SUMMARY STATEMENT

PROGRAM CONTACT:
Joy Boyer
301-402-4997
boyerj@exchange.nih.gov

(Privileged Communication)

Release Date: **11/02/2009**

Application Number: **2 R01 HG005277-07A1**

Principal Investigator

JUENGST, ERIC T PHD

Applicant Organization: CASE WESTERN RESERVE UNIVERSITY

Review Group: **ZRG1 GGG-N (02)**
Center for Scientific Review Special Emphasis Panel
Ethical, Legal and Societal Implications of Genetics

Meeting Date: **10/29/2009**
Council: **JAN 2010**
Requested Start: **04/01/2010**

RFA/PA: **PA07-070**
PCC: **X5JB**

Project Title: **Anticipating Personal Genomic Medicine: Impact and Implications**

SRG Action: Priority Score | Percentile

Human Subjects: **30-Human subjects involved - Certified, no SRG concerns**
Animal Subjects: **10-No live vertebrate animals involved for competing appl.**
Gender: **1A-Both genders, scientifically acceptable**
Minority: **1A-Minorities and non-minorities, scientifically acceptable**
Children: **3A-No children included, scientifically acceptable**
Clinical Research - not NIH-defined Phase III Trial

Project Year	Direct Costs Requested
7	389,636
8	390,661
9	405,534
10	416,349
TOTAL	1,602,180

DC Recommended

ADMINISTRATIVE BUDGET NOTE: The budget shown is the requested budget and has not been adjusted to reflect any recommendations made by reviewers. If an award is planned, the costs will be calculated by Institute grants management staff based on the recommendations outlined below in the COMMITTEE BUDGET RECOMMENDATIONS section.

2R01HG005277-07A1 Juengst, Eric

RESUME AND SUMMARY OF DISCUSSION: The proposed studies will investigate ethical, legal, and social issues associated with personalized genomic medicine (PGM) specifically focusing on how the various promises of PGM are interpreted by those with critical roles in shaping the way PGM emerges as a social practice. The studies should result in a number of significant publications on the important topic of translational genomic medicine; however, it is unclear to some reviewers whether policy change or norms will result. While the reviewers agree that the principal investigator and research team are outstanding, the environment of the Center for Genetic Research Ethics and Law is excellent, the combination of social science, qualitative and quantitative methods is powerful, and the plans for engagement of minority interviewees are improved, they also note several weaknesses. Productivity was moderate during the previous project period. It was not entirely clear to some of the reviewers how the parts of this very large and complex project would be integrated or how the various parts would engage the constituency being studied. In addition, some reviewers felt that not enough attention was paid to exploiting the social network that would grow from the project. These weaknesses somewhat reduced the reviewers' enthusiasm for the application.

DESCRIPTION (provided by applicant):
Project Summary "Personalized genomic medicine" (PGM) is being promoted as a "new paradigm for health care" and a major goal for translational genomic research (TGR). In addition to overcoming TGR's remaining scientific hurdles, achieving that goal will involve addressing a number of ethical, legal, and social challenges. Some of those challenges reflect the ways that different social policies and health care economies will complicate TGR's ability to realize PGM as a viable health care paradigm. But other challenges might emerge from the goal itself, depending upon how PGM is interpreted by those who shape it as a social practice. This project explores this suggestion by documenting how PGM and its most attractive virtues are interpreted by those involved in defining them for TGR and society, and the challenges and choices they are encountering in the process. PGM is a goal that unites a wide array of biomedical initiatives, from medical sequencing, gene expression, and pharmacogenomics research to public health, clinical, and commercial services. Its promissory virtues are precision diagnosis and risk prediction, individualized therapy, prevention, health promotion, and patient empowerment. Different proponents of PGM interpret and rank these promises differently, with different implications for the realization of PGM as a health care paradigm. We focus on four sets of interpreters that will have particularly important roles in shaping the way PGM emerges as a social practice: (1) the scientists, research sponsors, companies, and policy organizations that promote PGM as a biomedical paradigm; (2) the journals, public review bodies and educational institutions that mediate the implementation of this paradigm; (3) the health care institutions and professionals that pioneer the paradigm by providing PGM services in practice; (4) the patient-based organizations that increasingly help shape its public reception. Our empirical studies of the views of these social co-producers of PGM will then be used to generate an analytic map of their different visions, designed to draw out their ethical, legal, and social implications for TGR and health policy. The "translational pipeline" of genomic research will have many branches towards its distal end. This project is designed to anticipate the directional choices that these branches will require, so that the PGM that TGR finally delivers into the complicated plumbing of our society is as clean and safe as possible.

