Analysis of NIH's FOA's to Stimulate Research on Human Subject Research (HSR) Ethics (ESA Reference Number 09-1014)

Introduction:

The National Institute of Health's (NIH) Office of Extramural Research (OER) has the important role of providing oversight, tools and policy guidance needed to administer and manage the extramural research projects that NIH supports, including ensuring the compliance of grantees with Federal regulations regarding the protection of human subjects in NIH-sponsored research. Recent developments in biomedical and behavioral research challenge the appropriate interpretation and application of human subjects protections policies and regulations, including the rapid growth of new interventions and technologies, increasing involvement of international populations in human subjects research, and concerns about financial conflicts of interest among researchers. To that end, OER has led an effort to stimulate extramural research programs aimed at studying ethical issues in the conduct of research involving human subjects (HSR). A series of 6 Funding Opportunity Announcements (FOAs) specifically designed to attract research projects studying HSR ethics was made available to the NIH extramural community between 1997 and 2007. Table 1 below lists the applications received under these HSR Ethics FOAs and the award made from these application pools.

Table 1: Applications Received Under HSR Ethics FOAs and the Awards Made From These Application Pools

Funding Opportunity	Title	Applications[1]	Awards
RFA OD97-001	Informed Consent in Research Involving Human Participants	82	17
PA99-079	Research on Ethical Issues in Human Studies	47	16
PA02-103	Research on Ethical Issues in Human Studies	75	19
PA06-367	Research On Ethical Issues In Human Subjects Research (R03)	17	6
PA06-368	Research On Ethical Issues In Human Subjects Research (R21)	33	14
PA06-369	Research On Ethical Issues In Human Subjects Research (R01)	5	1
PA07-277	Research On Ethical Issues In Human Subjects Research (R01)	23	5
Total		**282**	**78**

Data Source and Methodology:

The primary data source for information about these HSR applications and projects was the Information for Management Planning, Analysis, and Coordination II (IMPAC II) database. To identify the universe of applications received in response to these funding opportunities, the Request for Application (RFA) / Program Announcement (PA) numbers listed above were used as a starting point to collect application records by year that were associated with each RFA/PA. These applications were then used to find all other applications that had a similar triplet of information that included the Activity Code (e.g. R01), the funding Institute or Center (e.g. HG) and six digit Serial Number issued by the Institute/Center. This method allowed for the identification of additional applications for which records in IMPACII were missing the RFA/PA number value or had incorrect RFA/PA number values.

This same triplet of information was used to roll up all original and revised applications into one "project". Most applications received by the NIH for R01 applications are not funded on the first attempt, and therefore this analysis combines all applications submitted for a particular grant into one "project". Values for fields, such as the Sponsoring Organization were selected from the last application received (funded or unfunded).

[1] Applications represent unique projects and include the initial application and all subsequent revised applications.

It was decided to only include application records received in response to these RFP/PAs that were assigned Council Rounds prior to May 2009, thus allowing sufficient time for the application to be reviewed and the outcome of the review to be reflected appropriately in IMPACII.

For the analysis of New Investigators, it was necessary to derive a New Investigator Code that considered prior applications from the Principal Investigator (PI) identified on the HSR project. The existing New Investigator code in IMPACII is not sufficiently populated throughout the entire time period of this study. For the purposes of this analysis, if a PI had no prior significant NIH independent research award, he or she was considered a New Investigator[2].

When looking at the study sections to which HSR projects were assigned for review, it was necessary to develop two categories of review sections, 'standing' and 'special emphasis panel' or 'SEP'. These categories were derived from the Study Section Code in IMPACII; those applications with a study section code beginning with 'Z', or those with the code 'SPEPOD' were coded as 'SEP' and all other applications were coded as 'Standing'.

For the analysis of topics of applications, several sources of information were used to populate the abstract. If an approved abstract existed in the Abstracts_T table, then it was used. If not, the summary statement from the study section records was used. In addition, a small number of projects had abstracts in a historical section of Query View Report System (QVR) that were not otherwise available. For projects within the HSR ethics group, each abstract was read and the project assigned one Topic category and one Affected Group category. The definitions of the Topics and Affected Group are included in Appendix A. For projects within the Research Integrity and Ethical, Legal, and Social Implications (ELSI) groups, each abstract was read to determine if the application dealt with human subjects research ethics and if so, it was then categorized using the same Topics and Affected Group definitions.

For use in developing comparison groups, the Human Subjects Code value was used to define whether research involved human subjects and therefore was similar in research thrust to the HSR ethics projects. Previous anecdotal evidence suggests that research involving human subjects encounters distinct issues during review, therefore general human subjects research applications serve as an optimal comparison group for the HSR ethics projects in this analysis. Applications coded with a human subject code of 10 were defined as not involving human subjects; all other codes were considered human subjects research and eligible for inclusion in the comparison group.

