The implementation team invited public comment on its draft. To submit comments to the team, emails were sent to advancehsr@umn.edu. The public comment period began May 18 and continued through June 1. The team considered all feedback, created a response and finalized the work plan for the June 11th Board of Regents meeting.

Categories assigned align with work plan sections: Policy, IRB, Scientific Review, Conflict of Interest, PAR/Investigations, Psychiatry, Education, Metrics, External/Community. All team members reviewed all comments and responses.

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<th>#</th>
<th>Comments/Feedback</th>
<th>Faculty, Staff, Student, External</th>
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<th>Category (Report Section)</th>
<th>Response</th>
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<tr>
<td>1</td>
<td>When situations arise, like the present pressure on the administration to change the methods that we regulate research on humans, the pressure is to go with the regulators who do not have to stay and live with the newly created regulations. Please do not regulate human subject's research so tightly that we can no longer afford to do it. The existing is difficult enough.</td>
<td>Faculty</td>
<td>5/6/15</td>
<td>Policy - undue burden (Section 14 Accountability Metrics: IRB Protocol Review Process)</td>
<td>We agree that we must find the appropriate balance such that research participants are protected without excessive burden on the investigator and without unnecessary regulation. The committee recognizes that this may take some time to sort out. The clarifications we have made to the report based on public comments should help to explain our intent that while some of the changes apply broadly, others are targeted at specific types of studies that require more attention to ensure participant protection. Any new policies and practices will review administrative burden as a part of their implementation.</td>
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<td>2</td>
<td>Overall this is an impressive step forward. There are some ambiguities, however, that I'd like to see clarified, and there is at least two large issues that needs to be considered that I feel is missing:</td>
<td>Faculty</td>
<td>5/18/15</td>
<td>IRB (Section 4 IRB Membership)</td>
<td>2.1 We agree that clarification was needed and we have changed the report to indicate that the changes regarding compensation for IRB</td>
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1. What changes will apply to the non-medical IRBs? It needs to be clear which changes apply only to medical IRBs and which also will apply to social and behavioral sciences. In particular, I think it would be a mistake to change the policies and procedures regarding:

* compensation
* required attendance
* record keeping
* departmental scientific review

only in the medical IRBs, while not applying these best practices across human subjects research protection.

2. What does it really mean for CTSI to manage Psychiatry research? The bullets talk about training and related items, but the real question is who gets to approve the research proposal (is the director of CTSI taking over for the Psychiatry head?), under what conditions will the authority be returned to the department? Who makes that decision? And will it be possible to recruit an excellent head if the department will remain under "experimental receivership" after he or she takes over?

3. One of the issues I feel is a challenge for the IRBs is the lack of specific expertise. While this plan might address that issue for subjects with impaired consent capacity, it isn't clear that it addresses that problem in other areas. Should the other IRBs also specialize (e.g., having certain IRBs with specific expertise on cancer therapy trials or surgical trials)? Should the IRB maintain, in addition to its standing panels, stand-by panels of experts who are "on call" when specific studies warrant consulting them? Our IRB did this years ago with Internet research (though in practice, the expert panels was rarely consulted).

COI (Section 15)
Scientific Review (Section 6)
Psychiatry (Section 11)

members, required attendance, and record keeping will apply to both the medical and non-medical IRBs. Departmental review for non-medical studies will not be changed as no issues have been identified with the current model.

2.2 We agree this needs more clarity. Language has been added to Section 11 documenting that CTSI will work with the Director of Research for Psychiatry to. This will include overall project management and coordination of participant activities. We note in the report that CTSI had been in discussions with Psychiatry to perform this transition prior to the preparation of this report. We are simply accelerating the process. We also note that when the new Chair of Psychiatry is named CTSI will work closely with that individual to structure the research infrastructure in Psychiatry according to the way they would like it done.