PUBLIC HEALTH RELEVANCE:
A major goal of genomic research is to develop health care tools that can achieve more precise diagnoses and risk predictions, individualized therapy, prevention, health promotion, and greater patient empowerment. The proponents of these advances call their goal "personalized genomic medicine." But many different parties are involved in shaping this vision for health care, and their different interpretations of its virtues carry different ethical, social, and legal implications. The purpose of this

project is to study how some of the most influential parties who are promoting, implementing, providing, and using "personalized genomic medicine" understand its promises and potential pitfalls. This understanding will allow us to define the policy choices that lie ahead for researchers, health care providers, and the public as translational genomic research moves closer to its goal.

CRITIQUE 1:

Significance: 3
Investigator(s): 2
Innovation: 5
Approach: 4
Environment: **1**

Application #: 2 R01 HG005277-07A1

Principal Investigator(s): Juengst, Eric

Overall Impact:

Strengths

- Excellent team
- Case CGREAL great base for operations; superb record of fostering collaboration and cooperating and productive scholarship
- Topic clearly “hot” and emerging, important
- Research plan entails interacting with the system under study, with consequent possibility of improving policies
- Research plan, in effect, would create a social network focusing on the research topic

Weaknesses

- Very large, almost ponderous set of independent projects
- Methods seems to be continuation of ongoing work
- The power of the social network that would grow from this large project is neither explicitly recognized nor exploited, so the project is likely to achieve less than it could. Appears likely to produce many papers, but what about policy change or norms? This proposal seems like distant armchair bioethics on a topic that is by definition very immediate, real-world, and has large consequences in real lives.
- No explicit plan for policy engagement

1. Significance:

Strengths

- Translational Genomic Medicine is a central concern
- Thoughtful critique would be quite useful,
- Good identification of constituencies and actors who will be engaged

Weaknesses

- Ambitious but sprawling approach. Feels like a collection of related projects.

2. Investigator(s):

Strengths

- Excellent team. Juengst is a national leader and has demonstrated skills in leading networks of scholars
- Great mix of social science, qualitative and quantitative methods
- Past work suggests the weekly calls are an effective management strategy

Weaknesses

- Lots and lots of people involved.
- Productivity of the past R01 for which this is a renewal seems to be 8 articles, five of them with a single lead author.
- Many trainees involved, but past publication record on the previous R01 does not show lead authorship emerging from their involvement.

3. Innovation:

Strengths

- The methods seem appropriate.
- Mix of methods.

Weaknesses

- There is not much sparkle. The prose promises conceptual reframings, and some of this is apparently different from the previous application (e.g., shifting to the specific constituencies rather than the previous "virtues and vices" diagram that was deemed 'clever" but inscrutable).
- The methods used to probe the anti-aging movement will be applied to a new domain, Personalized Genomic Medicine.

4. Approach:

Strengths

- Broad engagement of diverse constituencies
- Mix of qualitative and theoretical methods, with some quantitative social science
- This will likely produce a stream of many publications from the different teams

Weaknesses

- How will the very different themes be synthesized? The health care delivery models of the different clinics to be interviewed (and in some cases shadowed) will be similar in some ways and different in others. Likewise the interests and main concerns of diverse disease advocacy organizations. Likewise the medical curriculum and health professional training efforts. It is easy to see publications on each topic if this work is actually carried out. But what is the value of doing these things together? The real value of this project would be precisely in synthesis

and overarching themes, and particularly on policy translation of research findings, but there is little attention to how this value would be captured.

