Scientific Poster Abstracts from the
2009 AER Conference: Navigating the Future
Using the Belmont Compass

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<table>
<thead>
<tr>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>A Review of OHRP Compliance Oversight Letters-Update</td>
<td>3-4</td>
</tr>
<tr>
<td>A Systematic Review of Inclusion of Women of Childbearing Potential (WOCPO) in NIH Clinical Trials: Contraception and Pregnancy Testing</td>
<td>5</td>
</tr>
<tr>
<td>Assessment of Knowledge, Attitudes, and Perspectives of Faculty Members at Cairo University Towards Research Ethics</td>
<td>6-7</td>
</tr>
<tr>
<td>Disclosure of Genetic Research Results: Perspectives of IRB Members and Staff</td>
<td>8</td>
</tr>
<tr>
<td>Effects of Readability and Formatting on Recall of Consent Material Early and Late in the Semester</td>
<td>9</td>
</tr>
<tr>
<td>Ethical Implications of Asking Sensitive Questions</td>
<td>10</td>
</tr>
<tr>
<td>Evaluation of the Quality of Informed Consent in Clinical Researches: Healthy Subjects</td>
<td>11</td>
</tr>
<tr>
<td>Exempt Determination at One U.S. University</td>
<td>12</td>
</tr>
<tr>
<td>Genetics Research Review and Issues Project (GRRIP): Preliminary Results of a National Survey of IRB Professionals</td>
<td>13-14</td>
</tr>
<tr>
<td>Genetics Research Review and Issues Project (GRRIP): Preliminary Results of a National Survey of Genetic Researchers</td>
<td>15-16</td>
</tr>
<tr>
<td>Hope’s Role in Decision Making for Cancer Research Participation</td>
<td>17</td>
</tr>
<tr>
<td>Improving Recruitment in Clinical Trials: Why Eligible Participants Decline</td>
<td>18</td>
</tr>
<tr>
<td>Incarcerated Youth: Reactions to Participation in Suicide &amp; Self-Harm Research</td>
<td>19</td>
</tr>
<tr>
<td>Inclusion of Men in Clinical Trials: Do Interventions Pose Risk to Offspring and Should Men Use Contraception?</td>
<td>20</td>
</tr>
<tr>
<td>Inclusion of Minors of Childbearing Potential in Clinical Trials: Pregnancy Testing and Contraception</td>
<td>21</td>
</tr>
<tr>
<td>Information Overload: The Effect Of A Shorter Form On The Quality Of Informed Consent</td>
<td>22</td>
</tr>
<tr>
<td>Investigator Dissatisfaction with the IRB Approval Process</td>
<td>23</td>
</tr>
<tr>
<td>Medical Students and Research Ethics: Micro-Survey in Ufa, Russia</td>
<td>24</td>
</tr>
<tr>
<td>Not Just About Money: A Review Of The Literature Examining Self-Reported Motivations And Decision-Making In Healthy Volunteers</td>
<td>25</td>
</tr>
<tr>
<td>Parental Attitudes Toward Pediatric Biobanks</td>
<td>26</td>
</tr>
<tr>
<td>Paying Research Participants: Preliminary Results of Two National Surveys</td>
<td>27</td>
</tr>
<tr>
<td>Policy Development On Inclusion Of Subordinate Employees In Clinical Research: Identification Of Risks And Safeguards</td>
<td>28</td>
</tr>
<tr>
<td>Public and Biobank Participant Attitudes Toward Genetic Research Participation and Data Sharing</td>
<td>29</td>
</tr>
<tr>
<td>Quality of UPIRSO Reporting in Cancer Drug Clinical Trials</td>
<td>30</td>
</tr>
<tr>
<td>Research Participant Survey Project Part I: Focus Groups to Define Relevant Dimensions of the Research Participant Experience</td>
<td>31</td>
</tr>
<tr>
<td>The IRBs in Taiwan: A Status report 2008</td>
<td>32</td>
</tr>
<tr>
<td>What Does ‘Protection of Human Subjects’ Mean to a Social and Behavioral IRB?</td>
<td>33</td>
</tr>
</tbody>
</table>
A Review of OHRP Compliance Oversight Letters-Update
Authors: Carol Weil; Lisa Rooney; Patrick McNeilly; Karena Cooper; Kristina Borror; Paul Andreason

Background
The Office for Human Research Protections (OHRP), a component of the Department of Health and Human Services (HHS), is responsible for overseeing compliance with the HHS regulations governing research with human subjects (HHS regulations), and evaluates written substantive allegations or indications of noncompliance with the HHS regulations. In September 2003, OHRP’s Division of Compliance Oversight reported on the review of 269 compliance oversight determination letters issued to 155 institutions between October 1, 1998 and June 20, 2002. Now we describe a similar report of a review of 235 compliance oversight determination letters issued to 146 institutions between August 1, 2002 and August 31, 2007. Research questions: What percentage of institutions were cited by OHRP for various noncompliance? What is the distribution of OHRP citations of noncompliance? What are the trends that have evolved since our previous analysis?

Description of Research
Research methods: We reviewed 235 compliance oversight determination letters issued to 146 institutions between August 1, 2002 and August 31, 2007. Compliance oversight determination letters included in the analysis include those in which OHRP made a definitive citation of noncompliance with the HHS regulations and/or expressed concern about apparent regulatory or other deficiencies that resulted in the institution taking corrective action (hereinafter “citation of noncompliance”).

Results: The tables show the percentage of institutions cited by OHRP for various noncompliance and the distribution of OHRP citations of noncompliance. Table 1 shows that institutions were most frequently cited for noncompliance related to the initial IRB review process (56%), informed consent documents and/or informed consent process approved by the IRB (51%), IRB continuing review process (22%), and IRB policies and procedures (20%). Table 2 shows that the most common areas of noncompliance and deficiency involved informed consent documents and procedures (34%) and the process for IRB initial review of research protocols (20%). These were also the top two categories of citations in our previous review (27% and 25%, respectively). Table 3 indicates that almost two-thirds of the citations relating to IRB initial review of research protocols pertained to IRB failure to approve research protocols in accordance with HHS regulations at 45 CFR 46.111. This is a substantial increase over the percentage of these findings in our last review, which was about one third (153 citations vs 277 citations). Table 4 indicates that nearly a third of the citations of noncompliance involved matters related to informed consent, which is similar to our previous analysis. The most common informed consent citations were that consent documents failed to adequately describe the purpose, procedures, and duration of the research (23%) and the risks and discomforts of the research (23%).

Conclusions: Our current analysis demonstrates that, since our last analysis, there has been an increase in the percentage of institutions with citations of noncompliance regarding changes in research without prior IRB review and approval (25% in our previous analysis and 35% in our current analysis). Conversely, in our previous analysis, the number of citations of noncompliance in the category of written IRB policies and procedures was 88 (rank order #4), and in our current analysis it was 113 (rank order #3). This increase is statistically significant (113/762 vs. 88/1120; Chi-Square=23.1; p<0.00001). The analysis of these data provides OHRP with a reference point by which it may develop targeted guidance and educational programs to help strengthen protections for human subjects. Awareness of the most frequent problem areas identified by OHRP may allow institutions to take proactive measures before noncompliance occurs. Limitations: The letters examined only represent institutions that were involved with allegations or indications of noncompliance or underwent a not-for-cause evaluation (n = 146); the data do not represent a random sample of institutions that hold an OHRP-approved assurance. The vast majority of cases were for-cause evaluations by OHRP during the time period noted above. In addition,
for many evaluations the scope of research assessed was small, focusing on a single complaint and involving a limited sample of an institution’s human subjects research portfolio.
A Systematic Review of Inclusion of Women of Childbearing Potential (WOCP) in NIH Clinical Trials: Contraception and Pregnancy Testing

Authors: Maria Rita Vieira; Pamela Stratton; Christina Gonzalez; Izabella Khachikyan; Marnie Wagner; Lindsey Magaw; Shannon Liu; Tajana Pulanic; Patricia Battuello; Asma Idriss; Barbara Karp

Background

The 1993 NIH Revitalization Act required the inclusion of WOCP in clinical trials to assure generalizability of data to women. This study assessed whether written protocol documents addressed protections in studies of risk to WOCP/fetuses, specifically requirements for contraception and pregnancy testing.

Description of Research

Materials and Methods: NIH Intramural on-site clinical trials that included women and presented more than minimal risk were reviewed. We categorized each study as posing either ongoing risk (risk exposure extending over \( \geq 1 \) month) or episodic risk (interventions of risk performed periodically or over a period < 1 month, e.g., MRI, x-ray or brain stimulation). Each protocol, consent and minor assent form was reviewed by two independent reviewers and reconciled into a single dataset using NICHD Clinical Trials Database software.

