonization and/or disease. While looking at detection of carriers and prevention of transmission is important, ultimately the most successful interventions may include manipulation of the microbiome. The investigators may want to consider working in this area, especially since there is expertise in anaerobic cultures.

We agree with this comment and are planning to pursue this avenue of research.

3. It appears there may be 2 opportunities for patents (RT PCR for *C. difficile* carriage, MDR *A. baumannii* screen) and this could potentially provide funding for future studies.

We doubt that these patents would be commercially viable but will take this recommendation under consideration.

4. The work appears to be centered at UPMC except for the Kane long-term care study. Could larger sample sizes and more generalizable results be found by including other area hospitals?

Yes, most definitely, because, as pointed out by the reviewer, we performed our studies in only one hospital and one long-term care facility.

5. Regarding the minority training program, the summer program and post-baccalaureate program are admirable. Can longer term experiences, leading to grants and potential faculty positions be incorporated?

Given that the funding period has ended, we will not be offering additional minority training opportunities as part of this grant. However, we have already submitted other grant applications that do offer training in this area.

Reviewer 6:

1. Extend the training opportunities by not limiting to post baccalaureate minority trainees.
2. Enhance collaborations to more tertiary medical centers and community medical centers.
3. Spend efforts to explore the clinical applications of the modeling results.

We agree with all three of these recommendations and will take them into account when pursuing future grant and training opportunities.

Reviewer 7:

None.

No response required.

Generic Recommendations for the University of Pittsburgh

Reviewer 6:

Enhance exposure of the Center to all departments of the institutes and support the investigators to collaborate with other institutes inside and outside of the U.S. to extend these findings.

We will inform the University of this recommendation.

ADDITIONAL COMMENTS

Reviewer 1:

Although some of the stated objectives were met, and some components of the project are likely to have a beneficial impact, enthusiasm for this project is tempered by the fact that too many of the objectives were simply confirmatory of other published work. Moreover, discordant results from an MRSA RT-PCR assay that prevented one aim from being accomplished represent a missed opportunity, as this problem was not sufficiently investigated to determine the cause of the discordance. The *C. difficile* intervention and modelling aims were not completed, and other aims were not addressed conclusively due to underpowered studies.

This was a large project that involved some novel components and some findings that were confirmatory. This is the nature of infectious diseases research, in which the literature rapidly evolves and some studies that appear relatively novel at inception end up being less so by the time of publication. The discordant MRSA RT-PCR results were disconcerting to us and therefore that component was discontinued to avoid harm to patients. We initially intended to investigate and publish the mechanisms responsible for the discordant results but decided not to pursue this when several studies that addressed this issue were published. Decisions to discontinue or modify study aims were based on strong scientific grounds.

Reviewer 2:

Conclusions: Throughout the project, all major strengths were identified with few, if any, weaknesses; all projects met all or most of the stated objectives; and all of the projects are likely to have some beneficial impact.

I did not identify any weaknesses that require improvements.

No response required.

Reviewer 4:

- For the most part the investigators carried out the studies that were outlined in the proposal.
- Most aims resulted in publications in respected journals in a timely manner.
- An outstanding job was done with the recruitment of under-represented minorities and their training.
- The investigators integrated new technologies into their studies, defining the advantages and disadvantages of these approaches.

No response required.

Reviewer 6:

- A strong and solid center was established.
- Trainees were limited to post-baccalaureate minority trainees.
- Outside collaborations were limited.

No response required.

B. If the grant received a rating of “unfavorable,” please indicate the steps that you intend to take to address the criteria that the project failed to meet, and to modify the grant oversight process so that future projects will not receive “unfavorable” ratings.

Response: This project received a “Favorable” rating.

C. Additional comments in response to the Final Performance Review Report (OPTIONAL):

No response required.