Ethical, Legal and Social Implications (ELSI) Research Advisors Report to the National Advisory Council for Human Genome Research February 2005

Introduction

The ELSI Research Advisors (ERA) group was established in the Fall of 2000 to provide the National Advisory Council for Human Genome Research (NACHGR) with advice concerning the ELSI Research Program. As part of its mission, ERA is required periodically to report to the NACHGR on the status of the ELSI Program. The group participated in the planning process for the development of the AVision for the Future of Genomic Research@ article (Vision Document) that was published in *Nature* in April 2003[1] and has been involved in helping the ELSI Program shape new initiatives in response to the future directions for ELSI research that were presented in the document. This report briefly summarizes the ELSI Program=s progress since the Vision Document was published, identifies some areas of concern regarding the future of ELSI research, and argues for the importance of ELSI research for all components of the National Institutes of Health (NIH) and the need to encourage other parts of NIH to become involved in supporting this research.

The ELSI Program since the Completion of the Human Sequence

In the Vision Document, ELSI research issues are integrated throughout the **Grand Challenges** (GC) laid out for each of the three floors of genomic research: **Genomes to Biology, Genomes to Health and Genomes to Society**. They are specifically included in **Genomes to Biology** under GC I-5 regarding intellectual property issues. In **Genomes to Health**, ELSI issues feature prominently in GC II-4 on the provision of risk information in clinical settings and GC II-5 which focuses on ensuring that the benefits of the genomic revolution are made available to all. The third floor, **Genomes to Society**, focuses almost exclusively on issues that are addressed by the ELSI Program, including the development of policy options to ensure the safe use of genetic information and technologies (GC III-1), the exploration of the issues surrounding genetics and race and ethnicity (GC III-2), the genetics of Anormal@ traits and behaviors (GC III-3), and the ethical boundaries of genetic and genomic research (GC III-4). Following the publication of the Vision Document, the ELSI Program revised its regular (R01) and small (R03) research grant program announcements to incorporate these new grand challenges. These new announcements were released in January 2004.

In the last few years, the ELSI Program has supported a number of research initiatives in each of these areas. Within the **Genomes to Biology** floor, in 2002 and 2003, ELSI funded a pilot survey by the Kennedy Institute of Ethics and the Association of University Technology Managers (AUTM) to gather information on the licensing practices and policies of universities across North America. These data have been used as a foundation for the deliberations of the Institute of Medicine=s committee on AIntellectual Property Rights in Genomics and Protein-Related Research.@ In addition, in 2004, the ELSI Program issued a new Request for Applications (RFA) to study the role of laws and policies regarding intellectual property rights in genetics and

genomics research and development, and the effect of such laws and policies on progress in these fields and on commercialization, drug development, health care delivery, and the public health. These applications will be reviewed and funded in Fiscal Year (FY) 2005.

Within the **Genomes to Health** area, the ELSI Program has continued to fund a number of research projects focused on the safe and effective use of genetic technologies and risk information in clinical settings (GC II-4). These have included:

- an ongoing study at Boston University (PI: RC Green) examining genetic risk assessment and counseling for Alzheimer disease[2] and
- a new study at the Fred Hutchinson Cancer Research Center (S Ramsey) to develop a framework for evaluating the clinical and economic tradeoffs associated with genetic testing for colon cancer.

The ELSI Program has also funded a number of studies examining disparities in access to and use of genetic test information (GC II-5), including:

- an ongoing University of Pennsylvania study (K Armstrong) examining the impact of an individual=s level of distrust and the attributes of a genetic test and its delivery on willingness to undergo predictive genetic testing among African American, Latino and Caucasian populations[3] and
- a new study at the University of North Carolina (G Corbie-Smith) exploring the attitudes of African Americans and Caucasians regarding genetic research and colon cancer risk.

Within the **Genomes to Society** floor, the ELSI Program has funded a number of studies developing data upon which research and social policies can be based (GC III-1), including:

- an ongoing study at the University of North Carolina (G Henderson) examining the social construction and communication of benefit in gene transfer research,[4]
- a study (co-funded with NIEHS) at Arizona State University (G Marchant) to evaluate the legal, ethical and policy implications of the application of genetic susceptibility data to environmental regulation, and
- a new study by the American Society for Law, Medicine and Ethics (B Moulton) to investigate the issues surrounding DNA profiling and to educate policymakers so that they better understand privacy and civil liberty issues involved in the application of DNA technology to the criminal justice system.

