IRB DIRECTORS' PERCEPTIONS OF PROPOSED REVISIONS TO THE REGULATIONS FOR PROTECTING HUMAN SUBJECTS

BY

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Submitted to the graduate degree program in Clinical Research and the Graduate Faculty of the University of Kansas in partial fulfillment of the requirements for the degree of Master of Science.

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Date Defended: December 2, 2011

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ABSTRACT

In July, the U.S. Department of Health and Human Services (HHS), in association with the Office of Human Research Protections (OHRP) and the Food and Drug Administration (FDA), issued an Advance Notice of Proposed Rulemaking focused on modernizing the federal regulations for the protection of human subjects. Three areas targeted for revisions would have a substantial effect on how IRBs review human subjects research: ensuring risk-based protections, streamlining IRB review of multi-site studies and improving informed consent. The current study aimed to assess IRB Directors' perceptions of these proposed revisions and identify any barriers to implementation. The results of the study showed that IRB Directors agree that the federal regulations need to be updated and generally agree with the proposed revisions regarding mandating singe IRB review of multi-site studies and efforts to improve the length and complexity of informed consent forms. However, subjects did not agree with the proposed changes in regards to the new "excused" category, specifically the concept of allowing investigators to register studies with the IRB opposed to submitting for IRB review and approval prior to commencing research activities.

ACKNOWLEDGEMENTS

I would like to express my appreciation to my thesis committee members for their guidance and encouragement. Thank you to Won Choi, PhD, MPH for his continued support and advice throughout my completion of the Master of Science in Clinical Research program, to Tarris Rosell, PhD, DMin for his focused mentoring and tireless encouragement during my pursuit of independent study in research ethics, and to Jo Wick, PhD for her statistical guidance and for fostering my desire to explore ethical implications in clinical trials.

I would also like to extend a special thank you to Karen Blackwell, MS, CIP for providing me with my first professional opportunity within the Human Research Protection Program at the University of Kansas Medical Center as well as for encouraging my professional and academic development.

Lastly, thank you to Jerry Menikoff, MD, JD, Valorie Schroeder, MD and Daniel Voss, MS, JD, CIP for the many discussions and debates which have nurtured my interests in the ethical conduct of human subjects research.

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INTRODUCTION

In a July 22, 2011 news release, the U.S. Department of Health and Human Services (HHS), in association with the Office of Human Research Protections (OHRP) and the Food and Drug Administration (FDA), announced their intent to introduce a "proposal to improve rules protecting human research subjects."[1] The proposal, titled "Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators," was published in the July 26, 2011 Federal Register as an Advance Notice of Proposed Rulemaking (ANPRM).[2]

The purpose of the ANPRM was to solicit comments from the public on various enhancements and revisions that HHS was considering to the Code of Federal Regulations. Regulations pertaining to the protection of human subjects are listed in both Subpart A 45 CFR part 46[3] (regularly referred to as the "Common Rule") for all federally funded human subjects research, and 21 CFR parts 50, 56, 312 and 812[4] for research regulated by the FDA.

Acknowledging that the regulations have not "kept pace with the evolving human research enterprise, the proliferation of multi-site clinical trials and observational studies, the expansion of health services research, research in social and behavioral sciences, and research involving databases, the Internet, and biological specimen repositories, and the use of advanced technologies, such as genomics" (p. 44512), HHS proposes to modernize the regulations which have not been significantly revised since their adoption in 1991.[2] In the ANPRM, HHS targets seven areas for enhancement that have been criticized over the years:

I. Ensuring risk-based protections

II. Streamlining Institutional Review Board (IRB) review of multi-site studies

III. Improving informed consent

IV. Strengthening data protections to minimize informational risks

V. Data collection to enhance system oversight

VI. Extension of federal regulations

VII. Clarifying and harmonizing regulatory requirements and agency guidance

As evident by the title of the proposal, HHS's intentions are to enhance protections of human subjects and reduce regulatory burdens that are adversely affecting investigators and delaying the progress of valuable research. However, the realization of any enhancements in protections and reductions of regulatory burden will be determined by how effectively IRBs interpret and apply the final revisions. In most academic institutions, the interpretation of the final revisions and their subsequent translation into effective enhancements will be the responsibility of the directors of the administrative support offices for the IRB.

Focusing on the three targeted areas for revision which will have the greatest effect on how IRBs categorize, review and approve human subjects research studies (ensuring risk-based protections, streaming IRB review multi-site studies, and improving informed consent), the objective of the current research study is to:

I. Assess how IRB directors perceive the regulatory changes as proposed by HHS, and

II. Identify any potential concerns about or barriers to implementation of the revisions as proposed.

BACKGROUND

Commonly characterized as bureaucratic in nature, many investigators believe that IRBs have become overregulated and inefficient.[5,6,7,8,9] Contributing to this criticism is the fact that IRB effectiveness has historically been measured by administrative benchmarking opposed to the examination of the substance of IRB review and ethical issues at stake.[6,10] As Hyman (2007) noted:

> The use of forms as the locus for decision-making resulted in a check-the-box mentality among IRB personnel, where the substantive content of research was less important than the forms that had been submitted... These tendencies are worsened by the fact that evaluation of IRB performance is based on whether all forms and paperwork were filled out correctly, and whether IRB decisions were properly documented. [6] (p. 762)

The reality is that local IRBs are tasked with complying with best practices and standards set and enforced by the federal agencies and accreditation bodies. In addition, the ever-evolving research enterprise has introduced challenges in the form of increased workloads and difficulty recruiting new IRB members with valued expertise to volunteer their services. While some individual IRBs have tried implementing revised meeting schedules, increasing membership numbers to facilitate the rotation of members according to expertise and even paying members for their service to attempt to gain efficiencies and reduce delays,[11] the resources to implement these changes are not available to every IRB. The impetus of the sweeping reform called for by the research community must come from the federal agencies and accreditation bodies themselves. Until then IRBs, and the administrations they report to, will be afraid to redirect focus and deviate from accepted standards for fear of punitive actions.

The proposed revisions outlined in the ANPRM aim to provide the regulatory relief necessary to allow IRBs to more efficiently review human subjects research while maintaining meaningful protections. Specifically, the suggested changes in regard to ensuring risk-based protections, streamlining IRB review of multi-site studies and improving informed consent have the potential to allow IRBs to shift resources away from time-consuming activities and procedures that don't contribute significant protections.

Ensuring Risk-Based Protections

Wendler & Varma (2006) analyzed nine studies submitted to the Secretary of HHS under 45 CFR 46.407, a section of the regulations which allows IRBs to forward pediatric research studies to the Secretary that the IRB believes pose greater than minimal risk of harm to subjects without any prospects of direct benefit to the subjects. The investigators found that the research interventions in 8 of the 9 studies submitted to the Secretary for review actually did not pose risks greater than the level of risks that children encounter in daily life or during the performance of routine physical or psychological tests.[9] These findings illustrate one of the criticisms of the current regulations: that the level of scrutiny by IRBs does not always correlate with the level of possible risk proposed by the research.

To address this issue, HHS proposes several revisions to the Common Rule "intended to ensure that protections are commensurate with the level of risk of the research study"[2] (p. 44515). Though the proposed revisions do address the issue raised by Wendler & Varma (2006) by including more specific language to help IRBs make determinations of minimal risk, it is possible that other proposed changes will actually have a greater impact on IRB efficiency and/or function. Several of these proposed changes can assumedly result in tangible changes to the

review requirements for minimal risk studies which could translate into reduced IRB oversight. HHS hopes that by lessening some of the scrutiny on studies which do not pose greater than minimal risk, IRB resources can be re-directed to enhancing protections for studies which contain higher risk levels.