2.3 The medical boards will be expanded to include members from the departments that are high volume users of the IRB so that expertise will be available for the majority of research activities. In addition, ad hoc reviews will be used for studies for which expertise is not available on one of the IRBs. Limiting certain types of protocols such as oncology studies or surgery studies to just one board can create backlogs and delays for review compared to placing protocols on
4. The elephant in the room is the issue of conflicts of interest that DO NOT TRIGGER THE UNIVERSITY’S CRITERIA. It is very clear that we have serious individual and institutional conflicts around money that flows through appropriate channels. Faculty in many units (particularly in the AHC) are under intense pressure to raise their own salaries, and face very unpleasant reprisals (from loss of resources to clinical assignments) if they cannot do so. This impacts both untenured and tenured faculty. Even faculty outside the clinical fields (e.g., science and engineering, liberal arts, biological sciences) depend on grant funds for summer support, and in some cases to release them from some teaching obligations. Departments and Colleges are also under immense financial pressure--pressure that often requires sufficient research funding (and ICR) to sustain their budgets and staffs. A result is that everyone’s decision-making is inherently biased towards “take the grant and do what you need to keep it and get the next one.” This isn’t a problem that can be fixed, but it is a conflict that can be disclosed so that the IRB (and the public record) can make clear exactly how much PI (and other investigator) compensation and department/college ICR is at stake, giving the IRB and the public the tools to examine when there may be systematic relaxation of local standards that warrants more careful scrutiny. Honestly, until the University comes to grips with the fact that most of our serious research conflicts are ones that don’t trigger University reporting we cannot be seen as taking a serious approach to research ethics.

Thank you for moving swiftly and thoughtfully in putting together such a plan.

2.4 The committee recognizes that the pressure to receive grant money, federal or non-federal, is intense for many faculty at any research university, including the University of Minnesota. This is a larger problem than the one the Implementation Team is charged with addressing and is connected with how research is funded in the United States. The team suggests that discussion around this issue should occur in other forums, perhaps facilitated by faculty governance. As for conflict of interest that could impact protection of human subjects, the team feels that the changes proposed in Section 15 of the report are a step forward.

3 Required resources: The current HRPP office annual budget is $2.2M. The estimated cost for this action plan is a $5.5M one-time cost and an increase of a more extensive human subjects protection program annual budget, but this could be considered after the 4 medical boards are functioning.

Currently, the HRPP budget is part of the budget of University research cost pool. The annual
I would like to begin by thanking you for providing such a comprehensive review of IRB practices and recommendations. I greatly appreciate your efforts and your transparency in these matters, as well as the opportunity to offer feedback. I have a number of comments regarding specific aspects of the draft report. For convenience, these items are enumerated below:

1) The report calls for “timely assessment of all aspects of the proposed research.” I couldn’t agree more. Currently, the IRB often takes many months to get back to researchers on projects. This delays research progress and makes the academic enterprise very inefficient. Furthermore, there is little transparency in communicating the time that it will take to hear back regarding a given project. Often, one needs to call or email the IRB several times in order to get projects reviewed. This is frustrating. It would be better to have specific criteria and a specific timeline for reviewing projects.

2) The report states the following: “A process should exist to deliver information back to the participant on the outcome of the research they participated in.” However, in the interest of protecting the anonymity of participants, we often avoid collecting identifying information, including contact information. Protecting anonymity is important, and is encouraged by the IRB. However, it's difficult to accomplish this when researchers are expected to provide information to participants on the outcome of the research. There are other reasons why this may not be necessary, feasible, or even preferable. First, participants may not
understand the results presented to them, particularly when hypotheses involve complex interactions between variables that are unfamiliar to those who aren't trained in a given field. Second, many studies conducted in the social sciences utilize online contexts, such as Amazon’s Mechanical Turk, in which respondents may be taking multiple surveys. In these cases, precise awareness of the analyses conducted by researchers may inadvertently interfere with responses to future surveys. When participants are too informed about the precise hypotheses that researchers are testing, they may respond in ways that are congruent with hypotheses that are familiar to them from previous studies, rather than responding naturally. Although some degree of transparency is important, it’s likely not important for participants to have a complex understanding of the precise hypotheses that researchers are testing, and this may be detrimental to the research process.

3) Regarding the Dan Markingson case, was there any attention given to the probability that any one individual enrolled in a study would commit suicide, relative to individuals not enrolled in a study? As of 2013, the overall suicide rate in the U.S. was 12.6 per 100,000 people per year. This means that out of every 7937 people enrolled in studies for a given year, we would expect at least one person to commit suicide by chance alone. Moreover, among people with schizophrenia, suicide rates are substantially higher (Hor & Taylor, 2010), and among patients with bipolar disorder, 25-50% attempt suicide at least once (Jamison, 2000). Rather than going on a witch-hunt in response to one very tragic case, it’s important to first evaluate whether or not negative outcomes (e.g., suicide, depression, etc.) are statistically more likely among people enrolled in studies, relative to those with the same conditions who are not enrolled in studies. Would different IRB policies have actually prevented this tragedy? Is there any actual evidence that the drug increased suicidal thoughts and behavior among behavioral studies, and what parts are targeted to studies involving more than minimal risk or vulnerable populations.
participants, overall? Although preventing tragedies such as this is essential, it would also be a mistake to implement draconian regulations or prevent studies that are greatly beneficial to participants, even when there are occasional negative outcomes for a few participants. This is particularly true when there is no systematic evidence that these negative outcomes are associated with participation in a given study. These are controversial issues, but I think that they are important to consider if one is interested in good policy, rather than reactionary policy.