Results: 510 of 1640 studies met inclusion criteria. To date, 282 protocols, 305 consents, and 54 assents have been reviewed. Potential risk to WOCP/fetuses was explicitly addressed in 66% of protocols, 69% of consent forms and 26% of assents; 93% of studies posed ongoing and 7% posed episodic risk. Contraception was required 72% of studies posing ongoing risk and 29% of those with episodic risk. Subjects were informed of the need for contraception in 73% (ongoing-risk) and 32% (episodic risk) consent forms. Pregnancy testing was performed in almost all protocols (93% ongoing and 90% episodic risk), mostly at study entry. Pregnancy testing was repeated at least once a month in 9% of ongoing and 5% of episodic risk studies, and before interventions of risk in 32% of ongoing and 41% of episodic risk studies. Most protocols (96%) required that pregnant women be removed from the study. Contraception counseling was offered in 6% of protocols.

Conclusion: Pregnancy testing and contraception were not consistently addressed in studies posing risk. The safe inclusion of WOCP should include: 1. Clearly identifying the potential risks to WOCP/fetuses in the written protocol and consent documents. 2. Requiring contraceptive use and counseling in studies of ongoing risk. 3. Performing pregnancy testing beyond the initial visit, regularly and/or before interventions of risk as appropriate. 4. Delineating a plan for women who become pregnant during the study. Next steps: Our results highlight the need for a standardized approach to contraception use and pregnancy testing to ensure the safe inclusion of WOCP in clinical research.
Assessment of Knowledge, Attitudes, and Perspectives of Faculty Members at Cairo University Towards Research Ethics
Authors: Noha Asem; Henry Silverman

Background
There has been a recent increase in health research involving human subjects in the Middle East. Accordingly, concepts of research ethics have gained importance. However, little is known about the perspectives of faculty regarding research ethics, especially informed consent.

Objectives: To assess the knowledge, attitudes, and perspectives of the faculty members in the faculties of medicine, dentistry, and nursing regarding research ethics.

Description of Research
Methods: We developed a questionnaire consisting of close-ended questions and short case scenarios involving issues in research ethics. The survey consisted of the following domains: a) demographics, b) the importance of research ethics, c) the source of knowledge of research ethics, d) waiving informed consent, and e) informed consent issues involving vulnerable individuals. Responses were analyzed against several independent variables, e.g., faculty level and prior training in research ethics (i.e., read or taken a course in research ethics).

Participants: We administered the questionnaire to a convenient sample of faculty members.

Results: The number of participants included 135 faculty, 88 from Medicine, 19 from Nursing, and 28 from Dentistry. Of these participants, 60% were females and 40% were males; 33% were professors, 15% were assistant professors, and 52% were junior faculty. Regarding the importance of research ethics, more than 90% of all the faculty levels thought that human research should be submitted to an REC and that investigators need more training on research ethics and how to write an informed consent form. Regarding the source of knowledge of research ethics, 68% had read about research ethics and 52% had attended a course in research ethics; 48% reported having done both and 28% had done neither. Having read about research ethics or attended a research ethics course was more prevalent among the Nursing Faculty compared with the Medicine and Dentistry Faculty (p< 0.001). The percentage of respondents who thought it was proper to waive consent in the following situations were as follows: a) 38% in any study involving minimal risk; b) 36% in a study involving only the collection of blood samples; c) 84% when doing retrospective medical record research; d) 21% in a study involving withdrawal of an extra 5cc of blood from a child; e) 19% involving oncology patients who are unaware of their actual diagnosis; and f) 63% in a study involving prospective collection of an extra 10cc of bronchoalveolar lavage (BAL) fluid from patients undergoing the procedure for clinical purposes. Regarding informed consent in studies involving vulnerable populations: a) 33% believed that there is no need to give full information to participants with limited understanding; b) 17% thought it is just necessary to obtain the consent from the community leader of a village; c) 22% thought it is obligatory to obtain informed consent from a woman’s husband; d) 27% thought it is only necessary to obtain consent from doctors to enroll vulnerable individuals; and e) 17% thought it is proper to enroll vulnerable person if no one is available to give informed consent for them. Nursing faculty compared with Medicine and Dentistry faculty were less likely to agree to a) it is only necessary to obtain informed consent from doctors for vulnerable persons who cannot give informed consent; and b) a waiver of informed consent is appropriate in a study involving the prospective collection of an extra 10cc of bronchoalveolar lavage (BAL) fluid from patients undergoing the...
procedure for clinical purposes, (p< 0.005, and < 0.05, respectively). Individuals who had read about research ethics AND had taken a course in research ethics, compared to those who did neither, were less likely to agree that a) it is only necessary to obtain consent from doctors to enroll vulnerable individuals (p=0.05; and b) it is better not to inform potential research participants about the major risks of a study, since many might have concerns about such risks (p< 0.05).

Conclusions: A significant percentage of faculty from all schools and at all the different positions agreed with submitting research to an REC and also thought that more training was necessary. However, there might be an inappropriate regard for the value of informed consent, as many believed with waiving consent in different research scenarios. Also, there might be a concern with adequate protection of vulnerable participants, as many thought it was proper to include such participants in research without their consent or just with the consent of their doctors, and many thought it was not necessary to give detailed information to individuals with limited understanding. Having had prior readings AND taken a course in research ethics might affect these perspectives regarding consent waiver and the rights of vulnerable participants.

Next Steps: We recommend 1) enhanced training in research ethics for all members of the faculty and b) additional qualitative research studies to obtain a fuller understanding of faculty attitudes regarding issues in research ethics.
Disclosure of Genetic Research Results: Perspectives of IRB Members and Staff
Authors: Lynn G. Dressler; Roselle Ponsaran; Susan B. Trinidad; Nancy Gerson; Sue Lewis; Janell Markey; Debra Skinner; Nancy Press; Georgia Wiesner

Background
With the emergence of technologies that allow faster, less expensive, whole genome sequencing, the likelihood increases that clinically relevant research results will be revealed in genomic research. This coupled with the recent NIH GWAS policy suggesting that researchers and IRBs consider developing a plan to manage this occurrence has moved the controversial issue of return of individual research results to the forefront of genomic research. This study is part of a larger effort to assess experiences and perspectives of IRB members and staff regarding a number of issues in the review of genetic research proposals. Preliminary data obtained relating to the disclosure of genetic research results to individual research participants are the focus of this presentation.

Description of Research
Methods: This study involves semi-structured, in-depth interviews with IRB members and staff. Interviews are approximately 45-60 minutes in length and are conducted in person or by phone. Interviews are recorded and transcribed with individual identifiers removed to protect privacy. Coding and content analysis of interview text are performed independently by two analysts and compared for consensus.

Results: To date we have interviewed 22 IRB members and 8 IRB staff. Preliminary analysis indicates a range of responses to the question, Do you think genetic research results should be returned to research subjects? For some participants, initial response to this question was in favor of having results with clinical significance returned. On further probing with the questions: Who do you think should make the decision to return results? What criteria should be used to guide this decision?, the more complex ethical, scientific, and logistical aspects of this issue surface. Some participants indicated that this decision was outside the purview of the IRB, others indicated that the IRB did not have the expertise to make these decisions. Still other participants indicated that a moral obligation exists to divulge information if severe or life threatening or if an intervention was available. Several thematic areas are emerging: 1. the concern regarding the uncertainty and unreliability of research results; 2. the need for analytical and clinical validation of a research finding before returning results to a research subject; and 3. the desire for continued dialogue and a formal process to address this issue.

Significance: Return of individual genetic research results is a complex issue. If these themes remain prominent as our analysis proceeds, it may indicate an important area for policy development by organizations such as PRIM&R.

Additional Information
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Effects of Readability and Formatting on Recall of Consent Material Early and Late in the Semester
Authors: Rosemary Cogan; Michelle Gates; Angela Eaton

Background
If potential subjects do not know what they are being asked to do, the consent process becomes an empty ritual. To help make consent forms understandable, a reading level of 7th or 8th grade is recommended for adult subjects. Some also propose that “reader friendly” formats may facilitate consent form comprehension.

We carried out two studies of consent form comprehension. In Study 1, we assessed students’ ability to correctly answer questions about a consent form as a function of the reading level of the form. In Study 2, we assessed this ability as a function of both the reading level and the formatting of the consent form. In both studies, we also assessed students’ ability to correctly answer questions about the consent form as a function of whether they participated early or late in the semester.

Description of Research
Method: In study 1, 112 students in introductory psychology classes read a consent form written with a Flesch-Kincaid Grade level of 10, 13, or 16. In Study 2, 146 students in introductory psychology classes read a consent form written with a Flesch-Kincaid Grade level of 7 or 10 in one of three different formats. Participants in both studies then responded to a 10-item multiple choice questionnaire about the consent form.