For example, in order to eliminate the need for IRBs to consider the informational risks associated with a study, HHS proposes establishing mandatory data security and information protection standards for identifiable information. Informational risks are the risks of harm resulting from a breach of confidentiality or the misuse of identifiable data. Currently, without published standards to protect against informational risks, IRBs must assess the adequacy of data security procedures for each study individually. A systematic review of 16 studies evaluating IRB variation was conducted by Abbott & Grady (2011) in which they found that the literature shows a great deal of variation across IRB reviews of the same protocol.[12] By establishing mandatory standards that investigators must follow, variation among IRB reviews could be lessened. However, it is the gains in IRB resources resulting from reduced oversight that HHS highlights with this proposed revision. They believe that by establishing mandatory standards, the risk of harm resulting from breaches or misuses of information could be reduced to the extent that IRB review of these risks would not be necessary. Instead, IRBs would solely confirm that investigators have standard protections in place opposed to assessing the adequacy of proposed procedures for each individual study.

Another proposed change by HHS which could ensure commensurate risk-based protections is the elimination of continuing review requirements for all minimal risk studies. This would include studies initially approved under expedited procedures, as well as studies

approved by a convened IRB which have progressed to the stages of research activities which present no more than minimal risk such as data analysis or long-term follow-up of subjects. Currently, all non-exempt studies regardless of risk are required to undergo continuing review at least once per year until all research activities are completed. HHS questions whether or not annual review of studies which present no more than minimal risk of harm to subjects is an adequate use of IRB resources, especially when investigators already are required to submit any proposed changes and unanticipated problems for IRB review.

While the proposed changes of establishing mandatory data security and information protection standards and eliminating continuing review for minimal risk studies have potential to reduce regulatory burden for both IRBs and investigators, it is HHS's proposed changes to the categorization of exempt studies which could translate into the greatest amount of regulatory relief. Currently, the Common Rule includes an exempt category for minimal risk studies which meet certain criteria. This exempt classification generally covers studies involving the use of standard educational tests, survey or interview procedures, observations of public behavior and the review of existing data as long as the information obtained does not allow subjects to be identified and that any disclosure of the data outside of the research would not reasonably place subjects at risk of physical, psychological, financial or reputational harm. The regulations do not require IRB review of studies that qualify for an exempt classification; however, federal guidance and best practices do recommend that the determination of whether or not a proposed research study meets the criteria for an exempt classification be completed by the IRB. This has led to the common practice of IRBs requiring that exempt studies be submitted for some form of IRB approval, though this practice is not specifically mandated by the regulations.[13]

To attempt to remedy this situation in which IRB resources potentially are being over-used on research studies which pose the least risk, HHS is considering a complete re-evaluation of the exempt category. What they propose is to replace the exempt classification with a new "Excused" category. HHS explains that the change in terminology would clarify that these studies are no longer exempt from the regulations, but instead are excused from IRB review. For example, investigators would still be required to follow the regulatory requirements such as the proposed mandatory data security measures; however, IRB review of the study prior to implementation would not be required. In place of IRB review prior to implementation, HHS suggests that IRBs could institute a registration and tracking system to audit a portion of these studies. In effect, investigators would first register their study with the IRB. Then the investigator could either immediately begin research activities or begin after a short waiting period as determined by how the IRB decides to implement this change. Once registered, the IRB would have the information necessary to confirm that the study meets the criteria for an "excused" classification, and could also conduct post-registration audits on select studies to ensure that the investigators are following their proposed protocols.

Furthermore, HHS proposes to expand the criteria previously defined for exempt categorization so that the new "excused" category would include a broader spectrum of minimal risk studies. Specifically, they propose to remove the caveats regarding the identifiability of subjects and disclosure resulting in risks so that all studies involving standard educational tests, surveys, interviews and reviews of existing data involving competent adults would be included in the new "excused" category.

If all of the proposed changes discussed above were to be incorporated into the Common Rule, the regulatory burden surrounding the conduct of research studies which pose no greater than minimal risk of harm to subjects could be significantly reduced. To illustrate, consider an investigator who is proposing to conduct a survey of a sample of competent adults undergoing a surgery with the hopes of relieving back pain. The investigator proposes to conduct a quality of life survey prior to surgery, six months post-surgery and then one year after surgery. Assuming a within-subjects design, it would be necessary to record some sort of identifiable information for the purpose of matching subjects' responses. Under the current regulations this study would be classified as either "exempt" or "expedited," depending on the IRB's determination as whether or not the contents of the survey would be damaging to subjects if disclosed. The investigator would be required to submit an application for review and approval prior to implementation of any research activities. If the IRB approved the study under an expedited classification, the investigator would also be responsible for submitting an annual continuing review. If HHS's proposed revisions were implemented, this study would qualify as an "excused" study and the investigator would only need to follow the mandated data security standards and register the study with the IRB. The investigator would not need to wait for IRB approval before beginning the study, and would not need to submit any materials for annual continuing review.

This example is meant to illustrate how HHS's suggested revisions could reduce the regulatory burden for IRBs and investigators related to the review and conduct of minimal risk studies. But HHS does not only address minimal risk studies in the proposed changes presented in the ANPRM. Another aspect of IRB review that they have identified as being inefficient and needing enhancement are the regulations regarding IRB review of multi-site research studies.

Streamlining IRB Review of Multi-Site Studies

With the exception of studies of FDA-regulated medical devices, the regulations currently do not require that every participating site in a multi-site research study obtain approval from their local IRB. While IRB approval of some form must be obtained, the regulations allow for the local IRB to rely on the IRB approval from another IRB rather than conducting their own review. While some institutions use this flexibility in the regulations and rely on IRB approval from another institution or a central IRB, many still prefer to conduct their own review instead.

Loh & Meyer (2004) surveyed administrators at the then 125 accredited U.S. medical schools to examine their attitudes and perceptions of the use of central IRBs.[14] The authors found that 76% of U.S. medical schools had never used central IRBs. Of those schools that had never used a central IRB, the two main reasons cited for not using central IRBs were concerns about potential liability (74%) and a lack of local representation (86%). However, of the 24% that had used central IRBs, most were pleased with the quality of the review (79%) and the level of human subjects protection performed (84%). Most importantly, 79% reported that they were able to maintain excellent local oversight of the studies approved by the central IRB. These results suggest that when administrators commit to using central IRBs they are very satisfied with the results. However, with only 24% of U.S. medical schools committing to the use of central IRBs at the time of the survey, the concerns of liability and local representation clearly outweighed any prospects of optimizing local IRB resources.

In the ANPRM, HHS notes that the number of studies being conducted at multiple sites has increased over the years and is likely to continue to grow. They also cite the common criticisms of multiple IRB reviews for one study:

> In many cases, a local IRB for each institution does independently review the research protocol, informed consent documents and other materials, sometimes resulting in hundreds of reviews for one study. When any one of these IRBs requires changes to the research protocol that are adopted for the entire study, investigators must re-submit the revised protocol to all of the reviewing IRBs. This process can take months and can significantly delay the initiation of research projects…. Many commentators claim that multiple IRB reviews do not enhance the protection of human subjects and may, in fact, divert valuable resources from more detailed reviews of other studies. Relevant local contextual issues (e.g., investigator competence, site suitability) pertinent to most clinical studies can be addressed through mechanisms other than local IRB review. For research where local perspectives might be distinctly important (e.g., in relation to certain kinds of vulnerable populations targeted for recruitment) local IRB review could be limited to such consideration[s], but again, IRB review is not the only mechanism for addressing such issues. The evaluation of a study's social value, scientific validity, and risks and benefits, and the adequacy of the informed consent document and process generally do not require the unique perspective of a local IRB.[2] (pp. 44521-2)

The solution that HHS is contemplating is a revision to the regulations mandating that all participating sites in multi-site research studies rely on the IRB review of a single IRB. They stress that this mandate would not relieve institutions of their responsibility to ensure that research being conducted at their site follows regulations for protecting human subjects, but it would eliminate formal IRB review at each participating site. Recognizing that, as Loh & Meyer (2004) found, one of the main concerns institutions have about relying on external IRBs is related to liability, HHS agrees that any mandate requiring single IRB review of multi-site

studies must be accompanied with changes to the enforcement of regulations which would hold external IRBs accountable for regulatory requirements. Again, institutions would still be required to ensure that the conduct of studies at their sites follows regulations, but with these revisions they would not be held responsible for regulatory decisions made by the IRB.