4) A few places in the document, there are distinctions made between biomedical research and social/behavioral research. As I understand, the investigation pertains primarily to biomedical research, as it should. However, I would like to underscore the importance of distinguishing between these research areas. The National Research Council (NRC) has recently offered guidelines that are somewhat more flexible that current standard practices, and these guidelines also reflect those of the Office for Human Research Protection (OHRP), as well as the Department of Health and Human Services. Links to these pertinent sections of these guidelines are provided below:


In particular, the report suggests that research projects that pose minimal risk should be excused from IRB review:

"Studies where the research procedures involve informational risk that is no more than minimal risk (when appropriate data security and information protection plans are in place)"
This would almost certainly include the vast majority of research in the social and behavioral sciences, in which people are exposed to information that they are likely to encounter in everyday life, standard survey questions, etc. Indeed, even in experimental research involving the use of mild deception, risk to participants is generally minimal. Given the presence of secure data storage practices, informed consent, and debriefing to explain any deception that may have been used in the study, research in the Social and Behavioral Sciences should be largely excluded from the IRB review process. I sincerely hope that efforts made to protect human subjects and improve the human subjects review process will not result in unnecessary burdens on researchers in the social and behavioral sciences, whose research is of minimal risk to participants, almost without exception.

Thank you very much for your time and your thoughtful consideration.

5 Hello - My lab has IRB approval to collect peripheral blood from healthy donors to isolate particular blood cells, DNA/RNA, or proteins, and the data obtained is not connected to the donor. I believe obtaining certain human tissues through Univ. procurement facilities (Cancer Center) is non-exempt as well. While I see the need for an improved IRB procedure for clinical procedures, I hope this does not become a one size fits all application and approval process, and instead certain more low risk IRB protocols can be streamlined and customizable to the procedure. For instance, IACUC is a more module process in that certain basic information is provided and this is supplemented by relevant procedures as modules. Thanks.

Faculty 5/19/15 Org Chart Policy - undue burden

The changes at the IRB should further streamline the review process for your studies. Currently, a number of studies that are minimal risk such as yours are reviewed at the full board convened IRB meetings, In the future, all such studies will be triaged to the expedited review process so the turnaround time for your studies should be faster.
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<td><a href="https://drive.google.com/a/umn.edu/file/d/0B20cWO6w77sPUldJSjTUhicTRzd09mNGRrNVlyN3E3UE9v/view?usp=sharing">link to document</a></td>
<td>Faculty</td>
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<td>Org Chart</td>
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<td>We have added flow charts to the report appendix to help explain some of the new procedures. Many of the suggested language edits provided in this comment were incorporated into the revised report. We agree that we must find the appropriate balance such that research participants are protected without excessive burden on the investigator and without unnecessary regulation. The committee recognizes that this may take some time to sort out. The clarifications we have made to the report based on public comments should help to explain our intent that while some of the changes apply broadly, others are targeted at specific types of studies that require more attention to ensure participant protection. Any new policies and practices will review administrative burden as a part of their implementation.</td>
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<td>re: A more stringent structure for managing conflicts of interest, including a new policy that prohibits investigators from receiving personal compensation from industry while conducting a research study funded by that industry sponsor. I believe this is too broad a statement. There should be consideration of exceptions such as: 1) investigator initiated industry funded research which is not for the conduct of a clinical trial 2) performance of laboratory aspects of a clinical trial for which the UMN investigator is masked as to treatment assignment and has not enrolled patients in the trial I agree that investigators should not receive personal income for that</td>
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<td>Faculty</td>
<td>5/19/15</td>
<td>COI (Section 15)</td>
<td>Thank you for comments. We agree that the COI section of the report needed further clarification and this has been added. Investigators may continue to receive industry funding for research that includes salary support for the FTE devoted to the research. Investigators may continue to do consulting and engage in educational activities sponsored by industry while participating in a research study sponsored by the same company, but they may not receive personal income for that</td>
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compensation from industry while conducting a clinical trial funded by that industry sponsor, when this means enrolling patients in the trial or serving as a site or study PI.