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[2] This definition was based upon the current NIH definition of a New Investigator. http://grants.nih.gov/grants/new_investigators/#definition (accessed 12/31/2009)

Findings:

Impact of the selected FOAs on NIH's support for research in this area:

Table 2 below presents the total number of applications and awards for each for each of the HSR ethics FOAs by Fiscal Year (FY). In all tables where applications are listed by Fiscal Year, applications are counted in the year of the initial application. As seen in this table, the initial RFA OD97-001 resulted in about one third of the applications and one quarter of the awards for HSR ethics, PA99-079 and PA02-103 resulted in similar proportions, with the PA in 1999 having fewer applications and the three PAs issued in 2006 for the three activity codes resulted again in a similar number. PA07-277 was a reissuance of PA06-369 as these R01s were transitioned to electronic submission on Grants.gov, and therefore we will present data for these two PAs combined in the remaining tables.

Table 2: Applications and Awards by Fiscal Year and RFA/PA Number

FY	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total
OD 97-001 Applications	13	69												**82** 29%
OD97-001 Awards	13	4												**17** 22%
PA99-079 Applications		1	1	11	10	17	6	1						**47** 17%
PA99-079 Awards		1	1	5	2	5	2	0						**16** 21%
PA02-103 Applications						1	8	12	29	17	8			**75** 27%
PA02-103 Awards						1	2	4	4	7	1			**19** 24%
PA06-367 Applications											5	7	5	**17** 6%
PA06-367 Awards											2	3	1	**6** 8%
PA06-368 Applications											14	12	7	**33** 12%

FY	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	Total
PA06-368 Awards											6	8	0	14 18%
PA06-369 Applications											5			5 2%
PA06-369 Awards											1			1 1%
PA07-277 Applications												11	12	23 8%
PA07-277 Awards												4	1	5 6%
Total Applications	13 5%	70 25%	1 0%	11 4%	10 4%	18 6%	14 5%	13 5%	29 10%	17 6%	32 11%	30 11%	24 8%	282
Total Awards	13 16%	5 6%	1 1%	5 6%	2 3%	6 8%	4 5%	4 5%	4 5%	7 9%	10 13%	15 19%	2 3%	78

Table 3 shows the project funding rates by year for each FOA as well as the general R01 success rate for each year for human subjects research projects. Because this study combines revised/resubmitted applications into one project, the funding rates of the projects are generally higher than the published success rate calculation for applications.

Table 3: Project Funding Rates by Fiscal Year and RFA/PA Number

	OD97-001	PA99-079	PA02-103	PA06-367	PA06-368	PA06-369	PA07-277	Total
1997	100%							100%
1998	6%	100%						7%
1999		100%						100%
2000		45%						45%
2001		20%						20%
2002		29%	100%					33%
2003		33%	25%					29%
2004		0%	33%					31%
2005			14%					14%
2006			41%					41%
2007			13%	40%	43%	20%		31%
2008				43%	67%		36%	50%
2009				20%	0%		8%	8%
Total	21%	34%	25%	35%	42%	20%	22%	28%

As a control analysis, we collected application and award data for all research grants across the NIH that had human subject code values indicate human subject involvement. This comparison group was limited to new applications (type 1), R01, R03 and R21 activity codes, and were received within the same period of Council Rounds as the RFA/PAs studied. Table 4 shows the applications and awards by Fiscal Year and the Project Funding Rates for the comparison group of human subjects projects. Similar logic in combining revised/resubmitted applications into one project was used and the Fiscal Year presented is for the initial application.

Table 4: Applications and Awards, and Funding Rates by Fiscal Year for All Human Subjects

FY	Applications	Awards	Project Funding Rate
1998	5,871	1,979	34%
1999	6,831	2,271	33%
2000	7,293	2,366	32%
2001	7,807	2,573	33%
2002	8,529	2,789	33%
2003	9,718	2,837	29%
2004	11,447	3,028	26%
2005	11,567	2,791	24%
2006	10,803	2,484	23%
2007	10,017	2,449	24%
2008	9,527	2,280	24%
2009	8,944	1,400	16%
Total	108,354	29,247	27%

Overall, the project funding rate for the set of comparison group projects is 27% compared to 28% for the HSR Ethics projects. This difference is not significant at $p<0.05$. This suggests that the HSR Ethics projects have experienced similar funding rates when compared applications submitted across the NIH for human subjects during a similar time frame.

The following NIH Institutes and Centers (ICs) sponsored the Human Subject Research Ethics FOAs that are the subject of this study: Fogarty International Center (FIC), National Cancer Institute (NCI), National Center for Complementary and Alternative Medicine (NCCAM), National Heart, Lung, and Blood Institute (NHLBI), National Human Genome Research Institute (NHGRI), National Institute on Aging (NIA), National Institute on Alcohol Abuse and Alcoholism (NIAAA), National Institute of Allergy and Infectious Diseases (NIAID), National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institute of Child Health and Human Development (NICHD), National Institute on Deafness and Other Communication Disorders (NIDCD), National Institute of Diabetes and Kidney Diseases (NIDDK), National Institute of Drug Abuse (NIDA), National Institute of Environmental Health Sciences (NIEHS), National Institute of General Medical Sciences (NIGMS), National Institute of Mental Health (NIMH), National Institute of Neurological Disorders and Stroke (NINDS), National Institute of Nursing Research (NINR). Interestingly, we find that the National Center for Complementary and Alternative Medicine (NCCAM) was not assigned any applications in the selected group, and the National Instituted of Dental & Craniofacial Research

(NIDCR) was in fact assigned one application that was not awarded under the PA99-079 FOA.