Similar to the proposed changes for ensuring risk-based protections, HHS's suggestions on how to streamline the IRB review of multi-site studies clearly emphasize a reduction in the amount of scrutiny a study currently receives during initial IRB review. Proposing changes which would allow investigators to register "excused" studies and mandate single IRB review for multi-site studies could result in potentially significant reductions in both regulatory burden and delays in the initiation of research. The other theme that is inherent within these proposed changes is that HHS's intent is also to enhance protections of human subjects. It is clear that HHS believes that the current level of scrutiny during initial review does not enhance protections as much as actively monitoring studies while they are being conducted. Hence, proposing to allow investigators to register "excused" studies is accompanied with a proposal to implement an auditing system post-registration; and mandating single IRB review for multi-site studies is paired with a reminder that eliminating IRB review does not relieve institutions of their responsibilities to ensure the conduct of the study follows regulations. This emphasis on revising the regulations in order to allow IRBs to focus on areas that significantly affect the safety of human subjects is also inherent in HHS's suggestions for improving the informed consent process.

Improving Informed Consent

While many of the criticisms of the regulations and the current IRB system are centered around perceived bureaucracy and inefficiencies, research suggests that the area that the subjects

themselves, and parents of pediatric subjects, would like to see improved is the informed consent process.[15,16] Joffe et al. (2001) found that even when clinical trial subjects were satisfied with the informed consent process, the majority did not truly understand the information presented to them.[17] Additional criticisms suggest that consent forms have become too long and much too complicated for the average subject to understand.[18,19] Some critics have attributed the increased length of consent forms to language that has been added primarily for the protection of the institution rather than the subject.[20]

Currently, the Common Rule defines eight items that are required to be included in informed consent forms when applicable: a statement that the study involves research, a description of any foreseeable risks, a description of any possible benefits, a disclosure of appropriate alternative procedures or courses of treatment, a statement describing the extent to which confidentiality will be maintained, an explanation of whether compensation is available if injury occurs, contact information in case of questions and an explicit statement that participation in the study is voluntary. The only language that is specifically prohibited by the regulations is exculpatory language in which the subject is asked to waive any legal rights or release the investigator or institution from any liability.

To enhance the effectiveness of informed consent HHS is considering revising the regulations to include more specific standards for the content of informed consent forms. Their suggestions include:

> 1) Prescribing appropriate content that must be included in consent forms, with greater specificity than is provided in the current regulations; 2) restricting content that would be inappropriate to include in consent forms; 3) limiting the acceptable length of various sections of a consent form; 4) prescribing how information should be presented in

> consent forms, such as information that should be included at the very beginning of the consent form, or types of information that should be included in appendices and not in the main body of the consent form; 5) reducing institutional 'boilerplate' in consent forms (that is, standard language that does little to genuinely inform subjects, and often is intended to primarily protect institutions from lawsuits); and 6) making available standardized consent form templates, the use of which could satisfy applicable regulatory provisions.[2] (p. 44523)

Reactions to the proposed changes outlined in the ANPRM already range from excitement to reservation. The Society for Clinical and Translational Science applauds the proposed revisions and exclaims that "these changes in the Common Rule will be a common good"[21] (p. 313). Alternatively, the Association for the Accreditation for Human Research Protection Programs (AAHRPP) has stated that they believe HHS needs "to alter its approach to the proposed rulemaking so that the primary purpose is to protect human research participants…. Although the ANPRM states that one of the intentions is to enhance protections for research participants, the apparent primary purpose of the proposed rulemaking seems to be to reduce burden on researchers"[22] (p. 3).

What we don't know yet is how IRB directors perceive these proposed changes. Once revisions to the Common Rule are finalized, IRB directors and personnel will be tasked with digesting the final revisions and coordinating policies and procedures in order to translate those revisions into realized enhancements.

METHODS

This research study was approved by the Human Subjects Committee at the University of Kansas Medical Center (KUMC) under exempt category b(2). No information was collected that would allow the investigator to link responses to individual subjects. Study data were collected and managed using REDCap electronic data capture tools hosted at KUMC.[23] REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing: 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external servers.

Sample

Invitations to participate in this online survey research study were sent to a convenience sample of the IRB directors of the top 200 research universities as identified by 2010 Annual Report of The Center for Measuring University Performance.[24] Email addresses were obtained by reviewing each university's IRB website. For the purpose of this study, IRB director was operationally defined as the individual responsible for the day to day function of the IRB and supporting staff. Given the variation in the titles given to this administrative position, selection of individuals not specifically identified as IRB directors were prioritized in the following order: Director of Research Integrity, Director of Research Compliance, IRB Manager, Vice President of Research, IRB Coordinator and IRB Analyst. Additionally, the email invitation included the following statement to better reach the target population: "If you are not the IRB Director at your

institution, or the individual responsible for the function of the IRB and supporting staff, I would appreciate if you could please forward this invitation to the correct person."

Some of the top 200 research universities shared institutional affiliations and therefore IRBs. Also, several of the universities had more than one IRB. Therefore the total number of 206 potential subjects were identified and sent email invitations to participate.

Survey Instrument

The survey was comprised of six sections. The first two sections were designed to obtain participant and institutional demographics. Sliding Likert scales which allowed subjects to rate their level of agreement on a continuous range from 0-100 (0 = strongly disagree, 50 = neither agree or disagree, 100 = strongly agree) were used to query subjects about their perceptions of the current regulations. The third section included questions related to multi-site research studies and the use of central IRBs. The survey questions used by Loh & Meyer (2004) to survey U.S. medical schools about the use of central IRBs were replicated in order to examine if use of, attitudes toward and perceptions of central IRBs have changed in the last seven years. Then sliding Likert scales were used to query subjects about the proposed revisions to the review of multi-site research studies as proposed in the ANPRM.

The fourth and fifth sections of the survey used sliding Likert scales to query subjects about their level of agreement with the proposed changes regarding ensuring risk-based protections and improving informed consent, respectively. Throughout the sections about the proposed revisions subjects were also presented open-ended questions to allow for detailed comments. The final section of the survey included an open-ended question asking subjects to

provide any additional opinions on the other four areas of the ANPRM that were not covered in the current study. The complete survey is available in Appendix I.

Statistical Analysis

Data were analyzed using IBM SPSS Statistics version 20. Descriptive statistics were used to report participant and institutional characteristics as well as Likert scale values. Due to the skew of the Likert scale values, these data are described by medians ( ) and interquartile ranges (*IQR*), opposed to means and standard deviations.

Nonparametric tests were used to examine both whether perceptions (sliding Likert values) were significantly different amongst categorical variables and to examine significant correlations between categorical variables. The Mann-Whitney test was used for examining Likert values against categorical variables with only two possible values: type of studies reviewed ("biomedical and/or social/behavioral" or "social/behavioral only"), classification as an academic medical center (yes or no) and years of experience in human subjects protections ("5 years or less" or "more than 10 years"). The Kruskal-Wallis test was used examining Likert values against categorical variables with more than two possible values: number of active studies and average time to approval for the local IRB. Fisher's Exact Test was used in order to test for significant associations between categorical variables: use of central IRBs (yes or no), type of studies reviewed ("biomedical and/or social/behavioral" or "social/behavioral only"), classification as an academic medical center (yes or no) and number of currently active studies.

RESULTS

A total of 69 evaluable responses were collected following 206 invitations (33.5%). A total of 77 subjects submitted responses, however 8 subjects were removed from analysis

because they only responded to the personal characteristic questions and did not complete any of the questions regarding the proposed revisions to the regulations.

