Borrowed from Columbia

Rigor, Transparency and Reproducibility

Carrie Dykes, PhD

Research Engagement Specialist

Why is NIH Making More Work for Me?

NIH Mission

To seek fundamental knowledge about the nature and behavior of living systems and the application of that knowledge to enhance health, lengthen life and reduce illness and disability.

Key to this is scientific rigor: and one of NIH's goals is to 'exemplify and promote the highest level of scientific integrity, public accountability and social responsibility in the conduct of science'.

Key items

Rigor

scientific premise

Reproducibility

quality system in your lab

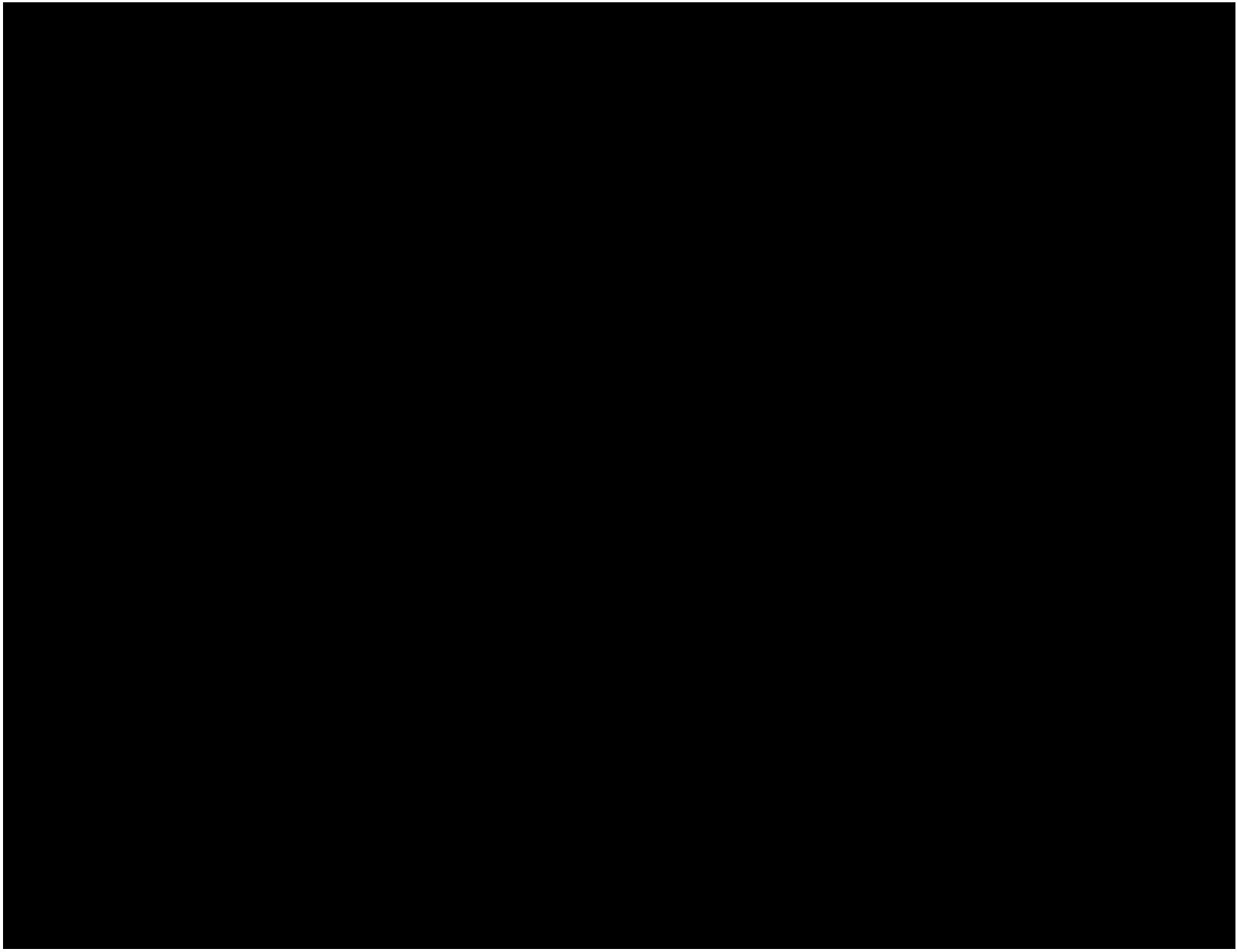
Transparency

Robust and unbiased results

Rigorous Experimental Design

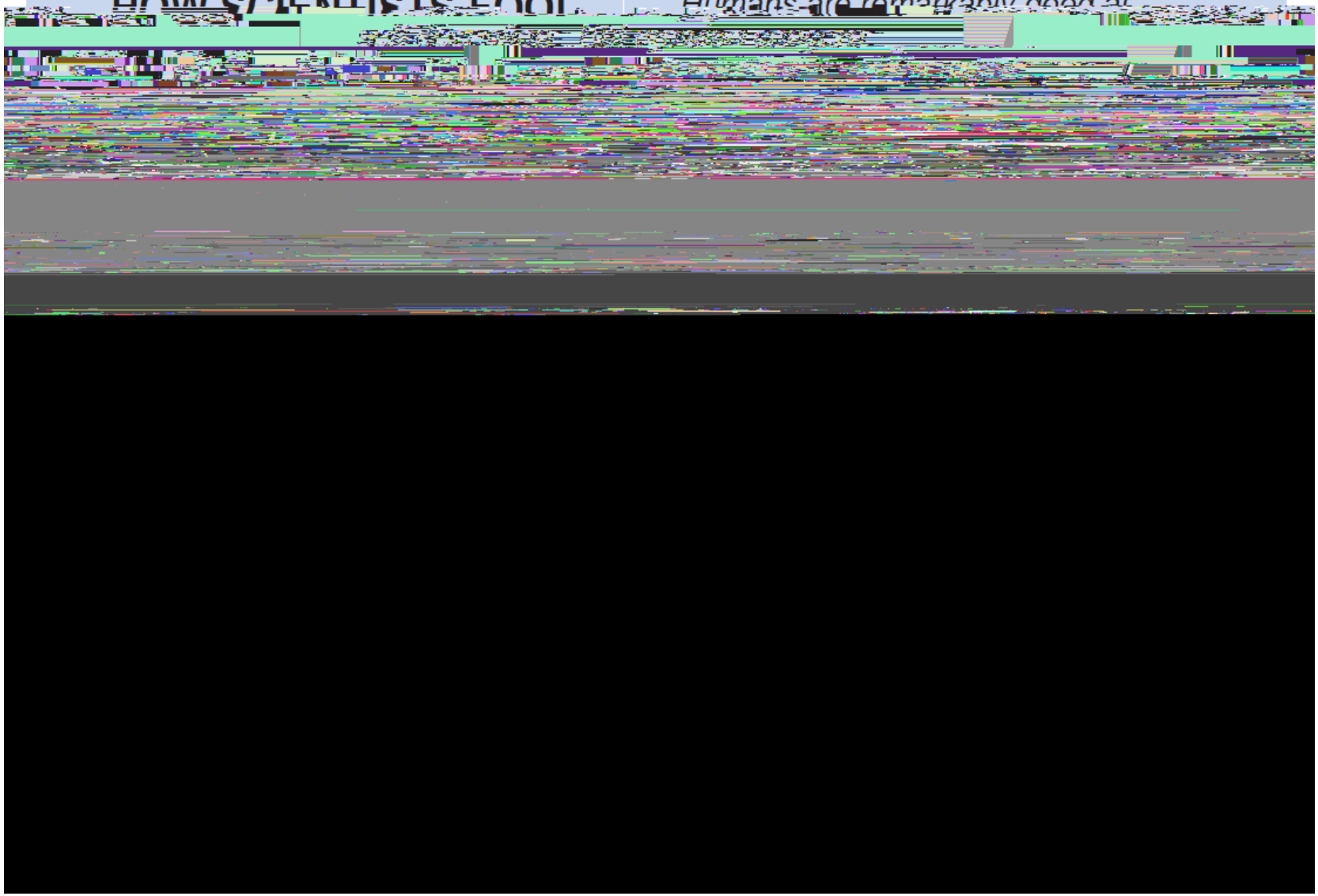
Scientific rigor is the strict application of the scientific method to ensure robust and unbiased experimental design, methodology, analysis, interpretation and reporting of results.