The applications and awards for each RFA/PA number are broken down in Tables 5 a, b, and c below by sponsoring Institute/Center.

Table 5a: Applications (Apps) and Awards (Awd) by Sponsoring IC and RFA/PA Number

IC	NCI	NIMH	NICHD	NHGRI	NINDS	NIA	NIAID	NHLBI	NIDA	NINR
OD97-001 Apps	20	14	11	6	9	8	6		4	
OD97-001 Awd	3	4	3	3	2	1	1		0	
PA99-079 Apps	17	4	2	4	5	1	2	4	2	
PA99-079 Awd	6	1	1	1	2	1	0	2	2	
PA02-103 Apps	13	8	7	6	1	7	7	11	4	3
PA02-103 Awd	3	5	2	1	0	3	0	2	2	1
PA06-367 Apps	3	4	1	3	2		1		1	0
PA06-367 Awd	2	1	0	2	1		0		0	0
PA06-368 Apps	10	1	5	2	2	3	4	1		5
PA06-368 Awd	3	0	3	0	1	1	3	0		3
PA06-369/PA07-277 Apps	6	5	4	3	2	1		1	1	2
PA06-369/PA07-277 Awd	2	2	0	1	1	0		0	0	0
Total Apps	69 24%	36 13%	30 11%	24 9%	21 7%	20 7%	20 7%	17 6%	12 4%	10 4%
Total Awd	19 24%	13 17%	9 12%	8 10%	7 9%	6 8%	4 5%	4 5%	4 5%	4 5%

Table 5b: Applications (Apps) and Awards (Awd) by Sponsoring IC and RFA/PA Number Continued

IC	NIGMS	NIAAA	FIC	NIEHS	NIDCR	NIAMS	NIDCD	NIDDK
OD97-001 Apps		4						
OD97-001 Awd		0						
PA99-079 Apps	1	1		2	2			
PA99-079 Awd	0	0		0	0			
PA02-103 Apps	2		3			1	1	1
PA02-103 Awd	0		0			0	0	0
PA06-367 Apps			1	1				
PA06-367 Awd				0				
PA06-368 Apps								
PA06-368 Awd								
PA06-369/PA07-277 Apps	2			1				
PA06-369/PA07-277 Awd	0			0				
Total Apps	5 2%	5 2%	4 1%	4 1%	2 1%	1 0%	1 0%	1 0%
Total Awd	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%	0 0%

Table 5c: Applications (Apps) and Awards (Awd) by Sponsoring IC and RFA/PA Number Continued (Totals)

IC	Total
OD97-001 Apps	82
OD97-001 Awd	17
PA99-079 Apps	47
PA99-079 Awd	16
PA02-103 Apps	75
PA02-103 Awd	19
PA06-367 Apps	17
PA06-367 Awd	6
PA06-368 Apps	33
PA06-368 Awd	14
PA06-369 / PA07-277 Apps	28
PA06-369 / PA07-277 Awd	6
Total Apps	**282**
Total Awd	**78**

8 sponsoring ICs received applications but did not make any awards, those ICs in table 5b above. When the number of awards granted by those ICs that receive greater than or equal to 6 applications is compared to the number of awards granted by the ICs that receive less than or equal to 5 applications, we observe that these awards are significantly underrepresented in the pool of awards.

Next, we analyzed the IC breakdown of the comparison group, and found that there were some differences between which ICs generally support human subjects research and those that received HSR ethics projects. The distribution of applications and awards for the comparison group by sponsoring IC is shown in Table 6 below.

NIAAA, NIAMS, NIDA, NIDDK, and NHLBI receive proportionally more grant applications for Human Subjects research broadly across the NIH than within the

universe of applications studied here. The ICs that did not participate in the HSR Ethics RFA/PAs but did in fact receive applications for human subjects research include National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Eye Institute (NEI), National Library of Medicine (NLM), National Center on Minority Health and Health Disparities (NCMHD) and National Center for Research Resources (NCRR) (underlined in the table).

Table 6: Applications and Awards of All Human Subjects projects by Sponsoring IC

Sponsoring IC	Application Number	Application Frequency	Award Number	Award Frequency
NCI	19,737	18%	5,430	19%
NIMH	11,481	11%	3,155	11%
NICHD	11,012	10%	2,576	9%
NHGRI	501	<1%	170	1%
NINDS	4,682	4%	1,177	4%
NIA	7,124	7%	1,881	6%
NIAID	6,855	6%	2,031	7%
NHLBI	9,839	9%	2,806	10%
NIDA	6,807	6%	2,148	7%
NINR	2,276	2%	642	2%
NIGMS	1,059	1%	270	1%
NIAAA	2761	3%	934	3%
FIC	11,64	1%	319	1%
NIEHS	1,688	2%	409	2%
NIDCR	2,548	2%	666	2%
NIAMS	3,327	3%	717	3%
NIDCD	1,978	2%	651	2%
NIDDK	7,348	7%	1,814	6%
NCCAM	2,244	2%	428	1%
NIBIB	1,380	1%	305	1%
NEI	1,636	2%	516	2%
NLM	567	1%	128	<1%
NCMHD	16	<1%	0	0%
NCRR	324	<1%	44	<1%
TOTAL	108,354		29,247	

Interestingly NCI, NIMH and NHGRI were represented in the HSR ethics group at greater proportion then among all human subjects research. The remaining IC's that funded at least one HSR ethics submission are all represented in similar portions among the broader definition of human subjects research.