Of the 69 evaluable responses, 63 subjects have been working in human subjects protections for more than 5 years (91.3%), and 49 subjects have been in charge of oversight of the function of the IRB for 4 years or more (71.0%) (see Table 1). Almost all subjects (95.7%) had familiarized themselves with the ANPRM prior to participation.

The number of currently active studies overseen by the subjects' IRBs varied with 33 subjects reporting that their IRB oversees 1000 active studies or less (47.8%) while 15 subjects reported that their IRB oversees more than 2500 active studies (21.7%). The 35 subjects from academic medical centers comprised 50.7% of the sample and 53 subjects reported that their IRB review both biomedical and social/behavioral research studies (76.8%). A total of 55 subjects reported that the average time to approval for studies submitted to their local IRB was 6 weeks or less (79.7%).

Using the sliding Likert scales ranging from 0-100, subjects reported that on average they believe that the current regulations promote effective protections of human subjects (= 75, *IQR* = 62.75 – 83.00) and that the current regulations promote efficient review of human subjects protections (= 54, *IQR* = 37.00 – 75.00) (see Table 2). Overall, subjects did not agree that the current regulations are adequate and do not need revised (= 32, *IQR* = 15.75 – 50.00); however subjects who direct IRBs that solely review social/behavioral studies believe that the current regulations are adequate and do not need to be revised (= 55, *IQR* = 39.75 – 74.00). This was significantly different ($U = 150.50$, $p < 0.005$) than subjects who oversee IRBs that review

Table 1: Characterization of Sample Population (n = 69)

Variable	*f (%)*
Years responsible for oversight of IRB	
- Less than 1 year	3 (4.3%)
- 1-3 years	17 (24.6%)
- 4-6 years	20 (29.0%)
- 7-9 years	12 (17.4%)
- 10 years or more	17 (24.6%)
Total years working in human subjects protections	
- Less than 1 year	0 (0.0%)
- 1-5 years	6 (8.7%)
- 6-10 years	30 (43.5%)
- 11-15 years	18 (26.1%)
- 15 years or more	15 (21.7)%
Familiarized with ANPRM prior to survey	
- Yes	66 (95.7%)
- No	3 (4.3%)
Number of currently active human subjects research studies	
- Less than 500 studies	13 (18.8%)
- 501-1000 studies	20 (29.0%)
- 1001-1500 studies	6 (8.7%)
- 1501-2000 studies	7 (10.1%)
- 2001-2500 studies	7 (10.1%)
- More than 2500 studies	15 (21.7%)
- Not able to answer*	0 (0.0%)
- Missing**	1 (1.4%)
Type of human subjects research studies reviewed by IRB	
- Biomedical only	3 (4.3%)
- Social/Behavioral only	12 (17.4%)
- Both biomedical and social/behavioral	53 (76.8%)
- Missing**	1 (1.4%)
Is your institution classified as an academic medical center?	
- Yes	35 (50.7%)
- No	33 (47.8%)
- Missing**	1 (1.4%)
Average reported time to approval for submissions to the local IRB	
- Less than 2 weeks	6 (8.7%)
- 15-21 days	11 (15.9%)
- 22-28 days	16 (23.2%)
- 4-6 weeks	22 (31.9%)
- 6 weeks – 3 months	4 (5.8%)
- More than 3 months	0 (0.0%)
- Not able to answer	4 (5.8%)
- Missing**	6 (8.7%)

*For certain variables which required that the subject had completed previous benchmarking calculations prior to completing the survey, subjects were given the option to answer "Not able to answer." **Subjects were not required to complete all questions in the survey. "Missing" refers to frequency of subjects who did not supply an answer to the question.

Table 2: Perceptions of Current Regulations Regarding the Protections of Human Subjects (n = 69)
Values given are subject's scores (0-100) on a sliding Likert scale which ranged from "Strongly Disagree" to "Strongly Agree." The higher the value, the greater the level of agreement with the statement.

Statement	Mean	Median	SD	Interquartile Range	Missing*
The current regulations promote effective protections for human subjects.	71.04	75	16.72	62.75 – 83.00	1
The current regulations promote efficient review of protections for human subjects.	55.25	54	22.47	37.00 – 75.00	2
The current regulations are adequate and DO NOT need to be revised.	37.21	32	27.74	15.75 – 50.00	1

*Subjects were not required to complete all questions in the survey. "Missing" refers to frequency of subjects who did not supply an answer to the question.

biomedical studies only or both biomedical and social/behavioral studies (= 30, *IQR* = 9.00 – 40.00).

Ensuring Risk-Based Protections

While subjects agreed with the proposed revisions to eliminate continuing review for expedited studies (= 75, *IQR* = 32.25 – 90.75), and full committee studies which have progressed to data analysis only (= 90, *IQR* = 68.00 – 99.00) or long-term follow-up only (= 75, *IQR* = 50.00 – 91.75), they did not agree with concept of mandatory data security standards replacing IRB review of informational risks (= 27, *IQR* = 10.00 – 56.00) (see Table 3). The proposed revisions which subjects disagreed with the most on average were those pertaining to the new "excused" category. Subjects did not agree that allowing investigators to register their "excused" studies prior to implementation was a good idea (= 13, *IQR* = 0.00 – 55.00), and if this revision were to be implemented 35 subjects reported that they believe a week long or more waiting period before an investigator could begin a study following registration with the IRB

Table 3: Perceptions of the Proposed Revisions Regarding *Ensuring Risk-BasedPprotections* (n = 69)
Values given are subject's scores (0-100) on a sliding Likert scale which ranged "Strongly Disagree" to "Strongly Agree." The higher the value, the greater the level of agreement with the statement.

Statement	Mean	Median	SD	Interquartile Range	Missing*
Mandatory data security standards					
If mandatory data security and information protections standards were implemented, indicate how comfortable you would be with the IRB no longer being responsible for review of a research study's plan for minimizing information risks.**	36.02	27	29.60	10.00 – 56.00	10
Elimination of continuing review for minimal risk studies					
I am comfortable with the IRB no longer conducting continuing review on…					
- Expedited studies	62.50	75	32.83	32.25 – 90.75	9
- Full review studies in data analysis only	77.84	90	27.33	68.00 – 99.00	8
- Full review studies in long-term follow-up only	67.68	75	29.47	50.00 – 91.75	9
Changing "Exempt" to "Excused"					
Allowing investigators to begin research activities for "excused" studies without formal IRB review prior to implementation is a good idea.	29.30	13	35.22	0.00 – 55.00	8
Shifting resources from pre-implementation review to post-implementation monitoring for "excused" studies would be a more efficient use of resources.	30.02	22	32.42	1.00 – 50.00	8
Shifting resources to post-implementation monitoring would result in more effective protections of human subjects than pre-implementation IRB review.	29.29	20	30.55	2.00 – 50.00	10
Including all survey-type research with competent adults into this new "excused" category, regardless of the type of data being collected, is a good idea.	44.22	50	33.90	8.25 – 70.00	11

Variable	Frequency	Percentage
If a waiting period was required before an investigator could start an excused study, how long of a waiting period do you think would be appropriate?		
- Less than 3 days	8	11.6%
- 4-6 days	12	17.4%
- 7-10 days	14	20.3%
- 11-14 days	13	18.8%
- More than 14 days	8	11.6%
- Missing*	14	20.3%

*Subjects were not required to complete all questions in the survey. "Missing" refers to frequency of subjects who did not supply an answer to the question.
**For this survey question Likert scale ranged from "Very Uncomfortable" to "Very Comfortable."

would be appropriate (50.7%). Overall, subjects did not agree that shifting resources from pre-implementation review to post-implementation monitoring would be more effective (= 20, *IQR* = 2.00 – 50.00) or more efficient (= 22, *IQR* = 1.00 – 50.00). However, subjects with 5 years of experience or less agreed with the proposed revisions regarding mandatory data security and the proposed "excused" category which was significantly different that subjects with more than ten years of experience (see Table 4).