The ELSI Program has funded 11 studies as the result of two ELSI genetic variation RFAs[5] and is currently supporting a consortium of 21 researchers who are looking at the issues surrounding genetic and genomic research and race and ethnicity (GC III-2). These include:

- ongoing studies such as the project at the University of Georgia (C Condit) exploring the feasibility of producing messages about human genetic variation that are non-discriminatory in their impact on public attitudes[6] and
- new studies such as the University of Pennsylvania project (P Sankar) examining why researchers use race and ethnicity in forensic and medical genetic research, and what

researchers think are appropriate generalizations and applications of their findings.

The ELSI Program has funded a small number of projects examining the issues surrounding the genetics of traits and behaviors (GC III-3), including:

- a study by the Hastings Center (E Parens) to develop tools and resources for open and informed public discussion about behavioral genetics[7] and
- a study by the University of Michigan (E Singer) exploring and analyzing public beliefs about genes and the environment as causes of behavior.[8]

In the final **Genomes to Society** Grand Challenge that explores the potential ethical boundaries of genetic and genomic research (III-4), the ELSI Program has funded a substantial body of work by a team at Case Western (E Juengst) examining the issues surrounding genetic enhancement[9] and a series of small research grants at the University of Maryland (M Sagoff) analyzing the potential impact of genetic and genomic technologies on concepts of humanity.[10]

In addition to the Grand Challenges, the ELSI Program is currently funding projects in four cross cutting areas: Education, Conferences, Training and Resources. The largest portion of this cross cut funding is currently devoted to Education projects, including:

- an ongoing project at Dartmouth University and Howard University (RM Green) to prepare college and university faculty to develop and teach courses on ELSI and
- a new project by SoundVision Inc. (B Scott) supporting the development of radio broadcasts on genetics and ELSI issues specifically targeted to minority populations.

However, in order to allow the ELSI Program to focus more attention on funding research grants, at the recommendation of its advisors the NHGRI has not reissued its education grant (R25) program announcement. The Program will continue to fund education grants that are currently obligated, but will gradually phase out that portion of the portfolio. The ELSI Program will continue to fund conference grants, training grants and a small number of resource grants.

Table 1 lists estimated budget totals for FY 2004 in each Grand Challenge and Crosscut area.

Table 1. FY 2004 Estimated ELSI Totals by Grand Challenge

Grand Challenge	**FY 2004 Total**
I-5. Intellectual property	$699,113
II-4. Genetic Risk Information in Health Care	$7,551,419
II-5. The Health of All	$1,173,074
III-1. Policy Options for the Use of Genetic Information	$2,898,860
III-2. Genetics, Race and Ethnicity	$1,786,814
III-3. Genetics and Normal Traits/Behaviors	$489,985
III-4. Boundaries of Genetic Research	$74,250
Crosscut	
Crosscut 1: Education	$2,958,820
Crosscut 2: Conferences	$139,666
Crosscut 3: Training	$200,000
Crosscut 4: Resources	$527,077

FY 2004 ELSI Total	$18,499,078

Persistent Challenges Faced by the ELSI Research Program

The ELSI Program has been the subject of many critical assessments since its inception. These have ranged from focused analyses by science policy or ethics scholars to more in-depth, formal evaluations by panels of experts and advisors.[11,12, 13,14] The most recent evaluation was completed in 2000 by the ELSI Research Planning and Evaluation Group (ERPEG). This group issued a report in January 2001 which included a series of recommendations to strengthen the Program.[14] More recently as part of the April 2003 planning process, the ELSI Research Advisors, working with an ad hoc policy group, published a brief white paper examining the "Role of ELSI Research in the Future of Genomics Research."[15] This paper was used in the development of the Vision Document and provided the ELSI Program with specific recommendations to enhance ELSI research following the completion of the sequence.

Several recurrent concerns have been raised in each of these reports about the ability of the ELSI Program to fulfill its mission to anticipate and address the implications of genetic and genomic research. These include:

- The need for increased integration between ELSI and genetic and genomic research,
- The need for the more effective translation of ELSI research findings to accessible products that can inform policy deliberations, and
- The need to support the continued expansion of the disciplinary and demographic diversity of the ELSI community of researchers.