Table 7 shows the funding rates for the projects submitted to each IC under each RFA/PA number, and the table includes the reference point for all R01, R03 and R21 applications submitted to each IC during the same council rounds as those found within our HSR ethics data set. The last column, titled All Human Subjects allows comparison of project funding rates more broadly.

Table 7: Project Funding Rates by Sponsoring IC and RFA/PA Number

Sponsoring IC	OD97-001	PA99-079	PA02-103	PA06-367	PA06-368	PA06-369/ PA07-277	Total	All Human Subjects
NCI	15%	35%	23%	67%	30%	33%	**28%**	28%
NIMH	29%	25%	63%	25%	0%	40%	**36%**	27%
NICHD	27%	50%	29%	0%	60%	0%	**30%**	23%
NHGRI	50%	25%	17%	67%	0%	33%	**33%**	34%
NINDS	22%	40%	0%	50%	50%	50%	**33%**	33%
NIA	13%	100%	43%		33%	0%	**30%**	26%
NIAID	17%	0%	0%	0%	75%		**20%**	38%
NHLBI		50%	18%		0%	0%	**24%**	29%
NIDA	0%	100%	50%	0%		0%	**33%**	32%
NINR			33%		60%	0%	**40%**	28%
NIGMS		0%	0%			0%	**0%**	25%
NIAAA	0%	0%					**0%**	34%
FIC			0%	0%			**0%**	27%
NIEHS		0%		0%		0%	**0%**	24%
NIDCR		0%					**0%**	26%
NIAMS			0%				**0%**	22%
NIDCD			0%				**0%**	33%
NIDDK			0%				**0%**	25%
Total	**21%**	**34%**	**25%**	**35%**	**42%**	**20%**	**28%**	**27%**

HSR Ethics applications to the following ICs fared better than those similar mechanisms involving human subjects: NIMH, NICHD, NIA, NIDA and NINR.

Until recently, the field of Human Subject Research ethics has been largely a field that does not seek support from the NIH. Because of the importance of research in this area to improving biomedical health, it is a goal of these RFA/PAs to bring bioethicists into NIH supported projects as new investigators to tackle issues particularly relevant to the NIH mission. Table 8 indicates that roughly 2 in 3 of the applications within this study group were submitted by new investigators. When considering more recent funding opportunities, however, the proportion of applications by new investigators is higher, in some cases approaching 90%. Using data available from OER, in the last few years,

new investigators have made up around 25% of the R01 investigator pool, thus the HSR ethics projects are attracting applications from new investigators[3].

Table 8: Applications (Apps) and Awards by Investigator Type and RFA/PA Number

Investigator Type	New	Established	Total
OD97-001 Apps	61	21	82
OD97-001 Awards	10	7	17
PA99-079 Apps	35	12	47
PA99-079 Awards	10	6	16
PA02-103 Apps	44	31	75
PA02-103 Awards	6	13	19
PA06-367 Apps	15	2	17
PA06-367 Awards	5	1	6
PA06-368 Apps	25	8	33
PA06-368 Awards	10	4	14
PA06-379/ PA07-277 Apps	15	13	28
PA06-379/ PA07-277 Awards	3	3	6
Total Apps	**195** 69%	**87** 31%	**282**
Total Awards	**44** 56%	**34** 44%	**78**

In Table 9, the project funding rates by Investigator Type reveals that the overall funding rates for applications from Established Investigators is higher. It is interesting to note

[3] Data accessed from http://grants.nih.gov/grants/new_investigators/First_Time_R01_1962-2008.ppt on January 29th, 2010.

that the funding rates for PA06-367 and PA06-368 are higher for New investigators than the other RFA/PAs based mechanisms.

Table 9: Project Funding Rates by Investigator Type and RFA/PA Number

Investigator Type	OD97-001	PA99-079	PA02-103	PA06-367	PA06-368	PA06-369/ PA07-22	Total
New	16%	29%	14%	33%	40%	20%	23%
Established	33%	50%	42%	50%	50%	23%	39%
Total	21%	34%	25%	35%	42%	21%	28%

As one way to bring in new investigators, the NIH has grant mechanisms such as the R03 and R21 that require less preliminary data and allow for exploration. As can been seen in Table 10 below, the vast majority of applications received to the HSR ethics funding opportunities have been of the standard R01 mechanism. However, PA06-367 was specifically for R03 applications and PA06-368 was specifically for R21 applications. Referring back to Table 2, we see that the R21 mechanism was more popular among the cohort of applications submitted in response to the program announcements available since 2006. The proportion of R03 and R21 projects within the HSR Ethics group is less than the proportion of these mechanisms in the overall human subjects comparison group.