Use of Central IRBs and Comparison to Loh & Meyer (2004)

In 2004, Loh & Meyer found that 21% of medical schools surveyed had used a central IRB.[14] Seven years later, 94% of subjects in the current study who oversee IRBs at academic medical centers (n=35) and 58% of all subjects (n=69) report that they have used a central IRB (see Table 5). However, fewer subjects in the current study from academic medical centers agree that the central IRBs used provide quality protections of human subjects (57%) and quality scientific review (46%) compared to subjects from the previous study (84% and 79%, respectively) (see Table 6). Reasons for not using a central IRB were not able to be compared between studies because only 2 subjects in the current study from academic medical centers reported that they had never used a central IRB (5.7%). Use of central IRBs was significantly correlated with the review of biomedical research (r_s = .475, p < 0.001), classification as an academic medical center (r_s = .742, p < 0.001) and greater numbers of currently active studies (r_s = .457, p < 0.001) (see Table 7).

Table 4: Mann-Whitney Comparison of Perceptions of Proposed Revisions to the Regulations in Regards to Mandatory Data Security Standards and the New "Excused" Category by Years of Experience in Human Subjects Protection.

If mandatory data security and information protections standards were implemented, indicate how comfortable you would be with the IRB no longer being responsible for review of a research study's plan for minimizing information risks.*				
Sample	**n**	**(, *IQR*)**	**Test Statistic**	**Sig. (2-sided)**
5 years or less	5	(77.00, 34.50 - 84.50)	26.00	$p < 0.05$
More than 10 years	27	(20.00, 9.00 – 43.00)		
Allowing investigators to begin research activities for "excused" studies without formal IRB review prior to implementation is a good idea.				
Sample	**n**	**(, *IQR*)**	**Test Statistic**	**Sig. (2-sided)**
5 years or less	6	(73.00, 21.25 – 100.00)	18.00	$p < 0.05$
More than 10 years	27	(2.00, 2.00 – 25.00)		
Shifting resources from pre-implementation review to post-implementation monitoring for "excused" studies would be a more efficient use of resources.				
Sample	**n**	**(, *IQR*)**	**Test Statistic**	**Sig. (2-sided)**
5 years or less	6	(37.50, 24.50 – 100.00)	34.50	$p < 0.05$
More than 10 years	28	(10.50, 1.00 – 35.25)		
Shifting resources to post-implementation monitoring would result in more effective protections of human subjects than pre-implementation IRB review.				
Sample	**n**	**(, *IQR*)**	**Test Statistic**	**Sig. (2-sided)**
5 years or less	6	(55.50, 19.50 – 100.00)	30.00	$p < 0.05$
More than 10 years	27	(6.00, 6.00 – 30.00)		

*For this survey question Likert scale ranged from "Very Uncomfortable" to "Very Comfortable."

Table 5: Use of Central IRBs

Has your institution ever used a central IRB?	**n**	**Frequency**	**Percentage**
Total sample	69		
- Yes		40	58.0%
- No		28	40.6%
- Missing		1	1.4%
Academic medical centers	35		
- Yes		33	94.3%
- No		2	5.7%
Other types of institutions*	33		
- Yes		7	21.2%
- No		26	78.8%

* "Other types of institutions" includes all subjects who replied "No" to "Is your institution classified as an academic medical center."

Table 6: Attitudes Towards Using a Central IRB as Reported in Loh & Meyer (2004) (n=21) Compared to the Current Study Results (n=35).*

Statement	Strongly Agree (%)	Agree (%)	Disagree (%)	Strongly Disagree (%)	Unable to Answer (%)
Use of a central IRB has shortened the time to approval.					
- Loh & Meyer (2004)	11	42	11	21	16
- Current study	14	23	23	17	23
We are pleased with the quality and level of the scientific review performed by the central IRB.					
- Loh & Meyer (2004)	11	68	0	5	16
- Current study	17	29	9	9	37
We are pleased with the human subjects protection review performed by the central IRB.					
- Loh & Meyer (2004)	16	68	5	5	5
- Current study	17	40	9	9	25
We are able to maintain excellent local oversight for studies approved by a central IRB.					
- Loh & Meyer (2004)	11	68	5	5	11
- Current study	23	23	17	14	23
Use of a central IRB has attracted industry sponsors.					
- Loh & Meyer (2004)	0	5	32	16	47
- Current study	17	9	11	3	60

*Data for the current study was collected using a sliding Likert scale ranging from 0-100. In order to compare results to Loh & Meyer (2004), the current data was grouped into corresponding categories: 0-24 = "Strongly Disagree," 25-49 = "Disagree," 51-75 = "Agree," 76-100 = "Strongly Agree," 50 and missing values = "Unable to Answer."

Streamlining IRB Review of Multi-Site Studies

Though subjects reported on average that they agree that multiple IRB reviews of multi-site studies significantly delays the initiation of research (= 75, *IQR* = 65.00 – 91.25), they also believe that local IRB review of multi-site studies adds to the protection of local human subjects (= 64, *IQR* = 35.00 – 75.00) (see Table 8). In regards to the proposed revisions by HHS to mandate single IRB review of multi-site studies, subjects reported that they would agree with this new regulation as long as the IRB of record is held regulatorally accountable (= 74, *IQR* =

50.00 – 90.75) and legally liable (= 75, *IQR* = 50.00 – 95.50). Subjects were concerned, however, with how the IRB of record would be determined (= 72, *IQR* = 55.00 – 96.00).

Table 7: Significant Associations Between Use of Central IRBs and Local IRB Demographics.

		Review biomedical research (yes or no)	Academic medical center (yes or no)	Number of currently active studies.*
Use of central IRBs (yes or no)	Sig. (2-tailed)	p < .001	p < .001	p < .005
	N	68	68	68

* Number of currently active studies were categorized as "less than 500," "501-1000," "1001-1500," "1501-2000," "2001-2500," and "more than 2500."

Table 8: Perceptions of the Proposed Revisions Regarding S*treamlining IRB Review of Multi-Site Studies* (n = 69)

Values given are subject's scores (0-100) on a sliding Likert scale which ranged "Strongly Disagree" to "Strongly Agree." The higher the value, the greater the level of agreement with the statement.

Statement	Mean	Median	SD	Interquartile Range	Missing*
Multiple IRB reviews of multi-site studies significantly delays the initiation of research.	75.02	75	19.72	65.00 – 91.25	7
Local IRB review of a multi-site study adds to the protection of local human subjects.	57.37	64	25.47	35.00 – 75.00	10
If single IRB review was mandated for all multi-site studies, I'm concerned about how the IRB of record would be selected.	69.07	72	28.95	55.00 – 96.00	10
I would agree with mandating single IRB review for multi-site studies as long as the IRB of record is held regulatorally accountable for their review.	66.95	74	30.50	50.00 – 90.75	9
I would agree with mandating single IRB review for multi-site studies as long as the IRB of record is held legally liable for their review.	68.74	75	30.55	50.00 – 95.50	12

*Subjects were not required to complete all questions in the survey. "Missing" refers to frequency of subjects who did not supply an answer to the question.

Improving Informed Consent

Overall, subjects agreed that the current regulations need to be revised to provide more specific guidance on acceptable content in informed consent forms (= 77.50, *IQR* = 60.50 –

94.50) (see Table 9). Of all the revisions to the regulations proposed by HHS, subjects most strongly agreed that the regulations need to be revised to account for the fact that informed consent forms have become too lengthy (= 84, *IQR* = 66.00 – 100.00) and contain too much institutional "boilerplate" language (= 81, *IQR* = 61.00 – 97.50).