Results: Students did not differ in the number of correct answers on the consent form questionnaire as a function of the reading level of the consent forms in either study. In Study 2, students’ scores did not differ as a function of the three formats. In both studies, students who participated late in the semester answered significantly fewer questions about the consent form correctly than those who participated early in the semester, $F (1,106) = 5.74$, $p = .02$ and $t (94.2) = 2.24$, $p = .03$ respectively.

Conclusion: While reading level and format of the consent form were not related to students’ comprehension of consent forms, in both studies, students who participated early in the semester answered more questions correctly about the consent form than those who participated late in the semester. Although this may reflect selection bias, students experience more stress late in the semester. Situations requiring informed consent are often stressful (e.g., medical situations). Students late in the academic semester may be a useful non-clinical sample for learning to improve consent form comprehension for people under stress.
Ethical Implications of Asking Sensitive Questions
Authors: Grant Benham; Kristin Croyle; Frederick Ernst

Background
Research on abuse, self-harm, sexual and illegal behavior, frequently requires subjects to respond to sensitive questions about their behaviors or attitudes. In assessing the risk of such human subjects research, it is important to evaluate the extent of subjective levels of discomfort and distress and the probability of such occurrences.

Description of Research
One hundred and fifty-seven undergraduate students read an informed consent document and completed an 80-question anonymous survey containing sensitive questions on various aspects of behavior and personal attitudes to taboo topics. Questions were based on yes/no, Likert-type, or numeric responses, and included the following:

- "If I could have sex with someone against their will, without any chance of getting caught, I would",
- "I believe that I was sexually abused between the ages of 6 and 12",
- "How many times have you deliberately hurt yourself without trying to kill yourself?",
- "During the past 2 years, approximately how many times have you driven a car or motorcycle while intoxicated?".

The final section of the survey included questions related to honesty of reporting, perceptions of anonymity/confidentiality, level of distress/discomfort experienced while completing the survey, desire to discontinue participation, and perceived ability to discontinue participation.

Results: While the vast majority of subjects experienced no distress or minor distress, approximately 4.5% reported that a number of the questions were quite distressing. Almost 6% felt that the level of discomfort or distress experienced whilst taking the survey was more than they might experience in their regular life. Importantly, none of the subjects who reported finding the questions quite distressing felt that the level of discomfort/distress was more than they might experience in their regular life. Through anonymous response, 6% of the subjects reported that they wanted to discontinue their participation at some point during the session and 15% felt that it would have been "Difficult" or "Very Difficult" to discontinue participation if they had wanted to.

Conclusion: These results suggest that while a small proportion of individuals may experience distress or discomfort answering sensitive questions, this distress may be no more than they experience outside of the research setting. The collection of such data during studies on sensitive topics assists greatly in quantifying probability and magnitude of harm and may be important in determinations of minimal risk. Our results also suggest that while a consent process may emphasize the notion of voluntary consent and freedom to withdraw participation, some subjects still feel that halting their participation would be difficult. Additional data is needed to determine the factors influencing the likelihood and extent of experienced distress. It is also critical that we examine methods to improve subjects' sense of agency in withdrawing participation.
Evaluation of the Quality of Informed Consent in Clinical Researches: Healthy Subjects  
Author: Ihnsook Jeong  

Background  
This study was aimed (a) to assess the quality of informed consent process, in particular, to measure subjects understanding of basic components of informed consent, (b) to identify correlates of increased understanding with demographic characteristics, experience of clinical trial participation, and characteristics of informed consent process (IC).  

Description of Research  
Methods: Convenience sample of 188 subjects aged 20 and above participated in bioequivalence studies by Inje regional clinical trial center, Busan. Study instruments were self-reported questionnaire, which were modified Quality of IC (QuIC) developed by Joffe et al (2001), and Informed Consent Questionnaire-4 items (ICQ-4) developed by Guarino et al (2006). Data were collected from Feb to May, 2007, and analyzed with descriptive statistics to assess the quality of informed consent process, and t-test, X2 test, and paired t test to identify correlates of increased understanding of informed consent using SPSS version 14.0.  

Results: All 188 subjects were male, mean age of 24 years, about 94% of college and more education. About 40% of subjects have participated in clinical trials more than once, and 48% of them remembered when they signed informed consent exactly. Mean QuIC objective knowledge score (QuIC-A) was 68.7(/100) and perceived (subjective) understanding (QuIC-B) 78.7 before participating in clinical trials, and 68.7 and 80.4 after participating in clinical trials respectively. General quality of informed consent (ICQ-4) was measured after participating in clinical trials, and score was 78.3(/100). Some questions were consistently answered poorly. There was low but significant correlation between QuIC-A and B (r=0.371, p=0.004). Higher objective knowledge (QuIC-A) were associated with age(25 years old and above, t=-2.040, p=0.043), and education (college and above, F=7.080, p=0.001), Higher QuIC-B scores were associated with past experience participating in clinical trials(t=-2.211, p=0.028), and memorization of date signed informed consent(t=2.101, p=0.037).  

Conclusions: Quality of informed consent process is not favorable and lower than other studies in the US and Australia. Strategies to improve subjects understanding of informed consent need to be developed. And it is recommended to do further studies with a variety of clinical trials to identify related factors with understanding of informed consent or quality of informed consent process.  

Additional Information  
This abstract has been presented at the 10th Asian Bioethics Conference in Tehran, Iran from 26-29, April, 2009
Exempt Determination at One U.S. University

Authors: Monika S. Markowitz, PhD; Elizabeth B. Ripley, MD, MS; Pamela Dillon, PharmD; Thomas Eissenberg, PhD

Background
45 CFR Part 46 describes 6 categories of human subjects research that are exempt from the federal regulations. The Office of Human Research Protections guidance suggests that investigators should not make the final determination regarding the exempt status of their research. At Virginia Commonwealth University (VCU), exempt determination is made by a single IRB, or otherwise qualified, reviewer. This study was designed to evaluate the number and categories of exempt research submitted at VCU, types of investigators, accuracy of investigator determination of exempt status, changes required by the reviewer prior to determination, and time required for determination of exempt status.

Description of Research

Methods: All protocols submitted as exempt research to the VCU IRB between January 1, 2007 and April 30, 2008 were examined. Descriptive statistics were used.

Results: 212 projects from a variety of disciplines, mostly from the schools of Medicine, Education, and Pharmacy, were submitted as exempt research. Of these, 10 were withdrawn and 4 were determined as not human subjects research. Of the remaining 198 protocols, 189 (95.5%) were confirmed by exempt reviewers to be exempt research and 9 (4.5%) were upgraded to expedited review due to reasons including collection of sensitive information or recording identifiable data. Most exempt research conformed to Category 1, 2, or 4. Although investigators were correct more than 95% of the time about exemption status, the accuracy with which they chose the specific exempt category varied, with particular challenges noted for categories infrequently utilized at VCU. Most submissions (174/189, 92.1%) required a change to retain exempt status, primarily to the protocol. The time between protocol delivery to the IRB and approval of exempt status averaged 41 days (range: 19-50 days, median: 33 days). The longest periods were the time required for the investigator to provide a complete submission (i.e., supplying missing measures or signatures) which averaged 12.8 days (range: 1-11 days, median: 4 days) and time for the actual review which averaged 26.4 days (range: 9-32.5 days, median 19 days).

Conclusions: VCU Investigators correctly identified their research as exempt in more than 95% of exempt submissions. Process evaluation shows that the time for determination of exempt status relies on 1) complete submissions by investigators and 2) timely communication, as needed, between reviewer and investigator with the goal of retaining exempt review status, if possible. This study provides support for a reconsideration of VCU’s exempt review submission process.
Genetics Research Review and Issues Project (GRRIP): Preliminary Results of a National Survey of IRB Professionals

Authors: William L. Freeman; Amy A. Lemke; Georgia L. Wiesner; P. Pearl O'Rourke; Wylie Burke; Karen L. Edwards; Genetics Research Review and Issues Project (GRRIP) Study Team

Background
Human genetic research engenders several concerns about scientific methods and human research protection (HRP). No study has systematically identified and compared those concerns among both genetic researchers and IRB professionals. The GRRIP consortium -- a partnership of University of Washington Center for Genomics and Healthcare Equality, Case Western Reserve University Center for Genetics Research Ethics and Law, PRIM&R, and American Society of Human Genetics (ASHG) -- addressed that gap. Our main objective was to determine and compare attitudes and experiences of genetic researchers and IRB professionals about HRP in genetic research.

Description of Research
The study had two phases: 1) individual, semi-structured, in-depth interviews with genetic researchers and IRB professionals; and 2) national surveys of members of PRIM&R and ASHG. We used the key informant interviews to develop questions with similar wording for two anonymous, web-based surveys (one for each group) that assessed experiences with and views about HRP review of genetic research. The questions in both surveys covered four major topics: IRB application process; IRB review process; IRB functions; and specific genetic research issues including risks of participant identification, return of DNA test results to participants, and when to re-consent. ASHG and PRIM&R leadership provided key input into recruitment methods and survey question content and wording, and then invited their members to participate. University IRB review and approval was obtained for this research. Results from the national IRB survey are presented here; results from the key informant interviews with IRB professionals and the national survey of genetic researchers are presented separately.