5. Environment:

Strengths

- CGREAL got the highest rating of the initial 4 CEER P50 centers, largely because of Eric Juengst's leadership. He is famous for being highly collaborative and supportive.
- The infrastructure can certainly support this research effort.

Protections for Human Subjects:

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Inclusion of Women, Minorities and Children:

M1A - Minority and Non-minority, Acceptable

C3A - No Children Included, Acceptable

- This is an area that clearly got attention since the initial renewal proposal. There is much more explicit attention to including Morehouse, Howard, and other HBUCs. One lingering concern, however, is that the only "minority" group that seems to have gotten explicit attention is African Americans. Yet some of the strongest concerns are among American Indian tribes, and there is tremendous inconsistency among Latino/Hispanic groups in classification and how "populations" will be classified, and how genomics will play a role in health research on diseases of high priority (such as diabetes). The scholars on this grant are part of that literature and well aware of it, indeed among the leaders in thinking about it, but that is not reflected in the proposal.

Resubmission:

- The investigators have clearly fleshed out the plans for engagement of minority interviewees and gender balance. They have replaced the "virtues and vices" framework with a pragmatic constituency map that translates to a research approach that flows into the four aims. The previous critique of the approach as a rigid and too-narrow "template" is well defended in the resubmission as a seasoned team using general methods to think through a new set of problems.
- The investigators do not engage the "too early to be useful" critique raised by Reviewer 2. That's too bad, because it is quite clear their approach explicitly intends to interact with and perhaps even deflect the roll-out of personalized genomic medicine. Indeed this is a virtue and far preferable to Monday morning quarterbacking of what went wrong after fateful choices and historical pathways are already in place. This feature of the methodology is mentioned several times, but only in passing, and with little attention to turning it into a real value of the research through attention to policy engagement and activities other than scholarly publication.
- The critique that collaboration had not been nailed down has been rectified with a profusion of support letters, assembling a truly impressive group of collaborators.
- One component that apparently involved Max Mehlman has apparently been dropped from this proposal.

- The investigators appear to have taken most of the reviewers' comments to heart.

Renewal:

- This appears to be a renewal in the sense that some of the PIs are carried forward, but it is a largely new topic, and seems to be a substantial widening of the network, budget, and ambition.

Budget and Period of Support:

Recommend as Requested

Additional Comments to Applicant:

- Plans beyond scholarly publications that will arise naturally from the work would be good to lay out, to take advantage of the breadth and synthetic opportunities of this large project.

CRITIQUE 2:

Significance: 3
Investigator(s): 2
Innovation: 5
Approach: 2
Environment: 2

Application #: 3207944

Principal Investigator(s): JUENGST, E.T.

Overall Impact:

Strengths

- High potential impact in social understanding of and policy response to PGM
- Highly accomplished PI and excellent, experienced research team
- Relying on tested, established approach

Weaknesses

- Moderate level of productivity from grant for which this is a competitive renewal

1. Significance:

Strengths

- Documenting how principal stakeholders of PGM interpret its promise illustrating these findings through an analytic mapping process could lead to improved public understanding of PGM and better policy responses to the changes it will introduce.

2. Investigator(s):

Strengths

- The PI is a highly accomplished, productive researcher and is well suited to undertake the proposed research. He has assembled an outstanding research team and each member contributes an important useful expertise.
- Jennifer Fishman brings important methodological and theoretical acumen to the social science framing of the project
- Several of the team members have worked together previously and very successfully

Weaknesses

- Consultants are drawn from small group of experts, a choice that might limit ability of project to adequately account for other sources of influence, other stakeholders, or possible fissures within groups of stakeholders that are likely to shape the path of PGM

3. Innovation:

Strengths

- The combination of topic and methods in a project of this scope is novel.