Table 9: Perceptions of the Proposed Revisions Regarding *Improving Informed Consent* (n = 69)
Values given are subject's scores (0-100) on a sliding Likert scale which ranged "Strongly Disagree" to "Strongly Agree." The higher the value, the greater the level of agreement with the statement.

Statement	Mean	Median	SD	Interquartile Range	Missing
The current regulations need to be revised to provide more specific guidance on acceptable content in informed consent forms.	71.88	77.50	26.70	60.50 – 94.50	13
Consent forms have become too lengthy and the regulations need to be revised to address this issue.	77.68	84	24.33	66.00 – 100.00	12
Consent forms today include too much information that is not pertinent to the subjects (e.g., institutional "boilerplate" language) and the regulations need to be revised to address this issue.	75.70	81	24.43	61.00 – 97.50	12

DISCUSSION

The survey results of the current study show that IRB Directors are open to the idea of revising the regulations on protecting human subjects, but they do not agree with all of revisions proposed by HHS. Clearly, the IRB Directors surveyed are not satisfied with the current state of informed consent forms and are in favor of adding more specific language to the regulations in order to better define acceptable content and shorten the overall length of the form. One subject suggested the use of a "single page standardized consent document that explains what research is which is used for every study, because the concepts of research, voluntariness, informed consent, ability to opt-out are universal." In the ANPRM, HHS proposes creating standard consent form templates which satisfy regulatory requirements and also specify an appropriate order of content.

One template option HHS could consider would be to create a standardized section, as suggested by this subject, which describes the basic tenants of participation in human subjects research and could be required to precede protocol specific information to ensure that all subjects are presented with the same baseline information. Standard language such as this would not be difficult to incorporate into current institutional templates.

The limited requirements in the current regulations have given institutions a great deal of flexibility in tailoring consent forms to meet the needs of their subject community. However, some critics believe that that flexibility has resulted in consent forms which have deviated too far from their intended purpose which is to provide subjects and parents with the appropriate information to facilitate their ability to make the best decisions possible about participation.[18, 19] Given the results of past research,[15, 16, 17] improvements to the length and complexity of informed consent forms may be most appreciated by subjects and parents, much less IRB Directors and the IRB members responsible for review of these forms.

As with informed consent, subjects reported that they generally agreed with the proposed revisions regarding the streamlining of IRB review for multi-site studies; however, their open ended comments focused primarily on their concern for how the IRB of record would be determined and whether or not this mandate would truly reduce delays to the initiation of research. In the ANPRM, HHS acknowledged the difficulty in effectively regulating the selection of a single IRB of record and asked for comments on how to avoid "inappropriate forms of 'IRB shopping' – intentionally selecting an IRB that is likely to approve the study without proper scrutiny – be prevented?"[2] (p 44522) HHS does not, however, specifically address how they envision this mandate reducing review times other than noting that the process

of responding to multiple IRBs with revised protocols can cause delays. A concern raised by several subjects is that the time spent by the IRB reviewing a multi-site trial will just be replaced by other compliance committees such as radiation safety, biosafety, privacy, and conflict of interest. Fifty eight percent of subjects reported that their institution requires approval from other institutional committees prior to the initiation of research studies approved by central IRBs. One subject argued that "the belief that use of central IRBs is going to markedly expedite the IRB review and approval process totally ignores the requirement for multiple non-IRB committee reviews… and many of these committees have slower turnaround than the IRB."

Mandating single IRB review for multi-site studies would be a bold revision which would entail a great deal of planning prior to implementation. Though it stands to reason that this mandate could reduce delays and regulatory burden in terms of IRB review, as currently proposed it would not directly address all of the compliance factors which lead to delays in the initiation of multi-site studies. If HHS's intentions are to truly reduce delays to initiation of research they will need to consider bolstering this section of the regulations with specific guidance related to institutional reviews beyond the IRB.

Industry sponsors would undoubtedly be elated with this mandate for single IRB review, but as many subjects suggested, an elaborate regulatory infrastructure encompassing the IRB and other institutional committees would need to be designed and tested prior to implementation. As one subject suggested, "funds must be dedicated to studying and testing models which explore how to select lead IRBs, how to submit and share information and how to allocate risk and liability." I would also add an additional objective to this list to examine in more detail the times to approval for central IRBs compared to local reviews with an emphasis on including other

institutional committees in the outcome of total time to approval. Though use of central IRBs has increased among academic medical centers, 41% of subjects reported that their institutions have never used a central IRB. While institutions that have used central IRBs will already have policies and procedures in place for how to rely on outside IRBs and perform other necessary institutional reviews, institutions who have not yet used a central IRB and intend to participate in multi-site research would incur an additional administrative burden to meet these requirements. The research on testing models of implementation could greatly assist these institutions during their transition.

Though subjects had concerns about certain aspects of the proposed revisions for improving informed consent and streamlining IRB reviews of multi-site studies, they did agree with the overall need for revision to the regulations. The same cannot be said about the proposed revisions to ensure risk-based protections. While subjects were in favor of eliminating continuing review for expedited studies and full committee studies which have progressed to data analysis or long-term follow-up, they did not agree with eliminating IRB review of informational risks by establishing mandatory data security standards and strongly disagreed with the concepts behind the proposed "excused" category. When looking at the proposed revisions regarding ensuring risk-based protections as a whole, HHS's suggestions illustrate a shift in the philosophy of human subjects protections for minimal risk studies away from pre-implementation review and approval to registration and post-implementation monitoring; A philosophy with which most subjects in the current study clearly do not agree. Interestingly though, there was a significant difference in agreement with allowing investigators to register "excused" studies when analyzed by years of experience in human subjects protections. Subjects with 5 years of experience or less agreed with allowing investigators to register "excused"

studies while subjects with more than 10 years experience strongly disagreed. A limitation of the current study is that only 6 subjects reported having 5 years of experience or less, so the validity of this comparison should be questioned until a larger sample can be examined.

It is important to remember that the types of studies included in the new "excused" category are studies that previously would have been classified as "exempt," plus formally "expedited" survey studies involving competent adults which present no reputational, financial or legal risks. This means that even if the data were to be accidentally released it would not result in any harm to the subject. For a study such as this, what would be the purpose of an IRB review beyond confirmation that the investigator made a correct risk assessment? Why would a registration process to conduct this confirmation not be adequate? If volume is an issue and IRB Directors would like time to make this confirmation before investigators begin research activities, a short waiting period of a couple of days seems reasonable. In fact, several subjects reported that their current exempt reviews are completed within two days, so a mandatory waiting period longer than two days would actually hinder their current efficiency. So why are subjects so adamantly against this proposed revision?

Comments from subjects who did not agree with the registration of "excused" studies predominantly centered on a belief that investigators often times do not make correct determinations regarding the possible risks of their research. As one subject implored, "Researchers demonstrate an inability to correctly categorize research now; concerned that they will be able to do so in the future." Similarly, another subject believed that "many investigators will misapply the standards for the 'excused' category," doubted that investigators "will always assess the risks of what they are doing in an appropriate way," and went as far as to suggest that

"there will be abuse of determining just who is competent" (in reference to the "excused" category including all types of surveys with competent adults). Given the tenor of these comments, an important question to ask is: Are these realistic concerns that are based on years of experience and are evidence enough that a registration process for minimal risk studies will put subjects at increased risk of harm? Or, are these past experiences leading to irresponsible assumptions that could hinder the progress of minimal risk research?

In order to believe that a registration process for "excused" studies would not work one must either believe that (1) investigators as a whole cannot be trusted to consistently make correct decisions as to the risk-level of their study, or that (2) IRB review and approval of these minimal risk studies prior to implementation is necessary in order to protect subjects from possible risks. Factors that could contribute to an inability of investigators to make correct decisions about the risk-level of their study would be (1) inadequate education on determining risk-levels, (2) a disregard for the importance of compliance to regulations and (3) conflicts of interest.