Result: We received 204/2,777 IRB survey responses by June 1, 2009. Selected preliminary analysis of responses included:

- 58% reported that broad consent was acceptable to their IRB;
- 70% felt it was important that IRBs provide guidance for developing DNA repositories;
- 36% felt the NIH guidelines for genome-wide association studies were clear; 33% didn't know;
- 35% felt it was likely that participants would be personally identified in a study with coded genetic data;
- 79% believed researchers have an ethical obligation to return individual research results from a CLIA-certified laboratory if results would affect a person's health or healthcare;
- 57% believed re-consent was needed if researchers later wanted to use genetic specimens for investigating a related but different condition, and
- 83% for investigating an unrelated condition.

Limitations: These results are a preliminary analysis of responses received by June 1, 2009. Next steps. The GRRIP partners plan to use the findings from both this survey and the national genetic researcher survey to help develop possible consensus recommendations about HRP review of genetic research.

Additional Information
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Genetics Research Review and Issues Project (GRRIP): Preliminary Results of a National Survey of Genetic Researchers

Authors: Georgia L. Wiesner; Amy A. Lemke; Patricia A. Marshall; William L. Freeman; Karen L. Edwards; Genetics Research Review and Issues Project (GRRIP) Study Team

Background

Protocols submitted to Institutional Review Boards (IRBs) for genetic research are increasing in number and complexity. A collaboration between the Case Western Reserve Univ. Center for Genetics Research Ethics and Law, Univ. of Washington Center for Genomics and Healthcare Equality, American Society of Human Genetics (ASHG), and Public Responsibility in Medicine and Research (PRIM&R) has sought to assess experiences with and attitudes toward the regulatory review of genetic research. GRRIP was conducted in two phases: 1) qualitative interviews of researchers and IRB members, and 2) national surveys of the ASHG and PRIM&R memberships. Our main objective was to determine and compare attitudes and experiences of genetic researchers and IRB professionals about human research protection in genetic research.

Description of Research

Methods: An anonymous, web-based survey was sent to the ASHG membership in April 2009. The survey included questions on experience with the genetic research application and review process, views toward specific genetic research issues, and basic demographic information. A survey with identical thematic domains was simultaneously sent to the PRIM&R membership. University IRB review and approval was obtained for this research. The results from the ASHG genetic researcher membership survey are presented here, while results from the PRIM&R survey are reported separately.

Results: 368 of 4,908 ASHG members have responded to the online survey. The majority of respondents are female (54%), U.S. based researchers (82%), and involved in research as their primary activity. Most respondents (48%) reported 15 years or more experience in conducting human genetic research studies. Issues related to consent of subjects has caused considerable discussion with their IRB (51%), followed by procedures related to protecting personal information of research participants (35%), and return of results to participants (31%). When asked about whether a genetic project involved human subjects, 79% of participants indicated agreement with their IRB. However, 20% of participants indicated that there is disagreement with their IRB with regard to level of review required (eg either expedited or full review) for a genetic study. Finally, participants felt that review of research protocols should not be different for human genetic protocols. Limitations. These results are a preliminary analysis of responses received by June 1, 2009.

Next Steps: The GRRIP partners plan to use the findings from both this survey and the national IRB professional survey to help develop possible consensus recommendations about human research protection review of genetic research.

Additional Information

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Hope’s Role in Decision Making for Cancer Research Participation
Author: Kathleen Shannon Dorcy

Background
In my years as a research nurse I often encountered patients who said things like, "I am so happy I had the opportunity to meet you and be involved in this research, it gives me such hope." These statements lead me to draw the conclusions that research needs to be done in reference to explore the role of hope in decision making for participation in cancer research.

Description of Research

Question: Hope is an acknowledged dynamic in decision making of people relative to why they decided to participate in cancer research. Hope is a practice that is actively engaged in by health care providers, patients, & family members involved in cancer care & hope is generally assumed to be a positive influence in this process. Could hope actually be a coercive element in decision making in the informed consent process for participation in clinical research?

Methods: A descriptive study was undertaken to analyze interviews of 25 patients, 20 family caregivers & 10 attending physicians in a quaternary cancer research center to evaluate the employment of hope as an element of language when discussing decisions to participate in Phase II clinical research trials. Interviews were tape recorded transcribed analyzed using content analysis and discourse analysis to understand how hope was co-created in the interviews. How the word hope was articulated, either as a verb, or a noun often was indicative of how patients envisioned their current status. "Hoping" was generally contextualized by individuals who still felt that a cure was possible & that they had an active role in the course of their own care. Hope as a noun, as in the phrase, “my only hope” often represented a patient’s feeling of powerless in the situation & the passive role they could play in the course of their care. Informed consent is a legally mandated process that is to be free of all elements of coercion. Research participation requires patients must be consented under the strict regulatory guides lines of the Code of Federal Registration (CFR) 45 § 16:124. Intertextuality is a key concept in this ongoing analysis “for any text there is a set of other texts and a set of voices which are potentially relevant & potentially incorporated into the text” (Fairclough). This refers not only to the attributed voices of others but also to the pervasive voice, or even hegemonic presence of other texts & language used in re-contextualization in each text/discourse.

Conclusions: Shared historical/cultural meanings facilitate the co-production of hope between researchers and patients. The implicit assumption that hope is a good thing and a value for people, may have unacknowledged potential power in the care of people with cancer. Hope may be a dialectic concept inculcating suffering rather than relief from suffering. More analysis is needed to explore the role of hope in decision making.

Additional Information
I am a doctoral student at the University of Utah and have chosen to study hope because it is powerful shared co-creation between patients, family members and cancer care providers. it is vital that we begin to understand how powerful hope is in discussions with patients in both explicit and implicit levels of discussion. Hope is not to be diminished by my work rather it is to be safeguarded and honored. It is in recognition of the power of hope that we are able to consciously avoid placing patients in positions of undue risk or coercion for research participation by virtue of our own personal investment in hope.
Improving Recruitment in Clinical Trials: Why Eligible Participants Decline
Authors: Julie Brinnall-Karabelas; Mary Ellen Cadman; Susanna Sung; Carol Squires; Katherine Whorton; Maryland Pao

Background
Although the general public expects researchers to develop innovative treatment approaches, the recruitment of participants into clinical trials continues to be a challenge. What are some of the deterrents to research participation for subjects who met basic inclusion criteria for mental health studies?

Description of Research
Methodology: From 2001-2008, the Centralized Office of Recruitment Evaluation (CORE) performed prescreening interviews of potential research subjects who initiated contact with NIMH with a request to be evaluated for inclusion in clinical trials. There were 977 individuals found to be eligible for inclusion in clinical trials who ultimately chose not to participate in research.

Results: By self-report, responses of individuals who chose not to participate fell into the following categories: a result of specific protocol requirements (34%), inconvenience (33%), financial reasons (3%), decided to participate in research elsewhere (2%) and, lastly, for other reasons not mentioned above (29%). Conclusions: There are a variety of issues that researchers should take into consideration when developing protocols. If investigators want to increase research participation, they need to understand what makes subjects decline participation after proving eligible. Potential subjects report they are more willing to participate in trials if they are: offered in an outpatient setting, conducted over a shorter period of time, have less intrusive and/or time consuming procedures, provide compensation, made available outside of the typical work schedule, have more flexible inclusion/exclusion criteria and if they offer novel treatments.

Limitations: A limitation of this study was that the categories of decline were limited in scope when collected as the primary purpose of the database was to maintain screening data.

Next Steps: Biomedical research facilities would benefit from including detailed screening follow-up questions that identify the specific reasons potential subjects decline participation in studies even after self-initiating contact and being determined to be eligible for research participation in mental health studies. Further investigation could identify modifiable factors to promote recruitment within clinical trials.
Incarcerated Youth: Reactions to Participation in Suicide & Self-Harm Research
Authors: André Ivanoff, PhD; Henry Schmidt III, PhD; Hillary Nammack, MS

Background
Incarcerated youth are multiply vulnerable and require special protections in research. Introducing the topic of suicidal behavior suggests even greater sensitivity is needed in reviewing such research, however no data exist on this topic. This study addresses the reactions and understanding of this population to participating in a research study concerning self-harm and suicidal behavior.

Description of Research
Following the pilot validation of the newly developed “Suicide & Self-harm Scale” (Schmidt, Ivanoff et al.) conducted by the Washington State Juvenile Rehabilitation Administration (JRA), this study was undertaken to explore youth reactions to participating in this research and their understanding of research in general. All youth still in residence (49 of 67) were approached, invited to participate, and then reassented: 47 youth participated. Youth were administered the Reactions to Research Participation Questionnaire (RRPQ-C; Kassam-Adams & Newman, 1998) and 8 focus groups were held across the four youth institutions. Themes represented in the focus group included general understanding of research, recall of participation, voluntariness of participation, harm or benefit of participation and general views of conducting research with incarcerated youth.