Table 10: Applications (Apps) and Awards (Awd) by Activity Code and RFA/PA Number

Activity Code	R01	R03	R21	Total
OD97-001 Apps	82			82
OD97-001 Awd	17			17
PA99-079 Apps	47			47
PA99-079 Awd	16			16
PA02-103 Apps	75			75
PA02-103 Awd	19			19
PA06-367 Apps		17		17
PA06-367 Awd		6		6
PA06-368 Apps			33	33
PA06-368 Awd			14	14
PA06-369/PA07-277 Apps	28			28
PA06-369/PA07-277 Awd	6			6
Total Apps	232 82%	17 6%	33 12%	282
Total Awd	58 75%	6 8%	14 18%	78
All Human Subjects Apps	67,954 63%	14,542 13%	25,858 24%	108,354
All Human Subjects Awd	18,835 64%	4,451 15%	5,961 20%	29,247

When comparing project funding rates for the different grant mechanisms, we see that R03 and R21 applications are funded at a higher rate, as shown in Table 11 below. Interestingly, the HSR Ethics R03s and R21s experience a higher project funding rate than those in the comparison group, consistent with a goal of bringing investigators new to this research area to projects on ethics.

Table 11: Project Funding Rate by Activity Code and RFA/PA Number

Activity Code	OD97-001	PA99-079	PA02-103	PA06-367	PA06-368	PA06-369/ PA07-277	Total	All Human Subjects
R01	21%	34%	25%			21%	25%	28%
R03				35%			35%	31%
R21					42%		42%	23%
Total	21%	34%	25%	35%	42%	21%	28%	27%

The data presented in Tables 10 and 11 suggest that applicants are taking advantage of the R03 and R21 offerings and are in fact faring better than those who submitted to the R01 version of the same offering.

Research proposals on the topics included in HSR ethics may require review by scientists familiar with ethics and/or HSR issues. An analysis of Study Section types is presented in Table 12 below. The overwhelming majority of applications across all funding opportunities were reviewed by Special Emphasis Panels, or SEPs.

Table 12: Applications (Apps) and Awards by Study Section type and RFA/PA number.

Study Section	Standing	SEP	Total
OD97-001 Apps	1*	81	82
OD97-001 Awards	0	17	17
PA99-079 Apps	2	45	47
PA99-079 Awards	1	15	16
PA02-103 Apps	9	66	75
PA02-103 Awards	1	18	19
PA06-367 Apps	4	13	17
PA06-367 Awards	2	4	6
PA06-368 Apps	8	25	33
PA06-368 Awards	2	12	14
PA06-369/PA07-277 Apps	2	26	28
PA06-369/PA07-277 Awards	0	6	6
Total Apps	26 9%	256 91%	282
Total Awards	6 8%	72 92%	78

*One of the initial applications received under RFA 0D97-001 was reviewed as a resubmission by a standing review committee.

Table 13 shows that applications reviewed by the SEPs have a higher funding rate than those reviewed in Standing review groups.

Table 13: Project Funding Rates by Study Section Type and RFA/PA Number

Study Section	OD97-001	PA99-079	PA02-103	PA06-367	PA06-368	PA06-369/ PA07-277	Total
Standing	0%	50%	11%	50%	25%	0%	**23%**
SEP	21%	33%	27%	31%	48%	23%	**28%**
Total	**21%**	**34%**	**25%**	**35%**	**42%**	**21%**	**28%**

223 different individuals submitted one or more HSR applications, and 68 individuals were awarded research funding under these FOAs.

133 different organizations submitted applications to these HSR funding opportunities, but only 49 institutions actually received at least one of the 79 awards. The following table (Table 14) lists the applications and awards for those organizations that received 2 or more of the HSR awards studied.

Table 14: Application and Awards from Organizations with More Than Two Awards

Organization	Total Applications	Percent of Total Applications	Total Awards	Percent of Total Awards
Johns Hopkins University	16	5.7%	6	7.6%
University Of Michigan At Ann Arbor	7	2.5%	5	6.3%
University Of Massachusetts Medical School Worcester	4	1.4%	3	3.8%
University Of California San Francisco	5	1.8%	3	3.8%
University Of Pennsylvania	6	2.1%	3	3.8%
Baylor College Of Medicine	5	1.8%	2	2.5%
Case Western Reserve University	3	1.1%	2	2.5%
Duke University	7	2.5%	2	2.5%
Fordham University	2	0.7%	2	2.5%
Fox Chase Cancer Center	2	0.7%	2	2.5%
Massachusetts General Hospital	3	1.1%	2	2.5%
Mount Sinai School Of Medicine Of NYU	3	1.1%	2	2.5%
Nemours Children's Clinic	3	1.1%	2	2.5%
Treatment Research Institute, Inc. (tri)	3	1.1%	2	2.5%
University Of Alaska Anchorage	2	0.7%	2	2.5%
University Of Chicago	4	1.4%	2	2.5%
University Of Illinois At Chicago	5	1.8%	2	2.5%
University Of New Mexico	7	2.5%	2	2.5%
University Of North Carolina Chapel Hill	6	2.1%	2	2.5%
Veterans Medical Research Foundation/San Diego	2	0.7%	2	2.5%

Topical Areas:

Of the 282 applications under study, abstracts were identified for 276 applications. Each abstract was read and the project assigned one Topic category and one Affected Group category. The definitions of the Topics and Affected Group are included in Appendix A.