NIH expects applicants to describe how they will achieve robust and unbiased



HOW SCIENTISTS FOOL

Humans are remarkably good at



Transparency

Full Transparency in reporting experimental

Reproducibility-Quality Lab System

Equipment

Has equipment been maintained properly and calibrated?

Management

Who reports to who and who helps who with problems?

SOPs

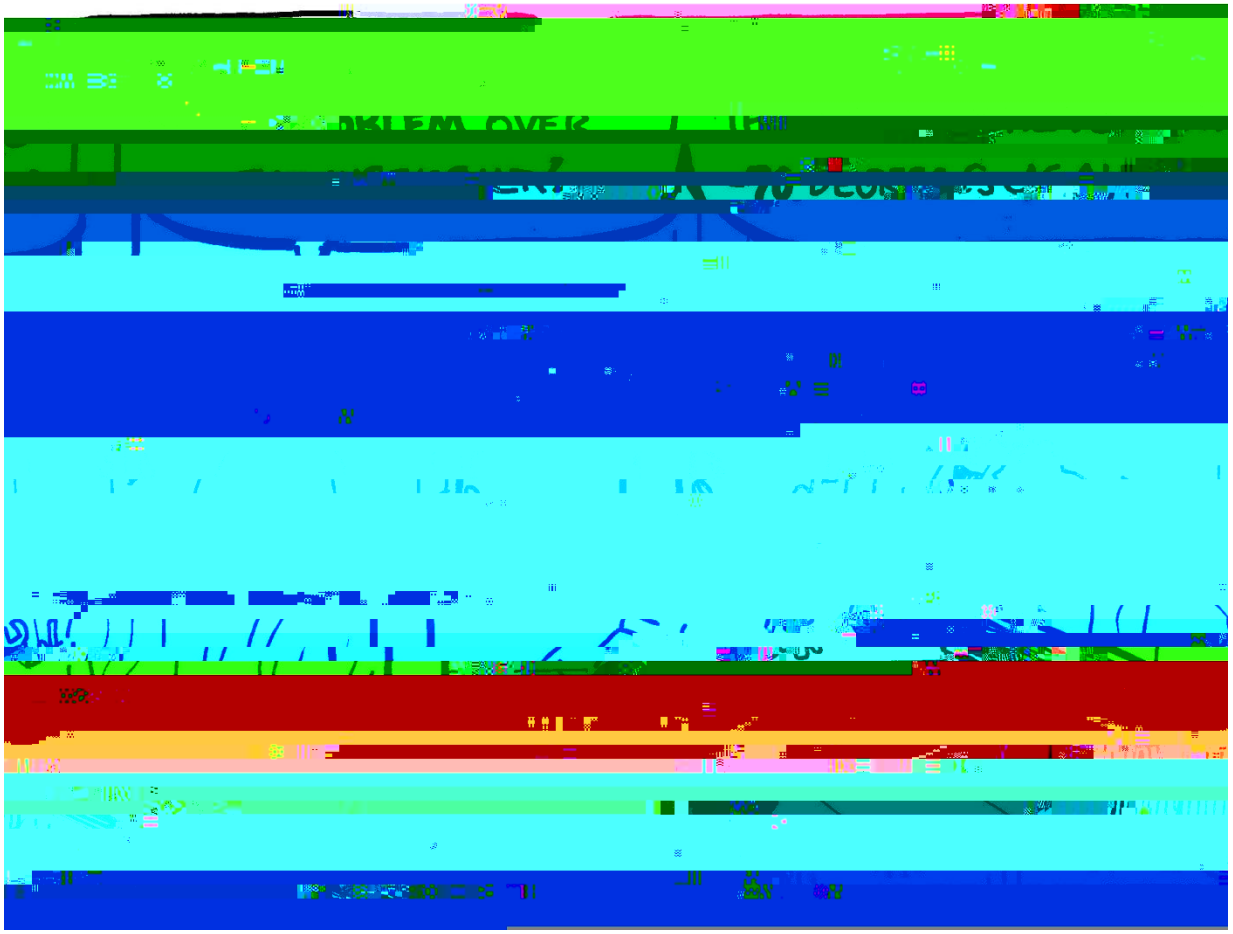
Are protocols documented are SOPs followed? Are deviations documented and corrected? Are the materials properly made, labeled,