Results of both the RRPQ-C and focus group transcripts indicate that the large majority of youth had positive appraisals of their participation, felt informed about the study and not coerced to participate, and did not feel answering the questions about suicide and self-harm was personally harmful. Further, some youth were able to articulate benefits to others that might come from such participation and a majority indicated they felt good about contributing in this way.

More information is needed about youth understanding of research and about participation in other types of social & behavioral research. Given the lack of published research on research participation with incarcerated youth, results of this study will hopefully be used to help inform questions frequently posed by IRBs reviewing protocol with this population. A larger participation study is also underway at JRA, expanding and extending these findings.
Inclusion of Men in Clinical Trials: Do Interventions Pose Risk to Offspring and Should Men Use Contraception?

Authors: Maria Rita Vieira; Pamela Stratton; Izabella Khachikyan; Christina Gonzales; Marnie Wagner; Lindsey Magaw; Shannon Liu; Tajana Pulanic; Patricia Battuello; Asma Idriss; Barbara Karp

Background
It is widely assumed that fetal malformations are caused only by mutations in female germ cells. Recently, it has been shown that damage to the sperm due paternal drug exposure may adversely affect their offspring. Moreover, some drugs stored in adipose tissue are released long after drug dosing. Such drug exposure may pose risk to men planning to father children. The purpose of this study is to determine 1) what interventions or drugs can damage male germ cells and thereby cause fetal harm, and 2) to evaluate if clinical trials with interventions posing such risk require contraception during the exposure period.

Description of Research
Materials and Methods: Articles published between 1983-2005 were searched through Scopus, PubMed and DART using key words: “teratogens AND paternal or paternal exposure or semen or spermatozoa or sperm” to identify drugs and interventions mutagenic to male germ cells. Protocols and consent forms from NIH Intramural clinical trials were reviewed to determine if the risk to offspring were identified and if contraceptive use was required.

Results: Literature review identified 3 main sources of risk to male germ cells: chronic use of cytotoxic drugs, and high dose radiation or heavy metal exposure. For example, male rats treated with alkylating agents (cyclophosphamide or methylnitrosourea) sired fewer live offspring and survivors often had behavioral abnormalities and somatic malformations. Radiation exposure in male mice caused skeletal abnormalities in their offspring. Of 262 clinical trials including men, 80 used an intervention of risk to sperm. 17 specifically acknowledged this risk in the protocol. 45 required men to use contraception.

Conclusions: 1) The literature documents the teratogenicity of paternal exposure to certain drugs and radiation. 2) Research studies with such interventions should require male contraception; however the use of contraception was not consistently addressed in studies we reviewed. The safe conduct of trials posing risk to sperm should: 1. Specifically acknowledge the potential risk to male germ cells and future offspring; 2. Require contraceptive use during treatment phase and beyond, when appropriate.

Next Steps: Our results highlight the need for a standardized approach to studies using interventions of risk to spermatogenesis.
Inclusion of Minors of Childbearing Potential in Clinical Trials - Pregnancy Testing and Contraception

Authors: Maria Rita Vieira; Pamela Stratton; Christina Gonzales; Izabella Khachikyan; Shannon Liu; Lindsey Magaw; Marnie Wagner; Tajana Pulanic; Patricia Battuello; Asma Idriss; Barbara Karp

Background
Protections for women of childbearing potential in clinical trials must extend to minors. There may be concern that discussions of sexual activity, pregnancy testing and contraception are inappropriate for minors, however, investigators have an obligation to inform children and adolescents of the requirements and risks of research studies, appropriate to the participant’s level of understanding. The purpose of this study is to determine if clinical trials enrolling girls of childbearing potential (GOCP) 1) identify potential risks to GOCP/fetuses; 2) perform pregnancy testing; 3) have a plan for reporting pregnancy test results; and 4) inform minors and their parents of any requirement for contraception.

Description of Research
Materials and Methods: NIH Intramural on-site clinical trials that included minors and presented risk to GOCP/fetuses were reviewed. Each protocol, consent form, and minor assent form was reviewed by two independent reviewers and reconciled into a single dataset using NICHD Clinical Trials Database software.

Results: 103 studies included female minors. All studies excluded pregnant women. 94% exposed girls to a study drug or risk for ≥ 1 month; in 6% the exposure to a drug or intervention of risk was episodic. The risk was acknowledged in 69 % of protocols, 73% of parental consents and 23% of assents. Pregnancy testing was done at entry in 88% and during the study in 65% of trials. Contraceptive use was required in 64% of protocols with non-episodic risk and was mentioned in 68% of parental consents and 17% of minor assents. 29% of assents stated that pregnancy test results would be reported only to the minor and 31% stated that both the minor and parents would be informed. The remaining assents were silent on who would receive test results.

Conclusions: The protections of pregnancy testing and use of contraception were inconsistently applied in studies enrolling minors of child-bearing potential and irregularly conveyed to participants and their parents. Limitations: This single-site study should be verified through review of protocols, consents and assent forms from other institutions.

Next Steps: Our results highlight the need for a standardized approach to research with girls of reproductive age. The safe inclusion of adolescent girls mandates informing subjects of potential risks and protections, including pregnancy testing and contraception. Investigators must be prepared to handle complex and sensitive issues regarding teen sexuality and communication with their parents.
Information Overload: The Effect Of A Shorter Form On The Quality Of Informed Consent
Authors: Leanne Stunkel; Meredith Shannon Benson; Dr. Gabriella Bedarida; Dr. Ezekiel Emanuel; Dr. Christine Grady

Background
Many interventions intended to improve the quality of informed consent have been tested in patient volunteers, but Phase I healthy volunteers are understudied. Healthy volunteers may differ from patient volunteers in both their motivations to participate in research and their values. These differences may affect their experience of the consent process and their comprehension of study information. The objective of this study is to evaluate the quality of informed consent in healthy volunteers who receive 2 different consent documents in a Phase I study. We hypothesized that volunteers would (1) have the same level of comprehension after reading either consent form, and (2) be more satisfied with the concise consent form.

Description of Research
Methods: Subjects included all 140 volunteers screened for a specific Phase I clinical trial. Each of the individuals screened participated in our survey study, but one left the survey blank. Participants were randomized to a standard or concise consent form which differed by number of words, length and complexity of sentences, and readability level. After reading the form, participants completed a questionnaire designed to assess motivations, comprehension of study information, satisfaction with the consent form, and demographic information. Chi-square analysis was used to determine statistical significance between the two groups, and 0.05 was used as a benchmark for significance. The project had IRB approval.

Results: The two groups were similar on demographic variables. Understanding was high; means scores were 11.1/15 for the standard consent group and 11.5/15 for the concise consent group. There was no significant difference in comprehension or satisfaction with the forms between the two groups. Out of several demographic variables assessed, only increased education correlated with higher comprehension scores. Most participants’ primary motivations were financial (68% reported financial motivations). The mean comprehension score was significantly higher for participants who reported primarily financial motivations (12.0) than for those who reported primarily non-financial motivations (10.3, p = 0.0005). No participant who reported financial motivations scored below a 5/15. There was no correlation observed between previous research participation and higher comprehension scores.

Limitations: Our results may not be generalizable to participants in all Phase I studies. Finally, the concise consent and the questionnaire were written by the same investigators, which may have introduced an element of bias.

Next Steps: We are planning a similar study as part of a Pfizer First in Human study, and will revise the questionnaire to add some more difficult questions.
Investigator Dissatisfaction with the IRB Approval Process
Authors: Steven Pennell, MBA, MA; Dr. Ronald Maio; James Lepkowski, PhD

Background
Little empirical data, but much anecdotal information, characterize researcher experience with the human subjects regulatory system. The 2002 Institute of Medicine report, the 2003 National Research Council report, the 2005 Illinois White Paper, and the associated 2006 editorial in Science recommend collection of empirical data to guide HRPP operations, yet more progress is needed. Empirical data that reflect investigator experience with the regulatory system are important because: 1) the approval process is the core service IRBs provide to researchers; 2) perceived or real difficulty strictly following approved protocols may lead to disrespect, noncompliance, or scofflaw behavior; 3) IRBs facilitate the research mission of Universities and collectively affect the nation’s research enterprise. This research contributes to advancing knowledge about how researchers experience the human subjects regulatory system by asking: 1) what is the relationship between time to approve an application and researcher dissatisfaction with the IRB’s core service; 2) what are other correlates of dissatisfaction with the IRB approval process; 3) are these correlates system-related, characteristics of researchers, or both; and 4) what is the strength of the relationship among these correlates and investigator dissatisfaction?