Table 15: Applications, Awards and Project Funding Rates by Topic

Topic	Applications	% of Total Applications	Awards	% of Total Awards	Project Funding Rate
Participation Recruitment	57	21%	23	29%	40%
Treatment vs. Research	6	2%	2	3%	33%
Informed Consent	113	41%	32	41%	28%
Risks vs. Benefits	11	4%	4	5%	36%
Clinical Trials	28	10%	6	8%	21%
Drug/Alcohol Admin	0	0%	0	0%	--
Genetics	3	1%	2	3%	67%
Existing Data	1	0%	0	0%	0%
Privacy Protection	8	3%	2	3%	25%
Communication	4	1%	1	1%	25%
Emerging Tech	3	1%	0	0%	0%
Stigma	0	0%	0	0%	--
Oversight*	**40**	**14%**	**5**	**6%**	13%
Other	2	1%	1	1%	50%
Total	276		78		28%

*Significantly underrepresented in the pool of funded awards ($p < .1$)

RFA OD97-001 was specifically soliciting applications on the topic of informed consent; all other solicitations had a broader topical scope. The largest number of applications and awards were to those proposals about Informed Consent, which is consistent with the large number of applications in response to the first solicitation.

In table 16 below, we present an analysis of the topics for submitted under the Program Announcements only. In response to the PAs, Participation/Recruitment and Informed Consent were the most common application types and were more represented among the awards. Other topics were generally represented with small numbers of applications and awards. Interestingly, a large number of applications were received on subjects related to Oversight, but a small number (statistically significant) were funded.

Table 16: Applications, Awards and Project Funding Rates by Topic for the HSR Program Announcements only

Topic	Applications	% of Total Applications	Awards	% of Total Awards	Project Funding Rate
Participation Recruitment	49	25%	20	33%	41%
Treatment vs. Research	4	2%	1	2%	25%
Informed Consent	52	26%	21	34%	40%
Risks vs. Benefits	11	6%	4	7%	36%
Clinical Trials	23	12%	4	7%	17%
Drug/Alcohol Admin	0	0%	0	0%	--
Genetics	3	2%	2	3%	67%
Existing Data	0	0%	0	0%	--
Privacy Protection	8	4%	2	3%	25%
Communication	3	2%	1	2%	33%
Emerging Tech	3	2%	0	0%	0%
Stigma	0	0%	0	0%	--
Oversight*	**39**	**20%**	**5**	**8%**	13%
Other	2	1%	1	2%	50%
Total	197		61		31%

Table 17 shows the number of applications and awards broken down by the population under study. Proposals related to Vulnerable Populations were overrepresented in the pool of awards, while those related to Cross-Cultural populations were underrepresented.

Table 17: Applications, Awards and Project Funding Rates by Affected Group

Affected Group	Applications	% of Total Applications	Awards	% of Total Awards	Project Funding Rate
Vulnerable Population*	**106**	**38%**	**44**	**56%**	42%
Cross-Cultural**	**29**	**11%**	**3**	**4%**	10%
Disease Specific	33	12%	10	13%	30%
General Population	108	39%	21	27%	19%
	276		78		28%

*Significantly overrepresented in the pool of funded awards ($p < .1$)

**Significantly underrepresented in the pool of funded awards ($p < .1$)

As shown in Table 18, the proportion of applications and awards in the Affected Groups do not change significantly when limited to the applications received in response to the Program Announcements.

Table 18: Applications, Awards and Project Funding Rates by Affected Group for the HSR Program Announcements only

Affected Group	Applications	% of Total Applications	Awards	% of Total Awards	Project Funding Rate
Vulnerable Population	**77**	**39%**	**35**	**57%**	45%
Cross-Cultural	**25**	**13%**	**3**	**5%**	12%
Disease Specific	15	8%	6	10%	40%
General Population	80	41%	17	28%	21%
Total	197		61		31%

Analysis of Resubmission Rates for the Human Subject Research Portfolio

Many NIH grant submissions are eligible to compete multiple times, incorporating feedback from prior review cycles and additional preliminary data. Table 15 presents data for all proposals submitted to one of the seven Human Subjects Research solicitations. While proposals may have been resubmitted numerous times in the past, recent years have brought increased restrictions on the number of revisions, and no projects within the data set were submitted more than 3 times (initial (A0), A1 and A2). The *Success Rate* is the percentage of applications at a particular submission level that are funded.

Abandoned applications are those for which there are no subsequent connected applications. The *Resubmission Rate* is the percentage of unfunded applications that are resubmitted at the next level (eg. # of A2 applications / # of unfunded A1 applications).

Table 19: Resubmission Rates for All HSR Ethics Projects

	Applied	Funded	Success Rate	Unfunded	Abandoned	Resubmission Rate
Initial/A0	282	34	12%	248	164	34%
A1	84	32	38%	52	30	42%
A2	22	12	55%	10	10	-
Total	**282**	**78**	**28%**			

For various reasons, not all grant submissions are eligible to apply multiple times. Proposals in response to an RFA are generally not eligible for resubmission. The

process of revising and resubmitting a proposal takes time, and because our data set is limited to those application records that were reviewed prior to or during the May 2009 council round, it is possible that other proposals have been, or will be, resubmitted. 38 applications submitted between FY2007-2009 were not funded and not revised or resubmitted as of the council round in question, establishing an upper bound to the number of projects currently considered Abandoned that may be resubmitted.