Your Grant

Significance

Approach

Authentication of Key Resources Plan



Significance section

Explicitly state the *scientific premise* for the proposed project.

The general strengths and weaknesses of the prior research cited by the applicant, which form the basis for the proposed research

Strengths and Weaknesses of Supporting Data: Studies of inter-individual differences in leukocyte telomere length (LTL) have focused largely on middle age and elderly persons. These studies have established that adult LTL is influenced by heredity (17-22), by paternal age at conception (PAC) (1, 3-5, 23), and by environmental exposures (24-28) which augment oxidative stress. They have also provided compelling evidence that shortened LTL is related to cardiovascular disease (CVD), principally atherosclerosis (29-36), and reduced longevity (37-40). Yet empirical observations (41-46) and simulations (47) suggest that LTL at birth is a major determinant of LTL throughout the human lifespan, such that individuals endowed with short (or long) LTL at birth are likely to have short (or long) LTL later in life. Therefore, we posit that determinants of LTL at birth impact the evolution of health and disease throughout the life course. By identifying these determinants, we will provide a foundation for linking experience from conception to birth with health and longevity in later life (48). Accordingly, the present study has the potential to transform our understanding of population health by opening novel investigations of the pathways through which intra-uterine experiences are biologically embedded in the individual‘s constitution, and might be reflected in risk factors for disease which emerge in childhood and evolve thereafter.

Borrowed from Columbia

Approach Section

Again have specific sections in your grant titled

- Scientific Rigor
- Consideration of Sex and Other Biological Variables

Concern over biomarker reliability. We have revised our study design to restrict to the biomarkers with greatest reliability (interclass correlation coefficients [ICCS] from 0.49-0.55).

Authentication of Key Biological and/or Chemical Resources

Briefly describe methods to ensure the identity and validity of key biological and chemical reagents used in the proposed studies.

What is a key biological resource?