It should be safe to assume that investigators have the capacity to learn how to properly classify the possible risks of their studies. Chances are their fields of study are more complex in nature than the federal regulations. Educational materials can be easily created and presented to investigators to sufficiently educate them on the risk criteria of the "excused" category. A more realistic concern may be whether investigators believe that mastering this categorization in order to ensure compliance with the regulations is important enough to warrant their time and effort. As one subject commented, "Investigators don't have the time or knowledge to become educated sufficiently on the categorical determinations or requirements and will make many errors." It is

true that time is often an incredibly valuable commodity for many investigators, so further investigation may be warranted into examining investigators' perceptions of the importance of compliance in terms of minimal risk research.

The most important discussion about factors which could lead to an investigator incorrectly categorizing the risk level of study, would be the discussion of whether there are possible conflicts of interest in investigators making these determination about their own resarch. One subject argued against registration because he/she believed that "investigators are inherently conflicted when it comes to assessing our own work." Given the competitive nature of research, there is incentive for investigators to choose whichever review category provides the shortest delay to initiation of their research. Research into the validity of investigators' assessments of the risk of their own research could provide valuable information to assist HHS in their considerations of their proposed revisions.

As with a belief that investigators cannot be trusted to make their own risk assessments, another reason to believe that registration would not be adequate would be the argument that IRB review of these minimal risk studies would be necessary to ensure adequate protections of subjects. In other words, after controlling for the first assumption of incorrect categorization of risk, one would have to believe that the possible risks involved in this category of research can only be mitigated by IRB review and approval prior to implementation. To simplify even further, if the IRB doesn't review the study before the investigator begins, subjects are more likely to be harmed.

Again, to reiterate, the types of studies that would be included in this category are studies that present virtually no risk. Assuming that a study truly meets the criteria for the "excused"

category and the investigator does not deviate from the proposed activities, what are the additional protections that could be gained which would necessitate IRB review prior to implementation? Even if there is a concern about deviation from the protocol, this is not an issue that can be mitigated at initial review. Post-implementation monitoring would be necessary to identify and correct risk associated with deviation from the protocol.

CONCLUSIONS

Given the areas of the regulations targeted for revision in the ANPRM, HHS assumedly recognizes that any gains in the effectiveness and efficiency of human subjects protections must begin with regulatory relief. If, as critics have been arguing for years, the pendulum of human subjects protections has swung to the extremes of bureaucratic over-regulation, the implementation of HHS's proposed revisions would certainly provide a needed correction to more balanced regulations. In the end, any actual realization of gains will be dependent upon how IRB Directors interpret the final revisions and then adapt their administrative processes.

The objective of the current study was to assess IRB Directors' perceptions of the proposed revisions and identify any barriers to implementation. The results of the study showed that IRB Directors recognize the need for revisions to the regulations and generally agreed with mandating single IRB review for multi-site studies, eliminating continuing review for minimal risk studies and efforts to improve informed consent forms. On the other hand, subjects did not agree with the proposed revisions in regards to the new "excused" category and more specifically with the idea of allowing investigators to register these studies rather than submit for IRB review and approval prior to beginning research activities. The main barrier to acceptance of this

proposed revision is a distrust of investigators to adequately assess the risk associated with their study.

Mandated revisions such as single IRB review of multi-site studies, and more specified regulations such as those proposed for informed consent forms, leave little room for flexibility. However, if IRB Directors do not agree with the proposed revisions to ensure risk-based protections, such as the new "excused" category, they are free to implement institutional standards that are more stringent then the regulations themselves. If HHS believes that the current regulatory burden associated with minimal risk studies is unbalanced, the results of the current study suggest that more work needs to be done to convince IRB Directors that investigators can be trusted to conduct minimal risk research with minimal oversight.

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APPENDIX: Survey Instrument

Please complete the survey below. If you would like to save your progrss and return to complete later, click on "Save and Return Later" at the bottom of the page.

Introduction

Thank you for choosing to participate in this research study. This research study is being conducted through the University of Kansas Medical Center by Ryan McDowell, BS, CIP for satisfaction of thesis requirements for the Master of Science in Clinical Research.

In July, the Department of Health & Human Services (DHHS) released an advance notice of proposed rulemaking (ANPRM) titled Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators.

The notice includes proposed changes to the federal regulations regarding human subjects research protections. The following survey will ask your opinion on a selection of the proposed changes which would have the greatest effect on how IRB offices process human subjects research submissions. In addition, you will be asked questions about the number and types of human subjects research studies reviewed by your IRB as well your institution's use of central IRBs.

The IRB Directors of the top 200 research universities in the United States are being asked to participate in this research study. The survey will take approximately 20-25 minutes to complete. You may exit the survey at any time and return to complete at a later time.

In order to minimize the chance of a breach of confidentiality, you will not be asked to provide any identifiable information. In addition, the survey program being used will not record any electronic identification information from your computer (e.g., IP address). It is hoped that the information gained will help the investigators learn more about how IRB Directors perceive the proposed changes to federal regulations.

If you have any questions before or after completion of this survey, please contact Ryan McDowell at rmcdowell@kumc.edu.

To continue to the survey, please click "Next Page" below.

Participant Information

For how many years have you been responsible for oversight of the IRB(s) at your institution?

Less than 1 year

1-3 years

4-6 years

7-9 years

10 years or more

Including the time spent in your current position, for how many years have you been working in human subjects protection?

Less than 1 year

1-5 years

6-10 years

11-15 years

15 years or more

Please rate your level of agreement with the following statements.

The current regulations promote effective protections for human subjects.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The current regulations promote efficient review of protections for human subjects.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The current regulations are adequate and DO NOT need to be revised.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Before today, have you had an opportunity to familarize yourself with the advance notice of proposed rulemaking (ANPRM) introduced by DHHS?

Yes

No

Institution Information

How many currently active human subjects research studies does your IRB(s) oversee?

Less than 500 studies

501 - 1000 studies

1001 - 1500 studies

1501 - 2000 studies

2001 - 2500 studies

More than 2500 studies

Not able to answer

What types of human subjects research studies are reviewed by your IRB(s)?

Biomedical only

Social/Behavioral only

Both biomedical and social/behavioral

What types of subject populations are included in the research reviewed by your IRB(s)?

Adults only

Children only

Both adults and children

Does your IRB review any clinical research studies (i.e., patient-oriented research, epidemiological and behavioral studies, or outcomes and health services research)?

Yes

No

Is your institution classified as an academic medical center?

Yes

No

Use of Central IRB(s)

Has your institution ever used a central IRB?

Yes

No

Central IRB Details – Have not used central IRB

Please rate your level of agreement with the following statements.

My institution does not participate in multi-site research so there is no need to go outside.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The institution's IRB(s) works efficiently so there is no need to go outside.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The institution does not want to incur additional costs.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The institution is concerned about the liability.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The institution is concerned about the absence of local representation.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

The institution is unable to assess the quality/outcomes of the services used.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Is your institution planning on using a central IRB in the future?

Yes

No

On average, what is the total time for approval after submission to the central IRB?

Less than 2 weeks

15-21 days

22-28 days

4-6 weeks

6 weeks - 3 months

More than 3 months

Not able to answer

Central IRB details – Have used a central IRB

Is your institution currently using a central IRB?

Yes

No

Which protocols are or have been submitted to the central IRB? (Please check all that apply.)

NIH funded Industry funded

Foundation funded

Institutional/Departmental funded

Patient-oriented research

Clinical trials

Health services research

Prevention Social/Behavioral

For studies sent to the central IRB, do you also require a local review?

Yes

No

For local review of studies sent to central IRBs, what institutional committees need to approve protocols? (Please check all that apply.)

Local IRB oversight review before or after central IRB review

Pharmacy and Therapeutics

Radiation Safety

Oncology

Gene Therapy

Biosafety

GCRC/CTSU

Privacy

Conflicts of Interest

Scientific Review

Other

If Other, please specify:

Do you maintain ongoing oversight (e.g., Adverse Event review, annual renewal, amendments, close out, investigator qualifications) of the research approved by the central IRB?