The following table presents data for those proposals that are in response to one of the six Human Subjects Research ethics PAs.

Table 20: Resubmission Rates for the HSR Program Announcements only

	Applied	Funded	Success Rate	Unfunded	Abandoned	Resubmission Rate
Initial/A0	200	18	9%	182	103	43%
A1	79	31	39%	48	27	44%
A2	21	12	57%	9	9	-
Total	**200**	**61**	**31%**			

The resubmission rates and success rates for applications within the comparison group of human subjects research is presented in Table 21. Resubmission rates of the HSR ethics projects are similar compared to applications for All Human Subjects.

Table 21: Resubmission Rates for All Human Subjects

	Applied	Funded	Success Rate	Unfunded	Abandoned	Resubmission Rate
Initial/A0	108,354	14,680	14%	93,674	60,086	36%
A1	33,588	9,793	29%	23,795	14,517	39%
A2	9,278	4,731	51%	4,547	4,449	2%
A3 *	98	43	44%	55	55	-
Total	**108,354**	**29,247**	**27%**			

Human Subject Research Proposals Submitted to Funding Opportunities Supporting Studies in Research Integrity or Ethical, Legal and Social Implications (ELSI)

In addition to Funding Opportunity Announcements (FOAs) that are specific to HSR ethics, related FOAs may have also resulted in submission and funding of HSR ethics related research grants. These FOAs are listed below in Table 22, and solicited R01, R03, and R21 applications prior to 2008.[4] All proposals in response to these funding

[4] In addition, FOAs PA00-132 and PA00-133 included several applications and awards that were R13 or R25 mechanisms. None of these projects were related to Human Subjects Research and were excluded from all analyses.

announcements were reviewed to determine relevance to Human Subjects Research ethics issues, as determined by having a large component of study on the involvement of human subjects in research, as opposed to disease treatment or the implications of testing on patients.

Table 22: Research Integrity and ELSI Applications and Awards

Programs Area	RFA/PA Number	Mechanisms	Applications	Awards	HSR-ethics Related Applications	HSR-ethics Related Awards
ELSI	HG02-003	R01, R03, R21	24	5	10	2
ELSI	HG99-002	R01, R03	13	6	10	4
ELSI	PA00-132	R01, R03	46	16	6	2
ELSI	PA00-133	R01, R03	60	22	15	6
ELSI	PA04-050	R01	37	13	8	5
ELSI	PA04-051	R03	41	16	5	2
Research Integrity	NR07-001	R01	22	7	6	1
Research Integrity	RR07-003	R21	22	3	3	0
Research Integrity	RR07-004	R03	1	0	0	0
	Total		**266**	**88**	**63**	**22**

Sixty three projects, or slightly less than 1 in every 4, were determined to be related to Human Subjects ethics Research. Applications within the related FOA areas have an

overall success rate of 33.2%; the subset of HSR-related applications had a slightly higher success rate of 34.9%, although this is not statistically significant.

These projects were further analyzed to determine the specific topical area, IC, and mechanism. Results of this analysis are presented below in Tables 23 through 26.

Topic and Affected Population Analysis

As shown in Table 23, the majority of HSR applications received in these related FOAs dealt with Genetics research, followed by the topic of Participation and Recruitment. Funding rates by topic for this set of proposals show the same trends as the funding rates of proposals responding to the HSR specific solicitations, though with less statistical significance due to small numbers. While there were six applications focusing on issues related to Oversight, none of them were funded. Proposals focusing on Vulnerable Populations are significantly overrepresented in the pool of funded awards, compared to the overall pool of applicants.

Table 23: Applications and Awards to Related FOAs by Topic

Topic	Applications	% of Total Applications	Awards	% of Total Awards
Participation Recruitment	9	14%	6	27%
Treatment vs. Research	0	0%	0	0%
Informed Consent	2	3%	0	0%
Risks vs. Benefits	1	2%	1	5%
Clinical Trials	3	5%	1	5%
Drug/Alcohol Admin	0	0%	0	0%
Genetics	37	59%	12	55%
Existing Data	2	3%	0	0%
Privacy Protection	1	2%	0	0%
Communication	1	2%	1	5%
Emerging Tech	0	0%	0	0%
Stigma	1	2%	1	5%
Oversight	6	10%	0	0%
Other	0	0%	0	0%
Total	**63**		**22**	

Table 24: Applications and Awards to Related FOAs by Affected Group

Affected Group	Applications	% of Total Applications	Awards	% of Total Awards
Vulnerable Population	**24**	**38%**	**11**	**50%**
Cross-Cultural	3	5%	0	0%
Disease Specific	14	22%	6	27%
General Population	22	35%	5	23%
Total	**63**		**22**	

Analysis of NIH Institutes and Centers and Activity Codes

Over two-thirds of the HSR-related applications to these associated FOAs were submitted to the National Human Genome Research Institute (NHGRI). The remainder of the relevant applications was distributed over nine different ICs. The distribution of applications and awards, by IC, is displayed in Table 25.