Authentication of Key Biological and/or Chemical Resources

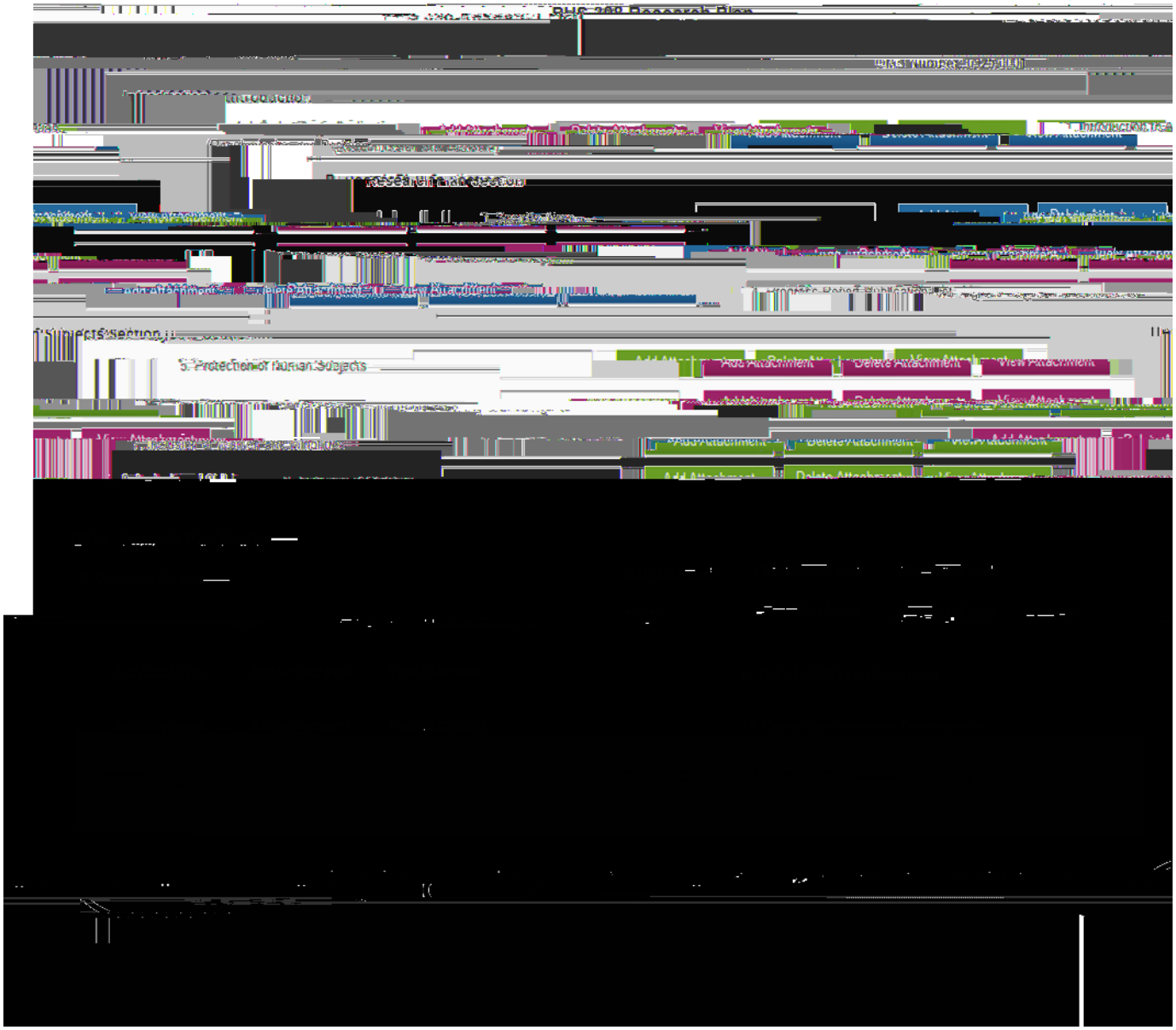
Researchers should transparently report on what they have done to authenticate key resources, so that NIH can develop understanding of consensus approaches.

You can use one description for multiple different resources in the same category (example: authenticating cell lines)

Actual data demonstrating that authenticated resources exist is not necessary

If a key resource is being made as part of the project or is under development, that should be in your research strategy, not this document.

