

Overall Impact/Penn Compact Innovation, Inclusion and Impact

This grant demonstrates strong innovation by approaching a novel treatment pathway in pulmonary hypertension. Successful execution of the proposed study would likely result in clinical trials in patients with an emphasis on improvement in quality of life. The PI is well-poised to execute the proposed work which appears feasible in her hands. Specific features of the approach demonstrate that the PI has experience in the area, but certain pitfalls and potential problems of the approach are not highlighted and addressed. In addition, more modern analytic approaches could have been suggested. If she executes this proposal successfully, the data will provide an important foundation for future extramural funding.

REVIEW CRITERIA

1. Significance:

Strengths

- Important problem and the investigator has already performed pilot studies to enlighten the approach
- Preliminary data suggest feasibility

Weaknesses

- There is the potential for new therapeutics that could lessen the impact of this treatment approach.

2. Investigator(s): including PI's career trajectory, Career development at early stages of career, Overall impact to investigator's research program

Strengths

- Dr. Smith has specific expertise in stepped wedge designs and other novel cluster randomization trials, which will be important for this study.
- Dr Smith has just received her first R01 and has just published a high-impact paper which forms the basis of this proposal, so that it appears that she is on an upwards trajectory
- Appropriately experienced staff and statistical analysts for the project

Weaknesses

None

3. Innovation:

Strengths

- Stepped wedge design may be considered innovative

Weaknesses

- While the analytic methodologies proposed are well-established, there may be more modern and sophisticated techniques that could be considered (e.g., Bayesian)

4. Approach:

Strengths

- Well-described study design
- Using appropriate end points
- Blinding of assessments will minimize bias

Weaknesses

- Certain pitfalls of the design were not discussed or mitigated. For example, drop-out is highly likely. How will the investigator minimize this during the study and address it in the analysis?

5. Environment:

Strengths

- Very good environment

Weaknesses

- None

6. Other Factors:

Prospects for future extramural funding

Matching support from other sources

Advancement of school or institutional objectives, such as interdisciplinary research

Undergraduate participation

- The application proposes having an undergraduate student assist with execution of the study
- The involvement of investigators from both the School of Medicine and Dentistry is a strength.
- As this is an area of recognized importance, execution of the aims would likely form the preliminary data for additional extramural funding
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7. Budget

___ Approved

___ Suggested modifications/justifications

8. Regulatory issues