The first concern is an acknowledgement of the fact that in order for ELSI research to be relevant, it must be grounded in cutting edge genetic and genomic research, and in order for this to occur, there must be close communication and collaboration between the two research communities. While there has been a general strengthening of the communication between genetic and genomic and ELSI researchers over the years, there has not been the kind of sustained collaboration that is needed to ensure the ongoing timeliness and relevance of ELSI research. This may be due in part to a conflict inherent in the establishment of the ELSI Program within the larger Human Genome Project. On the one hand, ELSI researchers have questioned whether the ELSI Program can maintain its ability to critically analyze the implications of genetic and genomic research when its funding is overseen by the same individuals who are responsible for the successful implementation of this research. On the other hand, genetic and genomic researchers often conflate the scholarly examinations of the implications of genetic and genomic research funded by the ELSI Program with the development and enforcement of human subjects research regulations which are actually developed and overseen by regulatory bodies like the Federal Office for Human Research Protections (OHRP). Thus, some ELSI researchers tend to be uneasy about the potential for the genetic and genomic research community to unduly constrain ELSI research and some genetic and genomic researchers tend to view ELSI as trying to slow down the research enterprise with unnecessary ethical hurdles and regulations. This somewhat natural, if misdirected, antipathy, coupled with a lack of systemic recognition and support for this kind of cross-disciplinary research within the academic and Federal research funding communities, has made collaborations between these researchers somewhat tenuous and

difficult to sustain.

The second concern goes to the fundamental fact that the ELSI Program is capable of producing a great deal of informative and relevant data, but that these data may not be presented in a form that is accessible to research, health and social policy makers. As a result, it is difficult to assure that ELSI findings are considered in the development of policies that address the implications of genetic and genomic research. While the ELSI Program has funded projects and convened meetings that have resulted in the development of policy options and standard of care recommendations,[a] and ELSI publications have been cited in the development of policies and legislation, as an extramural research program housed within the Federal Government, ELSI is statutorily Anot capable of developing or presenting in an effective manner specific policy recommendations to the Nation, the Congress, or the executive branch on the full range of problems presented by the Human Genome Project.@[16]

Over the years, the task of developing and presenting these recommendations has fallen to a variety of organizations, including the original ELSI Working Group (1990-1996), the ongoing Trans-NIH Bioethics Committee, the Secretary=s Advisory Committee on Genetic Testing (SACGT) and its successor the current Secretary=s Advisory Committee on Genetics, Health and Society (SACGHS) and the National Bioethics Advisory Committee and its successor the Presidents Bioethics Commission. While these groups have made use of ELSI research data in the development of policies and standards of care, none of them have been conversant enough with the totality of ELSI research to effectively and consistently translate the findings from this research to the various policy making communities, and, of equal importance, provide feedback to ELSI researchers regarding the data needs of these communities.

The final concern speaks to the need for the ELSI research community to continue to expand its range of expertise in order to maintain its ability to respond effectively to rapidly emerging scientific advances and concomitant policy needs. This requires not only the continual recruitment of individuals from different disciplines and demographic backgrounds into ELSI research, but an ongoing effort to train the next generation of researchers. The ELSI Program has been very successful in establishing a new field of research and a research community with great strength and depth of expertise, as indicated by the increasing number of competitive continuations of ongoing grants (several of which are cited above) and the frequent recruitment of ELSI researchers to provide expert testimony or to serve on advisory groups. However, it has not been as successful in supporting the recruitment and training of new investigators from disciplines and communities not currently well represented in the ELSI research community. While many factors may be contributing to this, one of the most obvious is the small number of

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[a]A notable product of one of these translational activities is the series of articles published in JAMA in 1997 by the Cancer Genetic Studies Consortium laying out recommendations for informed consent and follow-up care of individuals with genetic predispositions to breast, ovarian and colon cancers. To date, these publications have been cited more than 750 times in the scientific literature.

well-established research programs focused on ELSI research that can provide the incentives for multi-disciplinary work and the infrastructure to support the cross disciplinary training of new investigators.

The ELSI Centers Program

In response to these concerns and on the recommendations of its advisors, the ELSI Program issued a call for applications for the development of Centers of Excellence in ELSI Research (CEERs). The purpose of these CEERs is to encourage the development of broadly multidisciplinary research teams that can not only rapidly identify and respond to emerging issues, but also use the full spectrum of research and consensus building methodologies to translate the findings of ELSI research to useful policy and practice options. The three overarching goals of the program are to:

- Transcend the boundaries between genetic and genomic research and ELSI research;
- Translate ELSI research to safe, effective and just genetic and genomic policies and practices in research, health and non-medical settings; and
- Train the next generation of ELSI researchers to ensure disciplinary and demographic diversity.