Table 25: Applications and Awards to Related FOAs by Sponsoring IC

IC	Applications	% of Total Applications	Awards	% of Total Awards
NHGRI	43	68%	13	59%
NINR	5	8%	0	0%
NCRR	3	5%	0	0%
NCI	3	5%	2	9%
NIDA	2	3%	1	5%
NIGMS	2	3%	2	9%
NIA	2	3%	2	9%
NICHD	1	2%	0	0%
NIDCD	1	2%	1	5%
NIEHS	1	2%	1	5%
Total	**63**		**22**	

As shown in Table 26, the bulk of the applications and awards were the traditional R01 mechanism. There were also a small number of R03 and R21 type applications, and several R03 awards.

Table 26: Applications and Awards to Related FOAs by Activity Code

Mechanism	Applications	% of Total Applications	Awards	% of Total Awards
R01	47	75%	18	82%
R03	13	21%	4	18%
R21	3	5%	0	0%
Total	63		22	

Project Summary and Possible Future Directions

The above series of analyses provide NIH's Office of Extramural Research with a much better understanding of the impact of the selected Human Subject Research Bioethics funding opportunities offered to the research community since the late 1990's. New Investigators are applying to these programs, especially to PA06-367 and PA06-368, which provide R03 and R21 grant mechanisms respectively. Topic analysis reveals that there is interest in the bioethics community to conduct research in the area of Oversight, an area that hasn't been supported in the existing set of funding opportunities. Interestingly, analyzing the ELSI and Research Integrity funding opportunities revealed that there are some projects funded under these RFA/PAs that are in fact Human Subject Research Ethics projects. Compared to the HSR ethics RFA/PAs, however, these focus on Genetics and are in many cases funded by the Human Genome Research Institute (NHGRI).

Further analysis on these RFA/PAs could include the following:

- An analysis of the outcomes of the funded projects, to include publications, meeting presentations and standards of care. NIH's Electronic Scientific Portfolio Assistance (e-SPA) system could be a starting point for this type of outcome and impact analysis.
- An in depth analysis of the network of bioethicists conducting research in the United States, and whether these researchers applied for and were funded by the HSR ethics RFA/PAs. Using publication and grant databases, a subject category and research topic analysis could be conducted looking at existing researchers' areas of interest and how those areas may have been supported by the selected funding opportunities. In addition, network graphic and analysis could be used to model the network of researchers in this area and to identify those that have applied for and have been awarded NIH support.
- An analysis of bioethics research activities at other funding agencies, including the National Science Foundation (NSF) and other non-profit agencies, such as the Bill and Melinda Gates Foundation. This type of analysis would provide OER

with a better understanding of the bioethics funding landscape and could open up opportunities for collaboration and cross-fertilization.

Appendix A: Topic and Affected Group Definitions

Affected Groups (Who)	Description
Vulnerable Populations	children, pregnant women, fetuses, neonates, prisoners, diminished capacity, elderly, minority, socio-economically deprived
Cross-cultural	community issues, international populations, comparisons among groups
Disease Specific	ex. Cancer patients
General Population	anything else (default)

Topic	Description
PARTICIPATION RECRUITMENT	General comprehension of research and/or participation in research, decision making about participation, general or broad cognitive issues, methods to measure comprehension or decision making abilities in general; barriers to participation in general, Recruitment: including autonomy, coercion, use of incentives, compensation, re-contacting previous participants or eligible subjects, retention, access to research , disparities
TREATMENT VS. RESEARCH	Treatment verses Research – overlaps/boundaries, comprehension, coercion
INFORMED CONSENT	Informed Consent – including comprehension issues specific to consent and methods to assess, novel approaches, assent, special populations including those with diminished capacity, proxy consent, waiver of consent, non-written consent
RISKS VS. BENEFITS	Risks verses Benefits of participation, including non-physical risks (social, economic, psychological harm), environmental hazards, how participants view/comprehend risks, withdrawal of current medication
CLINICAL TRIALS	Clinical trials – design, use of placebo, inclusion of children, Complementary and Alternative Medicine (CAM), equipoise, palliative care, retention.
DRUG/ALCOHOL	Administration of drugs or alcohol to research participants

ADMIN	

Topic	Description
GENETICS	Genetics studies and data – identifiability of subject, data sharing, re-contact for consent or more info, providing results currently or in future, consent for specimen storage and/or future testing
EXISTING DATA	Research that uses existing data/ specimens; repository establishment and use, consent, identifiability, NOT GENETIC
PRIVACY PROTECTION	Protection of data, participant privacy, use of Certificates of Confidentiality, Electronic data sharing, identification of subjects in various data bases; data linkage
COMMUNICATION	Communicating results of research – to participants, to scientific community, incidental findings, in medical records, NOT GENETICS
EMERGING TECH	Emerging biomedical technologies (nanomedicine, synthetic biology, tissue engineering,) – justice, risks, intellectual property, oversight
STIGMA	Stigmatization of research participants
OVERSIGHT	Oversight of research by IRB's, Data Safety Monitoring Plans, reporting adverse events
OTHER	Other; specify

Appendix B: Description of Data Files Accompanying this Report

HSREthicsEvaluationReport_DataTables20100129.xls

This file contains the aggregated raw data used to create the following tables in this report: Table 1, 2, 3, 4, 5, 6, 7, 8, 9, 19, 11, 12, 13, and 14.

HSREthicsEvaluation_ProjectData20100129.xls

This file contains the project level data for all 282 applications analyzed in this project. The following fields are included.