Yes

No

On average, what is the total time for approval after submission to the central IRB?

Less than 2 weeks

15-21 days

22-28 days

4-6 weeks

6 weeks - 3 months

More than 3 months

Not able to answer

On average, what is the total time for approval after submission to the local IRB?

Less than 2 weeks

15-21 days

22-28 days

4-6 weeks

6 weeks - 3 months

More than 3 months

Not able to answer

Please rate your level of agreement with the following statements. The use of a central IRB has shortened the time to approval.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

We are pleased with the quality and level of the scientific review performed by the central IRB.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

We are pleased with the human subjects protection review performed by the central IRB.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

We are able to maintain excellent local oversight for studies approved by a central IRB.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Use of a central IRB has attracted industry sponsors.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Why did you choose to use a central IRB? (Please check all that apply.)

Our IRB was shut down by OHRP

Our local IRB is not currently functioning due to reorganization

We couldn't keep up with the volume of protocols

We feel there is less liability exposure using a central IRB

We believe that a central IRB provides greater credibility

Pressure from our investigators/researchers

Other

If Other, please specify:

Do you intend to continue to allow investigators to use a central IRB in the future?

Yes

No

If you've used central IRBs in the past and then discontinued that use, why did you discontinue the use?

Streamlining IRB Review of Multi-Site Studies

The federal regulations currently do not require that a separate local IRB review be completed at each institution participating in a multi-site research study (with the exception of studies involving FDA-regulated medical devices). However, many insitutions still conduct a local IRB review.

In the advance notice of proposed rulemaking, DHHS cites reports and studies which show that the practice of having numerous IRBs reviewing the same protocol results in significant delays and does not enhance the protections of human subjects. DHHS argues that "relevant local contextual issues (e.g., investigator competence, site suitability) pertinent to most clinical studies can be addressed through mechanisms other than local IRB review" (p11).

To remedy the delays and inefficient use of resources resulting from multiple IRB reviews of the same protocol, DHHS asks for public comments "on the feasibility, advantages, and disadvantages of mandating that all domestic sites in a multi-site study rely upon a single IRB as their IRB of record for that study" (p11).

Please rate your level of agreement with the following statements.

Multiple IRB reviews of multi-site studies significantly delays the initiation of research.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Local IRB review of a multi-site study adds to the protection of local human subjects.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

If single IRB review was mandated for all multi-site studies, I'm concerned about how the IRB of record would be selected.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

I would agree with mandating single IRB review for multi-site studies as long as the IRB of record is held regulatorally accountable for their review.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

I would agree with mandating single IRB review for multi-site studies as long as the IRB of record is held legally liable for their review.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

What additional concerns, if any, do you have with mandating single IRB review of mult-site research studies?

Ensuring Risk-Based Protections

Another issue that DHHS addresses in the advance notice of proposed rulemaking is ensuring that the level of IRB review required adequately correlates to the level of risk of the research study. DHHS cites criticisms that claim the current regulations do not match the level of review to the level of risk. A specific example given is "surveys that are unlikely to lead to any harm to subjects nonetheless undergo review by a convened IRB" (p3).

The following questions will introduce some of the proposed revisions to address these criticisms and ask for your opinion.

Establishment of Mandatory Data Security and Information Protection Standards

DHHS introduces the possibility of establishing mandatory data security and information protection standards in order to minimize the informational risks (or the risk of harm resulting from the unauthorized release of information about subjects) associated with research studies. The idea is that if researchers follow these mandatory standards then informational risks would be systematically minimized to the point where IRB review of these risks would not be necessary.

If mandatory data security and information protections standards were implemented, indicate how comfortable you would be with the IRB no longer being responsible for review of a research study's plan for minimizing information risks.

Very Uncomfortable	Neither Comfortable or Uncomfortable	Very Comfortable

What additional concerns, if any, do you have with mandating data securtity standards thus eliminating the need for theIRB to assess informational risks?

Elimination of Continuing Review for Studies That Present No More Than Minimal Risk

Another proposed revision would be to eliminate the requirement for continuing review of studies that present no more than minimal risk of harm to subjects. This would include all expedited studies as well as full review studies that have progressed to data analysis or long-term follow-up only. Included in this proposed revision is the caveat that continuing review could be required if the IRB reviewer determines that there is a justifiable reason why it would be appropriate for a specific study.

Please rate your level of agreement with the following statements.

I am comfortable with the IRB no longer conducting continuing review on most expedited studies.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

I am comfortable with the IRB no longer conducting continuing review on most full review studies that are in data analysis only.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

I am comfortable with the IRB no longer conducting continuing review on most full review studies that are in long-term follow-up only.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

What additional concerns, if any, would you have with the elimination of continuing review for minimal risk research studies/activities?

Changing "Exempt" to "Excused"

DHHS is considering significant changes to the current concept of the exempt category. Given historical confusion over the "exempt" label and other proposed revisions (such as the mandatory data security standards discussed earlier) the current exempt categories would be translated to a new category called "excused."

Studies in this new category would no longer be exempt from the regulations, but instead would be excused from IRB review prior to implementation. Investigator's could begin their research study after registering the study with the IRB rather than waiting for an IRB review to be completed before proceeding with research activities. DHHS proposes that instead, a tracking/audit system could be implemented effectively shifting resources from pre-implementation review to post-implementation monitoring.

In addition, DHHS is considering expanding the now "excused" categories to include more types of minimal risk studies. For example, DHHS recommends expanding exempt category 2 (45 CFR 46.101[b][2]) to include all educational tests, surveys, focus groups and interviews with competent adults regardless of any identifying information being collected.

Please rate your level of agreement with the following statements.

Allowing investigators to begin research activities for "excused" studies without formal IRB review prior to implementation is a good idea.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Shifting resources from pre-implementation review to post-implementation monitoring for "excused" studies would be a more efficient use of resources.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Shifting resources to post-implementation monitoring would result in more effective protections of human subjects than pre-implementation IRB review.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Including all survey-type research with competent adults into this new "excused" category, regardless of the type of data being collected, is a good idea.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

If a waiting period was required before an investigator could start an "excused" study, how long of a waiting period do you think would be appropriate?

Less than 3 days

4-6 days

7-10 days

11-14 days

More than 14 days

What additional concerns, if any, do you have with the proposed revisions to the regulations concerning "excused" studies?

Improving Informed Consent

DHHS describes criticisms of the informed consent process ranging from the length and complexity of consent forms to the amount of time IRBs spend editing/revising them. To address these concerns, DHHS is considering revising the regulations to ensure that consent forms:

1. Include all the appropriate content necessary,

2. Restrict inappropriate content,

3. Are not too lengthy by limiting the acceptable length of sections,

4. Include an appropriate order of information (e.g., specify what information should be at the beginning of the form), and

5. Do not include excessive "boilerplate" language (e.g., language intended to protect institutional liability).

Beyond revising the regulations regarding informed consent to be more specific, DHHS is also considering publishing standardized consent templates which would satisfy the new regulations.

Please rate your level of agreement with the following statements.

The current regulations need to be revised to provide more specific guidance on acceptable content in informed consent forms.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Consent forms have become too lengthy and the regulations need to be revised to address this issue.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

Consent forms today include too much information that is not pertinent to the subject (e.g., institutional "boilerplate" language) and the regulations need to be revised to address this issue.

Strongly Disagree	Neither Agree or Disagree	Strongly Agree

What additional concerns, if any, do you have with the proposed regulations regarding improvement to the informed consent process?

Other Proposed Revisions

The preceding survey included selected topics from the advance notice of proposed rulemaking which the current investigators believe will have the greatest impact on how IRBs function.

Are there other topics in the advance notice of proposed rulemaking that you feel will have a greater impact (positive or negative) on the protection of human subjects? If so, please explain: