Plan for Instruction in Methods for Enhancing Reproducibility

As the complexity and pace of science has increased, there have been increasing concerns that errors and/or lack of rigor in experimental design, analysis and execution have led to an increasing lack of reproducibility of research findings. Although errors and misinterpretations in science are generally corrected over time in the course of peer review and additional experimentation, the economic and temporal costs of "sloppy" science are substantial and unsustainable. NIH has developed plans to implement in stages an increasing emphasis on enhancing scientific reproducibility in its review of applications for both research and training grants. Although these requirements are not formally in place for the current round of T32 applications, we nonetheless plan to place a substantial emphasis on this issue in the training of trainees supported by our program.

We will ensure that all predoctoral and postdoctoral trainees obtain the knowledge and skills required to design and conduct rigorous, well-controlled experiments that consider all relevant biological variables, use authenticated biological and chemical resources, and apply appropriate statistical tests for data analyses.

Areas to be covered include the importance of developing a sound scientific premise prior to the initiation experimentation; developing a rigorous experimental design that is attentive to sample size, statistical power and statistical analyses; consideration of relevant variables such as sex; and authentication of chemicals, biological and animal strains. In human and population-based studies, we will emphasize additional key issues such as the importance of definition and representativeness of populations studied.

Ensuring that reproducibility of research is feasible depends on the type of research being conducted. Although our T32 program focused on epidemiologic and behavioral research which will be our primary emphasis, the EC believes that all trainees should have a basic understanding of rigor and reproducibility for basic and clinical research as well. In addition to the main areas above, our training will include the following key elements:

<u>Basic Research Studies</u>:

- Choice of appropriate cell lines
- Inclusion of adequate positive and negative controls
- Number of 'runs' to validate findings

<u>Clinical Trials:</u>

- CONSORT diagram and guidelines
- Registration of trial in clinicaltrials.gov
- Encouraging publication of study protocols
- Balance across study arms at baseline to assess known and unknown confounders
- Mediator/moderator analyses to assess mechanisms of effect
- Measures of effect size (e.g., Cohen's d value)
- Sources of potential bias (e.g. selective attrition) and their control
- Appropriateness of any post-hoc analyses
- Availability of systematic reviews and meta-analyses

<u>Epidemiologic Studies</u>:

- STROBE guidelines
- Model building strategies
- Applying criteria for causation (i.e., Doll and Hill)
- Availability of systematic reviews (e.g., Cochrane)
- Appropriateness of statistical analyses and control of potential sources of bias
- Statistical techniques for conducting sensitivity analyses (e.g., bootstrapping)

<u>Qualitative Research Studies</u>:

- Number of coders and coding scheme used to identify themes
- Appropriateness of qualitative software vs. coding by hand
- Achieving saturation of themes

- Using mixed methods to triangulate findings
- Member checking to assess validity of findings

We plan to utilize multiple methods to engrain critical principles and approaches to enhance training in research reproducibility throughout the program. These will include seminars and didactic sessions dedicated to this topic directed at both mentors and trainees beginning during the first year of the program. Drs. Strathdee and Patterson have been heavily engaged in editorial responsibilities and in the review of scientific research proposals for the NIH and other entities and will develop and present a seminar in this area at the during year 1 and annually thereafter. These will be supplemented by seminars organized by the Office of Research Administration, which is in the process of developing materials to address the issue of rigor. In addition to efforts dedicated to the topic *per se*, we will introduce key elements of concepts related to research reproducibility into other aspects of the training program. This would include, for example, affording attention to this topic in the course of reviewing journals at journal clubs and in the evaluation of the scientific literature in preparation for presentations. Special attention will be paid to this issue in the framing and execution of theses for PhD candidates supported by this program.

We recognize that as the importance of reproducibility of results gains further traction additional training vehicles and modules will be developed by us and by others. We will emphasize the importance of research reproducibility throughout the course of the program and will continuously introduce best practices in the area as curriculum in this area evolves.