Description of Research
To answer these questions the University of Michigan’s Institute for Social Research conducted an IRB-approved scientific survey among 1,800 Ann Arbor campus investigators in late Fall, 2007. The overall response rate for the web-based survey was 46%. Extensive focus groups preceded the survey to develop topic domains. A separate analysis indicated no nonresponse bias. Results from multivariate logistic regression modeling indicate several statistically significant outcomes: 1) investigators support the concept of ethical/regulatory review of research but take exception with how IRBs operationalize it; and 2) dissatisfaction with the IRB approval process is significantly associated with system-related outcomes and attitudes shaped by those outcomes. The time to approve applications is a key determinant of dissatisfaction: the odds ratio of dissatisfaction increases dramatically when approval times exceeds 4 weeks when controlling for other covariates in the model. Other significant system-related correlates are unanswered investigator inquiries to the IRB; IRB-required application changes; and difficulty using the application system. Attitudes like the perceived usefulness of IRBs and whether IRBs are regarded as allies also are important predictors. Investigator demographics are unrelated to dissatisfaction. The results suggest that reducing dissatisfaction with the IRB approval process will require recalibration of system-related features of HRPPs, above all reducing the time to approve applications. Examples will be provided. Repeated surveys will begin in Fall, 2009 to monitor system changes and their affect on key outcomes, including dissatisfaction with the IRB approval process.

Additional Information
A national survey is planned.
Medical Students and Research Ethics: Micro-Survey in Ufa, Russia
Author: Leyla Akhmadeeva

Background
Research ethics is still a new subject for medical students in Russia. It has to be taught briefly in the course of Bioethics, which is a compulsory part of the standard program required to be followed by all medical and dental schools in Russia. This subject has to be taken before students start clinical subjects (close to what you call "pre-med" in the US). Analyzing Russian medical papers I found out that the authors are often not aware of many simple ideas that have to be learnt at the university. That's why I did this small survey to get some evidence about knowledge of senior medical and dentistry students at our University in some problems of research ethics.

Description of Research
I put together a short questionnaire and distributed it to medical and dentistry students of the first year of clinical study and the final year – just before their graduation. I collected filled our questionnaires from 127 students. The questionnaire was printed out on paper and contained simple questions with 2 alternatives of answers ("yes" and "no"). Students were asked to mark the answer that they think applied. Nobody had to sign their names. The data showed that one student did not mark the answers clearly, so I manually analyzed the answers of 126 students.

Results: Although all students studied together the same disciplines, just less than a half (45.2%) answered positively to the question if they have ever had studied ethics of research involving human subjects (HRS). Four students (3.2%) left this field blank and I decided that they were not sure, but 65 (51.6%) students wrote that they have never studied it. Majority of students (84.1%) thought that HRSs have to be informed in details about the goals and the procedure of the research. The students' opinions about the right of a HRS to leave the trial without explaining the reason for this were different: 94 of them (74.6%) replied that a HRS has this right and 31 (24.6%) thought that (s)he doesn't. Fifty three (42.1%) students were sure that they can use the materials and data from HRSs when they are not aware that they participate in a trial.

Conclusion: Although this was a short pilot survey, I conclude that students at our medical university have limited knowledge about the basics of research ethics. Research ethics has to be taught more and better, and to include case discussions that students will remember.
Not Just About Money: A Review Of The Literature Examining Self-Reported Motivations And Decision-Making In Healthy Volunteers
Authors: Leanne Stunkel; Dr. Christine Grady

Background
We examined the literature on the motivations of healthy volunteers, and how participants reconcile competing motivations to make judgments about participation. Even among the recent literature on healthy volunteer motivations, little attention has been paid to decision-making processes, especially healthy volunteers’ assessment of the risks and benefits of participation. The purpose of this review is to summarize and characterize the current state of the literature on the self-reported motivations of healthy volunteers, and identify data on how participants make decisions about participation and weight risks and benefits. We hypothesize that healthy volunteers’ motivations for study participation are primarily financial, but that this financial motivation is often only one among others. Other factors, such as risks and trade-offs play a role in the decision-making process.

Description of Research
Methods: We performed a systematic search of PubMed for all studies which measured self-reported motivations of healthy volunteers to participate in research. We restricted results to English-language articles. The list was expanded using personal contacts and hand searching. Forty-two relevant articles were identified. Studies which measured motivations indirectly (willingness to participate, etc.) were excluded.

Results: Healthy volunteers are not motivated solely by financial remuneration. Only 9 of the 42 studies identified financial remuneration as the volunteers’ primary motivation. In fact, 22 of the 42 studies identified altruism to be the volunteers’ primary motivation. Several other studies identified volunteers’ primary motivations to be for personal benefit or the benefit of a family member or mixed motivations. Our final analysis will also take into account data on participant decision-making.

Limitations: This study only captures data on the self-reported motivations of healthy volunteers, so it is limited by participant reporting bias. Additionally, it is difficult to make comparisons between different types of studies, such as qualitative versus quantitative studies, studies of participants in a real study versus a hypothetical study.

Next Steps: We have secured IRB approval for an empirical study of healthy volunteer motivations for participation in Phase I drug development trials. The study will assess the motivations of healthy volunteers in three distinct countries who are participating in Phase I drug trials sponsored by Pfizer, and the factors they consider when making decisions about participation, as well as how these factors are related to certain sociodemographic characteristics of participants. We aim to determine the magnitude and nature of the motivating effect of financial compensation, and to identify the type and importance of other motivating and limiting factors.
Parental Attitudes Toward Pediatric Biobanks  
Authors: Jody Harland, MS, CIP; Lucy Miller, RN, BSN, CCRC; Eric Meslin, PhD; James Wolf, MA; Scott Denne, MD

**Background**
IRBs increasingly review research protocols which propose the creation of biorepositories (or “biobanks”); however, due to the scientific and ethical complexities of such studies, it can be difficult for IRBs to discern what concerns potential subjects may have relative to their participation and thus, what information should be conveyed to subjects. The establishment of pediatric biobanks can be more challenging due to the additional ethical and regulatory concerns about involving children in research. IRBs rarely have actual data available as to how such pediatric biobanks are viewed by families. As a result, this study sought to survey parents/guardians about their attitudes toward pediatric biobanking research. Research questions included whether parents/guardians have particular areas of concern about participation in a biobank and whether there was there any difference between the perspectives of parents/guardians of inpatients and outpatients. Our hypotheses were that areas of concern would relate to confidentiality and commercialization and that parents/guardians of inpatients would be more in favor of biobanking research than parents of outpatients.

**Description of Research**
**Method:** Survey questions were developed by a multi-disciplinary group (including physicians, nurses, a survey research expert, parents, a bioethicist, and an IRB expert) and were field tested. Parents/guardians of pediatric inpatients and pediatric outpatients at a large Midwestern children’s hospital were offered paper-and-pencil surveys in person.

**Results:** A total of 2179 surveys were returned (response rate of 72.9%). Results showed virtually no differences in response between parents of inpatients and outpatients in any category. Broad support for pediatric biobanking was noted regarding the parents/guardians’ allowance of their child’s blood to be included in a hospital biobank (80.3% ‘agreed’ or ‘strongly agreed’). Areas of concern included general opposition to the commercialization of biobank samples (61.4% were ‘opposed’ or ‘strongly opposed’ to such arrangements). Contrary to our hypothesis, respondents indicated that they trusted the institution to maintain their confidentiality (90.9% ‘agreed’ or ‘strongly agreed’). Respondents were generally concerned about commercialization, trusted the institution to maintain confidentiality, and were supportive of biobanking initiatives.

**Conclusion:** IRBs can use this data to inform their reviews of pediatric biobanking protocols. Due to the nature of a paper-and-pencil survey, limitations related to response bias and literacy may exist. We will share the results of this study with IRBs and plan to conduct focus groups with parents and children in an effort to obtain more detailed, qualitative information about attitudes toward pediatric biobanking.
Paying Research Participants: Preliminary Results of Two National Surveys
Authors: EBD Ripley; M Markowitz; F Macrina

Background
National and international guidelines provide guidance for paying research participants which is minimal at best and vague at worst. Ethical debate has both supported and questioned paying research participants. We are investigating the opinions, attitudes and practices toward paying research participants. To this end we are conducting, two national web-based surveys that collect such information from 1) NIH funded principal investigators and, 2) IRB Chairs

Description of Research
Methods/Results: Surveys have been completed by 442 investigators and 338 IRB Chairs. Investigators had a mean age of 48 years with 51% males. IRB Chairs had a mean age of 54 years and 61% were males. Both investigators and IRB Chairs viewed compensation for time spent (e.g., clinic visits, and procedures) as the primary purpose for paying participants. Forty percent of investigators and 35% of IRB Chairs thought that the risk of the study was extremely important in determining payment. There was agreement that reimbursement for expenses, compensation, and as an enrollment incentive were important reasons for payment. While investigators felt payment was important as a show of appreciation, IRB Chairs were divided on this reason. When considering study related factors for determining payment, investigators agreed that budget and anticipated difficulty recruiting were important factors and that the funding source was not important. However, they were divided on the importance of payment to attain the number needed for enrollment. IRB Chairs agreed that the anticipated difficulty of recruiting was important and that budget, funding source, and the number needed for the recruitment goal were not important in determining payment. Neither group thought that the income of the participant or the demographics of the study population were important in determining payment. Investigators and IRB Chairs recommended similar ranges of payment for specific study procedures such as clinic visits, blood samples, and overnight stays. There were only minimal differences between payment recommendations for therapeutic versus non therapeutic research. IRB Chairs relatively evenly represented panels that primarily reviewed biomedical and social-behavioral research. Seventy three percent had only 1 IRB at their institution. Nine percent of IRB Chairs said that the IRB panel never questioned the payment amount while 10% stated they always did. Payment not being clearly defined in the protocol was the most common reason for questioning the payment. Eighty eight percent required notice of the payment to be described in the consent and 60% included this in a separate section. For studies involving children, 33% said the payment was specified in the assent and 55% said it was in the parental permission form.