In September 2004, four full centers and three exploratory centers were funded. The first meeting of the researchers was held in February 2005. All of the funded CEER grants address issues highlighted in the Vision Document.

- The Duke center (B Cook-Deegan) proposes to explore the impact of publication, data and materials-sharing, patenting, database protection, and other practices that affect information flow in genomics research.
- The University of Washington center (W Burke) focuses on the clinical integration of genetic technologies and information for medically underserved communities, taking into consideration diverse voices that have often not been previously heard.
- The Case Western center (E Juengst) proposes to address issues related to genomics and genetics research, including commercialization, race and ethnicity, normal traits, and genetic enhancement.
- The Stanford center (M Cho) focuses on developing models for integrating ELSI concerns into neuro- and behavioral genetics research.
- The University of North Carolina exploratory center (D Bailey) focuses on the issues around the design and conduct of large sample gene discovery and disclosure studies.
- The Georgetown exploratory center (A Shields) is focused on health disparities.
- The Howard exploratory center (C. Royal) will explore the genomic and social identity issues surrounding the African Diaspora.

A CEERs Advisory Group (CAG) is being established to provide expert input on the individual Centers and on the CEERs program as a whole. For individual CEER evaluations, a site visit will take place in the third year to determine whether the Center is successfully meeting its individual goals and should continue to receive full funding and be invited to submit a competitive renewal; or is not meeting its goals and should begin to be phased out in its fourth

year. For the CEERs program evaluation, the CAG will participate in determining whether the program as a whole is successfully accomplishing the three broad goals outlined above.

Program Evaluation

Just as the evaluation of the individual CEERs and the overall CEERs program is crucial, it will be important for the ELSI Program to continue to evaluate its effectiveness in anticipating and addressing the implications of genetic and genomic research more broadly. It will be essential that the Program initiate a vigorous discussion of how to define endpoints and metrics for measuring successful ELSI research. For example, what are the relative merits of using the citation of ELSI publications in peer reviewed literature, in state and federal legislation, and in the development of standard of care guidelines as measures of success? The three broad goals set out for the CEERs program can be used as a starting point for this discussion, but ultimately they will need to be expanded and refined to more fully encompass the depth and breadth of ELSI activities. In addition to determining endpoints, the evaluation should focus on three levels of analysis: 1) the Project Level to determine whether individual projects are meeting their specific aims; 2) the Program Level to determine whether the ELSI Program as a whole is meeting its goals; and 3) Program Balance to determine the combination of study topics, funding mechanisms and types of projects that are most effective in accomplishing the program=s mission. This last level of evaluation will be particularly critical if the CEERs program moves forward as currently envisioned, consuming an increasing percentage of the ELSI budget set aside. Table 2 provides a projection of the percentage of the ELSI budget that will be devoted to the CEERs program through FY 2009.

Table 2. CEER OUTYEAR TOTAL BUDGET PROJECTIONS

Center PI		FY2004	FY 2005	FY 2006	FY 2007	FY 2008	*FY 2009*[1]
BAILEY	**P20**	$214,634	$214,503	$0	$0	$0	*$0*
SHIELDS	**P20**	$187,799	$187,763	$193,396	$0	$0	*$0*
ROYAL	**P20**	$220,091	$225,173	$231,926	$0	$0	*$0*
JUENGST	**P50**	$905,664	$1,040,969	$1,075,892	$1,131,308	$1,153,867	*$1,188,483*
BURKE	**P50**	$911,748	$900,847	$911,568	$938,767	$981,672	*$1,011,122*
CHO	**P50**	$689,985	$803,537	$827,201	$852,013	$781,129	*$804,563*
COOKDEEGAN	**P50**	$949,113	$975,766	$1,004,188	$1,034,917	$1,066,023	*$1,098,004*
TOTAL [2]		$4,079,034	$4,348,558	$4,244,171	$3,957,005	$3,982,691	*$4,102,172*
ELSI Total		**$3,454,034**	**$3,723,558**	**$4,194,171**	**$3,907,005**	**$3,932,691**	***$4,052,172***
Reissue @ $3M in 06 and 08				*$3,000,000*	*$3,090,000*	*$6,182,700*	*$6,368,181*
ELSI Set Aside [3]		**18,499,078**	**18,559,200**	$18,930,384	$19,308,992	**$19,695,172**	***$20,089,075***
% of ELSI Total [4,5]		**18.7%**	**20.1%**	**38.0%**	**36.2%**	**51.4%**	***51.9%***

[1] FY 2009 Estimate assumes competitive renewals of existing P50s are successful.

