Title of proposed program: Development of Surrogate Endpoints and Outcome Measures for Use in Drug Development Trials

Submitting Source: NIH

What is the major obstacle/challenge/opportunity that the Common Fund should address? What would the goals of the program be?

Better tools to identify individuals at risk of disease are needed in order to better target prevention and intervention strategies. It is increasingly difficult to conduct clinical trials of new agents when there are approved drugs that are at least somewhat effective. Current regulatory policy requires endpoints that are often prohibitive for large scale studies that are needed to test new agents for prevention or treatment. This requirement raises both ethical (allowing patients to reach severe endpoints) and financial (large numbers of patients required to see these outcomes) challenges in drug development. The development of reliable and viable surrogate endpoints for many diseases would facilitate the screening of potential new drugs and make more avenues available for prevention and treatment.

One of the most important ways to prevent the human and financial costs associated with disease is to develop techniques better suited to more accurately assess those at highest risk and identify and modify specific treatable components related to early disease processes. Imaging methods can be effective but not sufficiently informative or discriminatory to replace full blown disease as the primary endpoint in treatment trials. Newer imaging methods have the promise to overcome current limitations.

Researchers will analyze existing data sets and develop new resources that can be used as surrogates in drug development trials. Goals include:

- Studies that correlate defined parameters within relevant tissues with clinical outcomes following various treatments.
- Define the clinical context for use of imaging-derived measures.
- Define the clinical context for use of known biomarkers that offer the potential to be used as surrogate endpoints
- Define the level of evidence needed for these novel measurement techniques to be used as endpoints in clinical trials.
- Determine whether data from health care systems and electronic health databasescan be used to assess long-term safety and efficacy of treatments
- Work with regulatory agencies to encourage novel approaches to drug approvals including shorter, surrogate trials and longer monitoring in the field.

Why is a trans-NIH strategy needed to achieve these goals? What initiatives might form the strategic plan for this topic?

The lack of defined surrogate endpoints is a problem that affects many diseases and conditions and severely limits the conduct of clinical trials due to increased expense of following disease to its true endpoint. There are likely to be unifying factors that can be used to identify surrogate endpoints. Imaging parameters are perhaps the most likely to be developed with impact across many tissues, but molecular biosignatures are also likely. If investigators who are defining surrogate endpoints for individual diseases work together as a consortium, the general principles are more likely to be defined.

If a Common Fund program on this topic achieved its objectives, what would be the impact?

Surrogate endpoints will be developed for a handful of diseases, but the general principles by which surrogate endpoints are defined will be available for the community at large to adapt to their disease of interest.