Save this information in a single PDF file named “Authentication of Key Resources Plan,” and attach it on the R&R Other Project Information page of the application package


5. Protection of Human Subjects
Add Attachment
Delete Attachment
View Attachment

Review Criteria

Element of Rigor	Section of Application	Criterion Score	Additional Review Consideration	Contribute to Overall Impact?
Scientific Premise	Research Strategy	Significance	NA	Yes
Scientific Rigor		Approach		

Review criteria

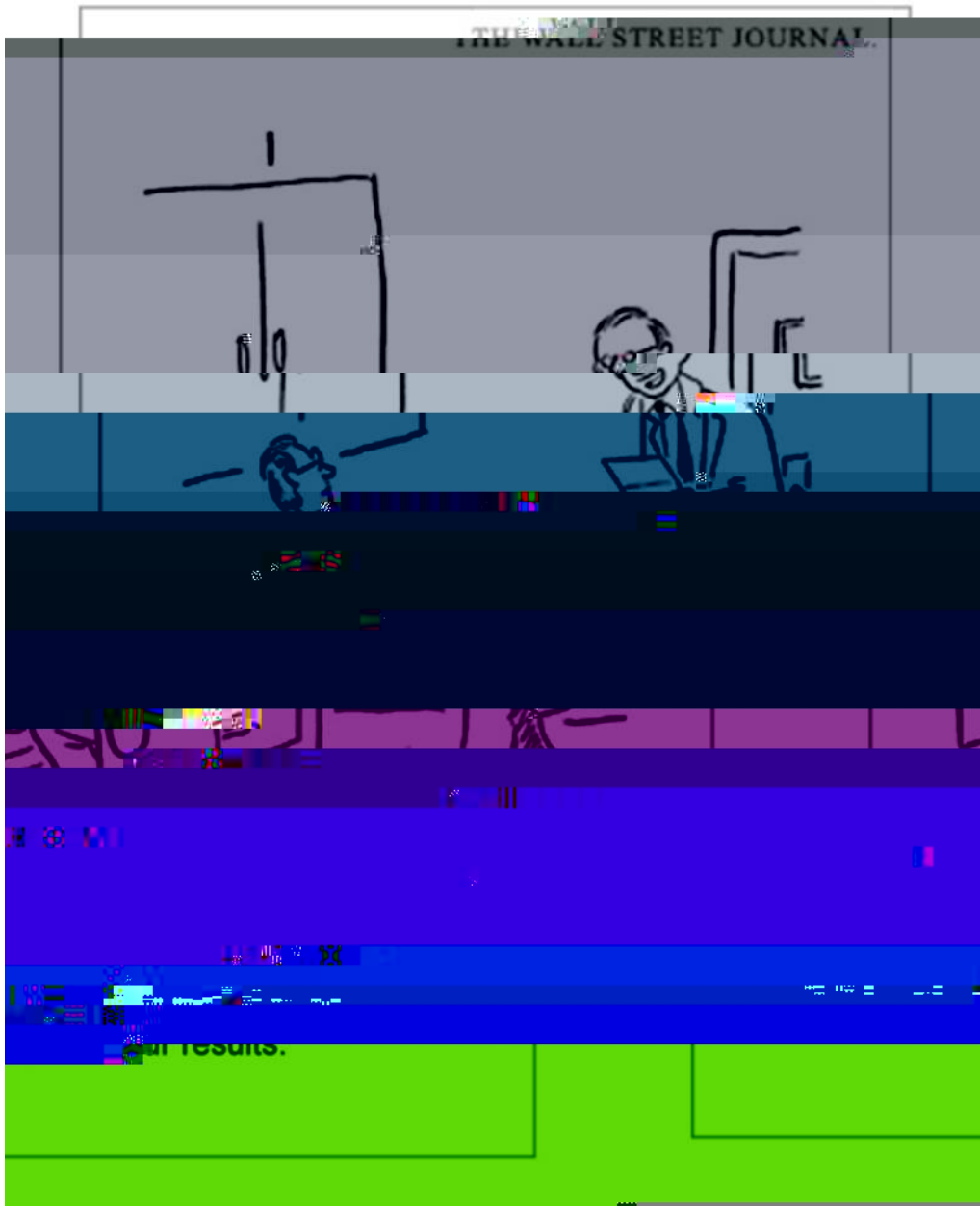
Reviewers will be asked to consider additional review questions in order to assess rigor and transparency

- Scored Review Criteria
  - Significance
    - Is there a strong scientific premise for the project?
    - The scientific premise will be reviewed as part of the **Significance** criterion, i.e., the importance of the problem, critical barriers to progress, how the proposed project will improve scientific knowledge, and how the field will change if the aims are achieved
  - Approach
    - Have the investigators presented strategies to ensure a robust and unbiased approach, as appropriate for the work proposed?
    - Have the investigators presented adequate plans to address relevant biological variables, such as sex, for studies in vertebrate animals or human subjects?