[2] Budget Figures reflect TOTAL Center budgets (i.e., ELSI budget contributions plus co-funding from DOE and NICHD)

[3] Based on projected 2% annual increase from FY 2005 base.

[4] Percentages are based only on NHGRI ELSI contributions and do not include additional co-funding from DOE and NICHD

[5] The jump in % of ELSI Total in FY 2006 is due to the fact that DOE was unable to commit co-funding to Cho and CookDeegan Beyond FY 2005, but may continue contributions, if funds are available.

Concerns for the Future of ELSI Research

With the long term commitment of funds to the new CEER grants, the current climate of no-growth federal budgets, and the continuing inflation of grant budgets across NIH, the ELSI Program has entered a new era of budget constraints. As in many agencies, the shortage of funds is already having an impact on the amount of the budget that can be spent on new investigator initiated research grants (less than 14.5% of the ELSI budget in 2005). Table 3 provides a brief summary of the downward trend since 2000 and the noticeable drop off over the last year. While this drop in funding for investigator initiated research is of concern, it is a not unexpected trade off caused in part by the creation of the CEERs program. Of perhaps greater concern is the impact that shrinking budgets will have on the ability of the ELSI Program to expand the diversity of its research portfolio and on its ability to provide support for new investigators from under represented groups and from disciplines in the law and humanities, who traditionally do not fare well in the NIH peer review system.

TABLE 3. Percent New and Total ELSI Expenditures by Research Mechanism FY 2000- 2005

FISCAL YEAR	FY 2000		FY 2001		FY 2002		FY 2003		FY 2004		FY 2005 Est.
TOTAL ELSI	$13,269,458		$15,006,647		$16,767,016		$18,023,110		$18,499,078		18,559,200
Percent Increase	20.32%		11.68%		10.53%		6.07%		2.57%		0.33%
	New	Total	New	Total	New	Total	New	Total	New	Total	Total Commit.
Centers (p20/50)		0	0	0	0	0	0	0	18.67%	18.67%	20.06%
Regular (R01)	25.01%	70.31%	19.26%	62.98%	13.38%	47.08%	32.99%	58.58%	6.75%	49.90%	47.83%
Small (R03)	0	0	0.48%	0.48%	2.84%	3.27%	2.39%	4.61%	0.40%	2.36%	2.57%
Education (R25)	9.69%	12.26%	7.82%	12.58%	7.20%	17.34%	8.94%	14.75%	1.01%	13.92%	11.58%
Resources (P41)	3.17%	3.17%	0	3.02%	5.96%	8.47%	0	2.40%	0	2.41%	0
Other (IAAs, Mtgs., Training, etc.)	14.04%	14.26%	10.08%	20.94%	11.26%	23.85%	6.47%	19.66%	0.49%	12.73%	3.47%
Percent Total	51.91%	100%	37.65%	100%	40.65%	100%	50.79%	100%	27.32%	100%	85.51%

ELSI Research as an NIH-wide Priority

Given these concerns and the low likelihood that additional funds will be made available to NHGRI in the near future, the base for funding of ELSI research must be expanded more broadly across the NIH. As a part of the HGP, the ELSI Program=s mission has focused specifically on the implications of genetic and genomic research, but the basic ethical, legal and social issues raised by the HGP apply much more broadly to all rapidly evolving biomedical technologies and research fields, such as nanomedicine, anti-aging medicine and xeno-transplantation, as well as

traditional biomedical and behavioral research involving racially and ethnically identified populations, children, the cognitively impaired and research focused on normal traits and behaviors like aging, intelligence and aggression.

Ten NIH Institutes signed on to the ELSI program announcements in 2004, and several also participated in the 1999 and 2003 ELSI Genetic Variation RFAs and research consortia, and the 1994 Cancer Genetic Studies and 1991 CF Genetic Studies RFAs and research consortia. While this record of participation by individual institutes indicates an underlying level of interest in ELSI research, it does not represent a strong institutional commitment by the NIH. For example, since 1999 the NIH has supported three NIH-wide program announcements calling for research (R01), training (T15) and career development (K01) applications that address the ethical issues surrounding research involving human participants. These announcements were part of the Federal initiative developed as part of the President=s 1997 apology for the U.S. Government=s support for the Tuskegee experiments and were intended to emphasize NIH support for ethics training and research. While these NIH-wide program announcements have resulted in a number of productive grants, the T15 and K01 announcements, which have already expired, have not been reissued, and the R01 announcement, which was due to expire in May 2005, was only recently extended for a single year while a decision is made whether it should be continued.

Recently, the NIH has launched two new trans-NIH initiatives: The Roadmap and the Public Trust Initiative. While ethics research is not currently incorporated into either initiative, the implementation of these initiatives may create a unique opportunity for the NHGRI and the NACHGR to encourage other institutes, and NIH as a whole, to make a more sustained NIH-wide commitment to supporting this type of research.

The Roadmap was launched in 2004 as a series of NIH-wide initiatives designed to Atransform our new scientific knowledge into tangible benefits for people.@ It focuses on three themes.

- The 1st themeBNew Pathways to DiscoveryBis designed in part to Afully capitalize on the recent completion of the human genome sequence and many recent discoveries in molecular and cell biology@ by ensuring Awide access to technologies, databases and other scientific resources that are more sensitive, more robust, and more easily adaptable to researchers' individual needs.@
- The 2nd themeBResearch Teams for the FutureBencourages the promotion of interdisciplinary research teams and new approaches to team-based research.
- The 3rd ThemeBRe-engineering the Clinical Research EnterpriseBpromotes the harmonization of clinical research regulatory processes and the development of enhanced infrastructures and more efficient mechanisms to translate basic research findings to clinical research settings. AA major goal of this initiative is to more fully involve and empower the public in the research process.@ [17]

Recognizing the importance of the public=s role in ensuring the success of biomedical research, after the initiation of the Roadmap the NIH Director established the NIH Public Trust Initiative (PTI) as an important adjunct to the Roadmap. The mission of the PTI is Ato promote activities and attitudes that foster understanding of, and build confidence in, the biomedical and behavioral health research that the NIH conducts and supports across the nation and throughout the world.@

"Specifically, the PTI seeks to:

- Increase the public=s understanding of how the NIH conducts and supports research;
- Enhance public involvement in the NIH research related activities;
- Enhance public access to, and understanding of, outcomes of research;
- Increase public involvement and participation in clinical research; and
- Strengthen interactions with the public regarding priority setting and stewardship of research for the public=s health."[18]

Ironically, despite the heavy emphasis placed on translating scientific knowledge to health care benefits in the Roadmap and on enhancing public trust in the PTI, neither program contains specific research initiatives designed to address how new discoveries will evolve from these enhanced research settings into the development of new health policies and practices, or to better understand the perspectives and concerns of the general public. An NIH-wide ELSI research program, focused on ensuring the safe and effective integration of new technologies into clinical settings and on examining public attitudes towards research technologies and information, would help to fill these gaps.

Just as ELSI research contributes to all levels of genomic research, it also can contribute to all aspects of the NIH Roadmap. Within the first theme, New Pathways to Discovery, ELSI work on intellectual property may help maximize public and private benefit by allowing for a more effective sharing of information among researchers and between the research community and the pharmaceutical industry. For the second theme, Research Teams for the Future, ELSI research not only can provide data on the interactions among cross disciplinary research teams, but also can provide a model for the value of inter- and multi-disciplinary studies that span not only biological and clinical research, but also include the social sciences, law and humanities. While other ICs encourage the integration of biological and clinical studies, and some social sciences studies, NHGRI=s ELSI Program is the only standing program that regularly includes researchers from law and the humanities. This research, which explores the impact of new biomedical discoveries on the human condition, is crucial to understanding and addressing issues involving the general public=s understanding and support for research, one of the major goals of the third theme, Re-engineering the Clinical Research Enterprise. Additionally, by supporting qualitative and quantitative social sciences research into individual and societal views of research and on the development and impact of regulations, guidelines and policies, the ELSI Program can help to provide data that can be used to harmonize research regulations and facilitate the translation of basic research findings to clinical research settings and ultimately to health care practice.