Weaknesses

- Neither the topic nor the methods are innovative

4. Approach:

Strengths

- Applying "social worlds and arenas theory," to this set of questions is an appropriate choice that is likely to produce useful insights
- Reliance on interviews appropriate and their conduct and analysis is well explained
- Summative exercise of developing an analytic map of ethical and policy choices well developed and fits well with the rest of the project framework

Weaknesses

- Occasional implication in proposal that the outcome is already known: That PGM of the future is simply a more robust version of the predictions and limited practices we see today. The investigators are too sophisticated to actually think this and it seems likely that the pre-ordained quality to the narrative has more to do with grant writing language than misconceptions on their part.
- Possible inadequate distance from the sense of inevitability that pervades much of the writing on PGM, especially in conceptualizing and writing about TGR

5. Environment:

Strengths

- Case Western Reserve and in particular the Center for Genetic Research Ethics and Law (CGREL) provide an excellent setting for the proposed work
- Relationships with investigators at additional sites seem well considered and resources at those sites are excellent as well.

Weaknesses

- None

Inclusion of Women, Minorities and Children:

G1A - Both Genders, Acceptable

M1A - Minority and Non-minority, Acceptable

Budget and Period of Support:

Recommend as Requested

CRITIQUE 3:

Significance: 3
Investigator(s): 1
Innovation: 2
Approach: 3
Environment: 1

Application #: 2 RO! AG020916-07

Principal Investigator(s): Juengst Eric

Overall Impact:

Strengths

- Outstanding team of researchers ensure likely success of project
- Focuses on personalized genomic medicine that is a major goal of the Human Genome Project

Weaknesses

- The direction that PGM ultimately takes is likely to depend on the science itself rather than what the identified mediators think of the science.

1. Significance:

Strengths

- Focuses on how the principle stakeholders interpret the promise of personalized genomic medicine
- Personalized genomic medicine is a major goal of the human genome project

Weaknesses

- Unclear whether these interpretations will actually play any important role in the actual development and/or use of PGM

2. Investigator(s):

Strengths

- Dr. Juengst, a well respected leader in ELSI research will have the main responsibility for this project along with Drs. Jennifer Fishman and Richard Setterstein who are both experts in their fields of sociology of medicine and aging.

Weaknesses

- None

3. Innovation:

Strengths

- Approaching PGM by looking at the underlying assumptions and way in which potential benefits are presented and at the ethical issues inherent in translational genomic medicine is new.

Weaknesses

- The methods in this project are not new or innovative.

4. Approach:

Strengths

- Interdisciplinary team with strong research experience in bioethics
- Have identified and detailed a new theoretical framework from medical sociology called "social worlds and arenas theory" that seems appropriate to their research focus
- Focus on three groups of mediators: journals. public committees and educational programs

Weaknesses

- Unclear to this reviewer what exactly is being done at the identified centers offering personalized genomic medicine

5. Environment:

Strengths

- The environment is excellent as the project will be based within the Center for Genetic Research, Ethics and Law at Case Western Reserve which is also part of the consortium of Centers of Excellence in ELSI Research.

Weaknesses

- None noted

Protections for Human Subjects:

Data and Safety Monitoring Plan (Applicable for Clinical Trials Only):

Inclusion of Women, Minorities and Children:

G1A - Both Genders, Acceptable

M1A - Minority and Non-minority, Acceptable

C3A - No Children Included, Acceptable

- Investigators have revised this section is response to reviewers comments.

Budget and Period of Support:

Recommend as Requested

THE FOLLOWING RESUME SECTIONS WERE PREPARED BY THE SCIENTIFIC REVIEW OFFICER TO SUMMARIZE THE OUTCOME OF DISCUSSIONS OF THE REVIEW COMMITTEE ON THE FOLLOWING ISSUES:

PROTECTION OF HUMAN SUBJECTS (Resume): ACCEPTABLE

INCLUSION OF WOMEN PLAN (Resume): ACCEPTABLE

INCLUSION OF MINORITIES PLAN (Resume): ACCEPTABLE

INCLUSION OF CHILDREN PLAN (Resume): ACCEPTABLE

COMMITTEE BUDGET RECOMMENDATIONS: The budget was recommended as requested.

Ad hoc or special section application percentiled against "Total CSR" base.

NOTICE: In 2008 NIH modified its policy regarding the receipt of resubmission (formerly termed amended) applications. Detailed information can be found by accessing the following URL address: http://grants.nih.gov/grants/policy/amendedapps.htm