Conclusion: While most factors and reasons for paying participants suggested general agreement as to importance, opinions do cover the spectrum. Further evaluation of these survey results are planned and are expected to help shape national practices in paying research participants.
Policy Development On Inclusion Of Subordinate Employees In Clinical Research: Identification Of Risks And Safeguards

Authors: Barbara Karp; Maria Rita Vieira; Marjorie Gillespie; Jennifer Morris; Alex Noury; Michael Chapple; Marnie Wagner; Marion Danis; Christine Grady

Background
Inclusion of an investigator's subordinates as research subjects poses ethical issues. 45 CRF Part 46 does not address this potentially vulnerable population. The Office for Human Research Protections (OHRP) considers research with employees to raise the same concerns as that with students, especially the prevention of coercion/undue influence and protection of confidentiality and free choice. In this review we surveyed research institutional policies to identify risks and to suggest guidelines to mitigate the risks.

Description of Research
Materials and Methods: We searched Google for policies on the inclusion of employees and subordinates in clinical research. We randomly selected 10 research institution policies for analysis. We independently identified additional risks associated with subordinate participation.

Results: All 10 institutions permitted research participation of employees. All stated that participation should be voluntary and free of coercion/undue influence. 8 policies placed employees in the same category as students, 8 identified compromised confidentiality as a potential risk, and 2 required that those who decline participation not be identified. 8 policies restricted recruitment to outside the presence of the supervisor. No policy explicitly addressed the participation of an investigator's subordinates. We independently identified the following concerns related to subordinate participation:

1. Coercion. Refusal may appear to jeopardize one's position as part of the research team. Conversely, agreement may appear to confer benefit, such as a financial bonus, better rating or more resources.
2. Conflict-of-interest. Subordinates have a stake in the success of the study and may be in a position to influence the outcome.
3. Privacy and confidentiality. The research may involve revealing sensitive information (e.g. HIV status, sexual activity, drug use, criminal activity) to co-workers or sensitive procedures (e.g. disrobing).
4. Scientific integrity and subject safety. Subordinates may under-report adverse effects so as not to jeopardize a supervisor's research.

Conclusion: The policies reviewed permitted employee participation in clinical research with varying protections. None of the policies reviewed addressed the ethical concerns raised by subordinate participation. We propose that subordinates should generally be excluded from research conducted by their own supervisors. An exception may be appropriate, however, for research that offers the prospect of direct therapeutic benefit.

Next Steps: Institutions conducting research should consider developing policies regarding the participation of the investigators’ subordinates in research studies.
Public and Biobank Participant Attitudes Toward Genetic Research Participation and Data Sharing
Authors: A.A. Lemke; W.A. Wolf; J. Hebert-Beirne; M.E. Smith

Background
Research assessing attitudes toward consent processes for high-throughput genomic-wide technologies and widespread sharing of data is limited. In order to develop a better understanding of stakeholder views toward these issues, this cross-sectional study assessed public and biorepository participant attitudes toward research participation and genetic research data sharing.

Description of Research
Study Objectives: The study objectives are:

1) to obtain in participants’ own words their attitudes toward collecting, analyzing and sharing genetic research data;
2) to compare attitudes between biorepository participants and the public; and
3) to offer recommendations for the consent process and sharing of genetic research data.

Methods: Six audiotaped focus groups (6-10 participants in each group) were conducted, including 3 NUgene biorepository participant groups and 3 general public groups in Chicago, IL. In addition, all participants completed a brief background information survey.

Results: Forty-nine individuals participated in six focus groups; 21 in three NUgene biorepository focus groups and 28 in three public focus groups. In the public focus groups, 75% of participants were women, 75% had some college education or more, 46% were African-American and 29% were Hispanic. In the NUgene focus groups, 67% of participants were women, 95% had some college education or more, and the majority (76%) of participants were Caucasian. More than half (56%) of the NUgene focus group participants were somewhat or very concerned about the confidentiality and privacy of medical information compared to 46% of the public group participants. Overall, approximately 75% of focus group participants were neutral or somewhat trusting of medical research. Five major themes were identified in the focus group data: 1) a wide spectrum of understanding of genetic research; 2) pros and cons of participation in genetic research; 3) influence of credibility and trust of the research institution; 4) concerns about sharing genetic research data and need for transparency in the National Institutes of Health (NIH) Genome-wide Association Study (GWAS) Policy; and 5) a need for more information and education about genetic research.

Conclusions and Next Steps: In order to increase public understanding and address potential concerns about genetic research, future efforts should be aimed at involving the public in genetic research policy development and in identifying or developing appropriate educational strategies to meet the public’s needs. Findings from this research will be used to inform key professional groups regarding concerns and potential changes needed in the consent and genetic research data sharing process.
Quality of UPIRSO Reporting in Cancer Drug Clinical Trials
Authors: Steven M. Belknap, MD; Christina H. Georgopoulos, BS; Paul R. Yarnold, PhD; William N. Kelly, PharmD; Dennis P. West, PhD

Background
Timely identification of previously undetected safety signals during clinical trials is an important unsolved problem. Approximately 20% of drugs approved by FDA are withdrawn or acquire a new black box warning after approval. Moreover, there is widespread public reporting of failure to detect and disseminate knowledge about serious adverse events. Our hypothesis is that current safety signal detection systems are inadequate.

Description of Research
Instruments used to detect, assess, and report UPIRSOs to IRBs have not been adequately studied as a possible cause of widespread safety signal detection failure. This study evaluates instruments used to report UPIRSOs to IRBs at all NCI centers as of 2007. We obtained copies of instruments from all 49 NCI centers & assessed them for utility in abstracting UPIRSO type, severity, and causality; pt demographics and safety monitoring; and consequent study conduct changes. Additionally, each form was awarded a score in two categories: “event description utility” (34 items) and “oversight description utility” (21 items). The “event description utility” score was a sum of the items within the categories of “the event description” (type, expectedness, seriousness, and patient outcome) “event severity”, “causality”, and “patient demographic descriptors” that were present on each form. The “oversight description utility” score was a sum of the items within the categories of “data safety monitoring information” and “changes to protocol and associated documents” that were present on each form.

A panel of experts formed the minimal dataset to define the key elements to describe the event and assess severity and causality. This dataset was used to develop a model adverse event form. Of 55 items considered essential for UPIRSO reporting, only 1 (event description) was present on all forms. 78% prompted for global introspection of the investigator, a method known to be unreliable. Only 7 centers had UPIRSO forms prompting the use of CTCAE taxonomy for description of event type and severity. Only 41% prompted for an assessment of event severity, & only half prompted for pt outcome. None used a validated method for assessing causality. >¼ of forms failed to prompt for causality. 2/3 of the forms did not prompt for demographic & clinical descriptors; ¼ did not prompt for a subject ID code, and ¼ did not prompt for whether the UPIRSO resulted in consent form revisions. These omissions effectively sever the link between UPIRSO reporting and source documentation, hampering oversight and auditing efforts of the IRB. Use of a validated tool to describe and assess event type, severity, and causality may lead to more timely, accurate identification of significant safety signals in cancer treatment. Electronic systems may make validated instruments for UPIRSO abstraction more available, eliminate considerable paperwork in clinical trials, facilitate data collection and subsequent audit trails, and standardize UPIRSO reporting.