The online description of the Public Trust Initiative states that the initiative rests on two "Basic Assumptions:

- Gaining and enhancing public trust is a top priority for the NIH.
- Enhancing public trust requires a long-term commitment.@[18]

The ELSI Program, with its Congressionally mandated 5% set aside of the HGP budget, was created as a long-term commitment by NIH to anticipate and address both individual and societal concerns about advances in genetic and genomic research. Most, if not all, of the ELSI studies

included within the Vision Document=s Grand Challenges are focused on gaining a better understanding of the public=s attitudes toward and use of new genetic and genomic information and technologies. For example, in addition to the studies already highlighted, the ELSI Program has funded an historical analysis of the concerns of Evangelical Christians about genetic interventions,[19] a study of the beliefs and attitudes of individuals of Hispanic descent regarding hereditary prostate cancer[20] and a new qualitative study of the impact of prophylactic mastectomy on the lives of women with BRCA mutations. While it is difficult to quantify the impact of studies like these and the many other similar studies funded by ELSI, the very existence of a federally funded program that takes the concerns of the public seriously enough to invest funds to explore and address these concerns can reasonably be expected to increase public involvement in and trust for biomedical research.

Conclusions

Since the completion of the first human sequence in April 2003, the ELSI Program has revised its program announcements and funding priorities to address the Grand Challenges identified in the Vision Document, and has already funded a substantial body of research in many of these areas. It has also released a targeted RFA on intellectual property issuesBone of the areas identified in the Vision Document as needing immediate attention. In addition, in response to persistent structural concerns about the ELSI research enterprise, the Program has established a Centers of Excellence in ELSI Research (CEERs) initiative that will enable sustained multi-disciplinary research and training, and enable the translation of ELSI research findings to products that can be used by the research, health and social policy communities.

In short, the ELSI Program is well positioned to move forward into the future of genetic and genomic research. Unfortunately, like much of the biomedical research community, the ELSI Program is faced with a shrinking budget just as it is launching a number of new initiatives. In order for the ELSI Program to fully support these initiatives, it will be essential to expand the base of support for ELSI research to include all of NIH. The decision not to reissue the NIH-wide K01 and T15 ethics announcements and the pending decision about the R01 announcement coupled with the launching of the new Trans-NIH Roadmap and Public Trust Initiatives create an opportunity to make the case to the rest of NIH for this expansion, since ELSI research can provide much needed support to both initiatives. For the Roadmap, ELSI research, through its clinical and social sciences research studies, can help to facilitate the translation of new discoveries from the bench to the bedside. With the Public Trust Initiative, ELSI research can provide conceptual clarity and a strong foundation of research data to help shape successful interventions to improve the public=s confidence in biomedical research.

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Henderson GE, Davis AM, King NMP et al. AUncertain Benefit: Investigators' Views and Communications in Early Phase Gene Transfer Trials.@ *Molecular Therapy* 2004.

5. **Genetic Variation Consortium Publications**. More than 30 individually authored peer reviewed publications or books have resulted from these two RFAs and one jointly authored publication. A selection of these publications follows.

Sankar P, Cho MK, Condit CM, Hunt LM, Koenig B, Marshall P, Lee SS, Spicer P. AGenetic Research and Health Disparities@ *JAMA*. 2004;291:2985-2989

Elliott C, Brodwin P. "Identity and genetic ancestry tracing." *BMJ* December 2002; 21-28(325): 1469-71.

Foster MW, Sharp RR. "Beyond race: towards a whole-genome perspective on human populations and genetic variation" *Nature Reviews Genetics*. October 2004;Vol. 5:790-796

Lee SS. "Race, Distributive Justice and the Promise of Pharmacogenomics: Ethical Considerations," *Amer. Jour. of PharmacoGenomics. 2003;* 3(6): 385-392.

Rothstein MA (ed.) *Pharmacogenomics: Social, Ethical, and Clinical Dimensions*. Wiley-Liss; (January 2003) 368p.

Sankar P, Cho MK. "Toward a new vocabulary of human genetic variation." *Science.* November 2002; 298(15): 1337-1338.

6. **CONDIT, Celeste M. "Race and Public Communication About Human Variation"** This grant has produced 6 publications to date, including:

Condit C. "What is 'public opinion' about genetics." Nat Rev Genet October 2001; 2(10): 811-815.

Condit CM, Parrott R, Harris TM "Lay understandings of the relationship between race and genetics: Development of a collectivized knowledge through shared discourse." Public Underst Sci. 11(4): 373-387 October 2002.

Condit C, Templeton A, Bates B, Bevan JL, Harris TM "Attitudinal barriers to delivery of race-targeted pharmacogenomics among informed lay persons." (385-392) and Bevan JL, Lynch JA, Dubriwny TN et al. "Informed lay preferences for delivery of racially varied pharmacogenomics." *Genetics in Medicine*. September/October 2003; 5(5): 393-399.