Additional Review

Authentication of Key Biological and/or Chemical Resources

For projects involving key biological and/or chemical resources, reviewers will comment on the brief plans proposed for identifying and ensuring the validity of those resources.



More 44.064 Tf1 0 0 1 194.

More, more information

Nature article on quality science

Help

ResearchHelp@urmc.rochester.edu

More examples

REPRODUCIBILITY AND RIGOR: Background for the scientific premise of this project is described above. The literature contains conflicting reports on the use of ultrasound for soft tissue and bone healing. A weakness in some investigations is the lack of critical calibrations of acoustic fields. Additionally, many studies focus on a narrow range of acoustic exposure parameters, thereby limiting understanding of underlying mechanisms and optimization potential. Our proposed project addresses these concerns and others in regards to scientific rigor. Ultrasound fields will be thoroughly calibrated before and after each experiment, and we have proposed investigating how different acoustic parameters (e.g. frequency, intensity, pulsing parameters, exposure duration) influence efficacy. Furthermore, we have incorporated blinding and randomization to reduce bias, have clear laboratory practices for data collection and analyses and transparency in reporting results. We have a quality system of operation in our laboratories, and ensure regular and proper training of investigators involved with experiments. In this project, we have incorporated testing of two important biological variables: we include experiments comparing responses in normal and genetically-diabetic mice, and between male and female mice. An important biological resource is the genetically-diabetic mouse model. This strain will be purchased from Jackson Laboratories, and glucose levels will be monitored as metrics of diabetes for each mouse. The response of diabetic mice will be compared to their strain-matched, non-diabetic controls. At the initiation of a protocol, the treatment site (i.e., left or right dorsal ulcer) will also be randomly chosen; the contralateral ulcer will serve as an untreated control. During daily exposures of individual mice, the treatment order (including sham exposures) will be randomized using a random number generator to avoid grouping identical ultrasound protocols in time. Separate investigators will be responsible for assigning treatment protocols, performing ultrasound exposures, and collecting data. For protocols involving data acquisition, the investigator will be blinded to treatment conditions and investigators will not be made aware of the treatment allocations until all data have been collected and analyzed. Based on our earlier studies using diabetic mice, and our other studies using normal mice to evaluate bioeffects of ultrasound, we anticipate that 9-10 mice per group will be required to evaluate significance. Dose response models of the various acoustic exposure parameters are utilized and threshold dependency will be assessed. Statistical analysis will be performed by one-way ANOVA followed by Tukey’s post-test. Results will be considered significant when $p<0.05$.

Denise Hocking U01

Questionnaire and medical record data.

Repeat questionnaires are administered by trained bi-lingual research workers to the

Limitations and Strengths.

The competitive renewal is responsive to recent epidemiologic and experimental evidence indicating that phthalates modulate thyroid function and reduce circulating thyroid hormone levels. These findings have important implications for child cognitive and behavioral function, as thyroid hormones during pregnancy and early childhood are critical to brain development. Even modest reduction may impact child mental, motor and neuropsychological function. Our preliminary research has shown a significant inverse association between maternal prenatal phthalate exposures and child mental development at age 3 years. However, limitations in the study design need to be recognized. Phthalates are ubiquitous contaminants, and measuring exposures is always a challenge given the potential for contamination and the fact that biologic half-lives are short. To address this, we will use phthalate monoester levels in urine samples from the mother during pregnancy and the child between ages 3-11 as our primary dosimeter of exposure