Additional Information
Sample size was complete in that it included all 49 NCI-designated cancer centers. Frequency distributions were calculated for the number of forms that prompted for answers for each item within a category. - see abstract - Limitations include ongoing improvements in electronic UPIRSO reporting to NCI that were not implemented in 2007. - Next steps include validation of the model reporting form developed in this project for improved quality and accuracy of safety signal detection and reporting.
Research Participant Survey Project Part I: Focus Groups to Define Relevant Dimensions of the Research Participant Experience

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Background
The self-described experiences of research participants may be excellent indicators of the ethical treatment of individuals in research, and of why participants stay or leave research participation. To identify dimensions of the research experience important to participants for the purposes of deriving and validating an outcomes survey instrument for broader fielding, a multi-center study was designed to conduct focus groups of research participants at the Rockefeller University, the Clinical Center of the National Institutes of Health, and at 6 additional CTSA/GCRC research centers.

Description of Research
Methods: Individuals enrolled as research participants within the prior two years were recruited to enroll into one of 12 focus groups in 3 categories: 1) individuals affected by a disorder under study; 2) individuals participating in a natural history study; and 3) individuals enrolled as normal/healthy volunteers. Research professionals in the areas of 1) IRB members/ethicist/RSA; 2) Research nurses/coordinators; and 3) investigators were recruited into 6 additional focus groups. Target enrollment was up to 92 research participants and 48 research professionals. Written informed consent was obtained/waived, according to the local Institutional Review Board. A single moderator conducted the participants’ focus groups across all centers but one. The professionals groups were all moderated by a second moderator. One of two observers attended all focus groups but one. The proceedings of focus groups were audio taped, and transcribed at NRC Picker, Inc where the names of individuals and centers were redacted. Transcripts were analyzed using NVivo software, and coded into planned categories based on the moderator’s guide.

Results: From May–November 2008, 85 research participants and 29 professionals participated in 18 focus groups at 8 centers. Participants were 45% male, age average 49.9 yrs (range19-86)), 58% white, 28% African American, 2% Asian, 2% Native American, 9% unspecified; 93% were not Hispanic. Participants’ experience with clinical research ranged from 1 to 20 studies, or more. Protocol types varied widely. Findings clustered around 16 main themes. Participants take part in clinical studies for a variety of reasons, often in combination. Altruism emerged as the most common reason. The four next most common reasons included the personal relevance of the study topic, for anticipated learning related to interest or health, to access new therapies, and financial compensation. Participants widely expressed disappointment if they did not receive individual test results during or after the study. Participants most often said they were happy with the Informed Consent process. The most commonly appreciated aspect of being in a study was the relationship that participants developed with the research team. This theme stands out as the strongest theme in the entire study. The focus was on the caring, respectfulness and responsiveness of the staff, often in the context of a long term relationship, and was cited as a reason to stay in a study.

Limitations: African American and Latino populations were somewhat underrepresented in the focus groups. The Western and southern parts of the US are not represented by the sample. The focus groups were conducted in English, potentially excluding non-English speaking research volunteers, though based on preliminary discussions, non-English speaking individuals are under-represented in research overall.

Next Steps: A survey instrument has been drafted and will be fielded in 2009-10 to approximately 5,000 research participants at 15 centers for validation and benchmarking purposes. The larger fielding/validation study will include a broader demographic.
The IRBs in Taiwan: A Status report 2008
Authors: Kwai-Fong Lee, MA; Hsiang-Ning Luk, MD, MS, PhD, CIP; Wen-Ta Chiu, MD, PhD; Wei-Hwa Lee, MD, PhD; Der-Zen Liu, PhD

Background
In the past ten years, there are nation-wide discussions and concerns about rights and safety of human subjects participating in clinical researches in Taiwan. Therefore, Department of Health (DOH) had launched Guidelines for the Organization and Operation of Medical Institutional Review Board (IRB) in late 2003. Taiwan Joint Commission on Hospital which was authorized by DOH accredited 26 IRBs during 2007 and WHO-SIDCER-FERCAP Recognition program recognized 16 IRBs from 2005 to 2008. We can see IRBs endeavor to reach global standard. However, there is no specific data to understand the clinical research scale in Taiwan and what kind of review is the majority. To answer this question, we focused on 16 IRBs, which were both accredited by DOH and FERCAP-SIDCER, and analyzed the composition, submission flow chart, review process, meeting frequency from website. These IRBs provided initial submission number of 2008 and categorized it into expedited and convened review.

Description of Research

Results: All these IRBs have sufficient Standard Operation Procedures, independent offices to operate and cover their functions. 56% of IRBs held the meeting once a month and 80% of members were affiliated with his/her institutions. Protocols would be previewed by 2-3 reviewers before it was scheduled on the convened meeting. There were 5089 initial submission in 2008 from respondent institutions. 72% of researches went through expedited review and convened review was 28%. Stripping away the fee of continuing review, changes in research, and other services, the average of initial review was about 1450 USD. The revenues of two hospital IRBs and one independent IRB were 0.58, 0.51, and 0.36 million respectively. Conclusion A complete and continuing training plan for members to review protocols is significant, especially for expedited review. Reviewers are primary gate keepers to determine whether the protocol fits expedited criteria or not. This study also provides useful information about the scale of clinical research and main IRB status in Taiwan.

Limitations: We received replies from 12 IRBs and therefore the rest of data could not be included in this study. Next steps There is an urgent need to have a governmental department to manage, counsel, accredit, and audit. Since IRBs consume lots of administrative working and teaching hospital or university may have their IRB/EC, electronic system and centralization would be the way we go forward.
What Does 'Protection of Human Subjects' Mean to a Social and Behavioral IRB?

Author: Diane S. Young

Background
Social and behavioral IRBs must take the federal regulations, better suited in many respects to medical research, and evaluate the research studies proposed by social scientists. Understanding what issues board members attend to and the dilemmas they discuss when reviewing full board studies is an important step in examining how social and behavioral IRBs contribute to the protection of human subjects. Questions: On what issues/topics does the full board focus? What are the dilemmas the board struggles with? Do scientist and non-scientist members introduce different kinds of considerations for discussion?

Description of Research

Methods: Full board IRB meetings over the course of one year at one Research University were audiorecorded and transcribed for manifest and latent content analysis. This case study includes 11 meetings, each approximately 2 hours in length. Transcriptions end with the June 2009 meeting. The research conducted at this university is predominantly social and behavioral in nature, providing a good fit for the case study. Content analysis is currently underway, with the first half of the year’s meetings examined for the identification of themes and general hypotheses. These findings will be further refined using the second half of the year’s transcripts and reported on.

Results: During the first 6 meetings, the full board reviewed 16 new protocols, 29 renewals, 12 amendments, and 1 unanticipated event. Concerns raised by board members were categorized into routine and new issues. Routine issues are common problems with protocols, regularly recognized by board members. New issues are concerns with protocols that the full board has not previously addressed and does not have a standard response for. Routine issues were raised in 26 areas related to the consent process and in 28 additional areas. New issues were raised in 13 different areas, 2 related to the consent process. In all cases, except for one, new issues were raised by scientist members of the board. Examples of new issues include different compensation rates for participants doing the same procedures at different times and whether parents should be informed about a recruitment practice involving their children.

Conclusions: Changing technologies, procedures and accepted wisdom about human subjects’ protections require board members to problem solve in new areas. Non-scientist members may need assistance in developing their unique contributions to the IRB.

Limitations: The study is carried out at one site. Next Steps: Results will be presented to the board to assist the board in developing standardized procedures for commonly occurring problems and to inform future training efforts in new areas. Replicating the study with additional IRBs will broaden understanding about current areas of concern addressed by social and behavioral IRBs.
Authors: Joan E. Sieber; Gerald Koocher; Patricia Keith-Spiegel

Background
Whistleblowing typically turns into a disaster for all concerned. This study sought to identify collegial alternatives to whistle blowing in responding to irresponsible science and to identify best practices for teaching and reinforcing responsible research.

Description of Research
Method: We conducted an online survey of 2,599 NIH grantees on their observations of bad science -- what they saw, how they responded, and, if they intervened, what the outcome was for them and for science. “Bad science” referred to any practices that damage the scientific record, including falsification, fabrication and plagiarism (FF&P) as well as errors introduced through bias, poor research design and management, inadequate data management, and questionable publication practices. We also conducted phone interviews with 135 of these PIs who supplemented survey findings with in-depth details.

Results: 84% of survey respondents reported having witnessed misconduct. In follow-up interviews, more than 50% described questionable practices, such as bias in study design and analysis, carelessness, and dubious publication practices, that did not meet the traditional definition of misconduct. 63% of those surveyed intervened, with nearly two-thirds rating the outcome as acceptable (satisfactory or at least not unsatisfactory). Many interviewees successfully handled questionable practices through informal and creative mechanisms.

Conclusion: Our survey indicates existing institutional misconduct policies may not be fully effective in detecting and managing all types of misconduct. Our interviews suggest collegial, informal interventions may provide a useful adjunct to these policies, particularly for questionable practices where whistleblowing may be unnecessary or even harmful.

Additional Information
A key product, in addition to some journal articles, is a user-friendly manual on how to respond to “bad science”. That manual can be found at www.ethicsresearch.com