7. **PARENS, Erik. "Tools for Public Conversation about Behavioral Genetics"**

Parens E. "Genetic Differences and Human Identities: On Why Talking about Behavioral Genetics Is Important and Difficult." *Hastings Center Report*. Special Supplement. January-February 2004: S1-S34.

8. **SINGER, Eleanor. Beliefs about Genes & Environment as Causes of Behavior.**

Singer E. et al. ARacial and Ethnic Variations in Knowledge and Attitudes about Genetic Testing,@ *Genetic Test.* 2004 Spring; 8(1): 31-43.

9. **JUENGST, Eric T. "Anticipating Enhancement: Ethical, Legal and Social Issues"** This grant and its two competitive continuations have produced 14 publications to date. A brief selection follows.

Juengst ET. "Can Prevention be Distinguished from Enhancement in Genetic Medicine?" *Journal of Medicine and Philosophy*. 1997; 22: 125-142.

Mehlman MJ. "How Will We Regulate Genetic Enhancement?" *Wake Forest Law Review*. Fall 1999; 34(3): 671-714.

Juengst ET, Binstock RH, Mehlman MJ et al. "Aging - Antiaging research and the need for public dialogue." *Science*, 299(5611): 1323-1323 February 28, 2003.

10. **SAGOFF, Mark. Concepts of Nature, Biotechnology, and the Human Genome.** This grant has produced 10 publications to date. A selection of these publications follows.

Sagoff M. AIntellectual Property and Products of Nature,@ *American Journal of Bioethics*. 2002; 2(3): 12-13.

Wasserman D. ASpecies and Races, Chimeras and Multiracial People.@ *American Journal of Bioethics*. 2003; 3(3).

Wasserman D. AThis Old House: The Human Genome and Human Body as Objects of Historic Preservation.@ *Politics and the Life Sciences*. March 2003; 22(1); 43-47.

11. Hanna KE. AThe Ethical, Legal, and Social Implications Program of the National Center for Human Genome Research: A Missed Opportunity?@ in *Society=s Choices: Social and Ethical Decision Making in Biomedicine*. RE Bulger, EM Bobby and HV Fineberg eds. Washington DC, National Academy Press, 1995. P.432-457.

12. Juengst ET (1996) Self-Critical Federal Science? The Ethics Experiment within the U.S. Human Genome Project. *Social Philosophy & Policy* 13(2): 63-95.

13. Spence A and M Rothstein. "Report Of The Joint NIH/DOE Committee To Evaluate the Ethical, Legal, and Social Implications Program of the Human Genome Project." December 1996.

14. ELSI Research Planning and Evaluation Group (2000) *A Review and Analysis of the Ethical, Legal, and Social Implications (ELSI) Research Programs at the National Institutes of Health and the Department of Energy.* NIH Publication No. 00-4867.

15. ELSI Research Advisors and ELSI Policy and Planning Group. *The Role of ELSI Research and Policy Activities in the NHGRI Plan.* *http://www.genome.gov/page.cfm?pageID=10005516*

16. U.S. House of Representatives Committee on Government Operations. "Designing Information Policy: The Need for an Independent Policy Review of the Ethical Legal, and Social Implications of the Human Genome Project." House Report 102-478, April 2, 1992, p.4.

17. NIH Roadmap Overview. http://nihroadmap.nih.gov/overview.asp

18. NIH Public Trust Initiative Mission Statement. http://publictrust.nih.gov/mission.cfm

19. **DAVIS, John J. AConcerns of Evangelicals about Genetic Interventions"**
Davis JJ "Ethical Concerns of American Evangelicals Relative to Genetic Interventions." *Ethics and Medicine* (Accepted for publication).

20. **ARAR, Nedal H. "Cultural and Ethical Issues in Genetic Family Studies"**
Arar NH, Plaetke R, Arar MY. et al. "Incorporating the Contextual Assessment Approach to regimens used in genetic family studies." *Genetics in Medicine*. November/December 2002: 4(6): 451-463.

Arar NH, Hazuda HP, Plaetke R. et al. "Familial Clustering of Diabetic Nephropathy: Perceptions and Risk Recognition Among Mexican-American Patients With a Family History of Diabetes." *Diabetes Spectrum*. 2003: 16(3): 136-142.