One thing I forgot to mention is the following, by investigator initiated grants from industry I am referring to grants from industry which require application and review and where the research and the data belong to and are analyzed by the investigator, and where the content of presentations and publications is controlled by the investigator and the company can't exercise control over the scientific process or output. I think this is very distinct from investigators participating in industry sponsored clinical trials where patient recruitment and follow up are essential components.

8 Thank you for the opportunity to weigh in with a seemingly minor -- yet actually pivotal -- recommendation on the draft work plan. In my academic field of English rhetoric, it is a truism that language both reflects and shapes reality, so I urge you to help shape a more egalitarian reality by jettisoning the word "subjects" when equated with human beings. Whether or not the writer or speaker means to, using the dehumanizing term "human subjects" suggests a hierarchy in which kingly or queenly researchers objectify, look down upon, and lord it over, subtly or otherwise, mere "clinical material" (to cite another phrase that caring academics should never deploy).

Synonymous noun phrases abound that acknowledge the equal worth of humans who so generously give informed consent for research, e.g., "human research participants," "study participants," "trial enrollees," "human volunteers." I would pick 1 such term and stick to it throughout your document.

This is a topic near and dear to my career. In fact, I

consulting or educational activity—the payment can go to the University. These changes will apply to all human studies research. Extensive changes were made in Section 15 to clarify these points.

Thank you for this insightful suggestion. We agree, and “research participants” will be used throughout the plan.
wrote my dissertation-turned-book, *First Do No Harm: Empathy and the Writing of Medical Journal Articles* (New York and London: Routledge, 2002), on this very topic: how patients are too often demeaned, because of the top-down power structure, by insensitive labels unwittingly applied to them by physicians, insurance companies, and others in the health care industry. We at this wonderful University of Minnesota should be above such condescending nomenclature and, instead, should take the lead in foregrounding, in word and deed, the dignity of all humans, including those participating in research.

Again, many thanks for the chance to offer this constructive idea. Relatively easy to implement, it would effect a sea change in tone whose positive impact, though hard to measure, would be profound.

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<th>5/20/15</th>
<th>IRB Protocol Review Process (Section 5)</th>
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Thank you for sharing your perspective on the implementation plan. Although it would be ideal to direct the studies you mentioned to just one IRB board, and likewise direct studies from other specialties such as Oncology, Surgery, Cardiology, etc., to just one board it may not be practical because of the backlog and delay for review at the IRB. This could be reconsidered after the 4 medical boards are functioning.

I would like to talk to the committee about research on typically developing, healthy children that is conducted here at the U of Minnesota, much of it in the Institute of Child Development in the College of Education.

This research does not quality as exempt or as minimal risk because it involves minors. However, I don't think it often is the type of research risk that you all were contemplating when you wrote these new recommendations.

Much of this child research goes to the social science IRB panel, but some has to go to medical panels.

The work that goes to medical panels may involve blood sampling, heart rate measurement (involving electrodes), and brain wave measurement (involving electrodes). There certainly are risk, but they are of a different level than the risk of randomly assigning patients to different treatment conditions. And there are consent issues, but the parents of the children we test are not typically in a vulnerable group. And, while sick
children who need treatments for medical reasons often cannot refuse procedures; healthy children who are doing research solely for research purposes can and do refuse to play our games and the child's refusal is always a reason to terminate the session. .....if for no other reason than you don't get good data from a child who isn't cooperating.

We are wondering if it would make sense to designate a panel that deals with healthy (i.e., not medically or psychiatrically ill) child research that could be appropriately calibrated to the nature of risk in that research.

10 I have read the report that you helped co-chair and am puzzled about whether it applies at all to researchers whose work is reviewed through the social sciences panel. It doesn't seem like it does. This clarification has implications for a variety of factors related to implementing the recommendations made.

Faculty 5/21/15 IRB Protocol Review Process (Section 5) We agree that clarification was needed and we have changed the report to indicate that the changes regarding compensation for IRB members, required attendance, and record keeping will apply both to the medical and non-medical IRBs. Departmental review for non-medical studies will not be changed as no issues have been identified with the current model.

11 One thing that is lacking in this assessment is addressing the efficiency and effectiveness of the practices in the HRPP team to review and track submissions. An electronic system that allows for consent tracking (versions and approvals), document tracking and submission processing essential to improve the IRB ability to improve efficiency and reduce errors. Likewise, they IRB needs to develop a different way of conveying stipulations and deferrals. The letters are wrought with errors and misinterpretation; which is often due to the unnecessary time lag between the meeting and letter completion. The disorganization of the IRB team is wasting University resources trying to track down and interpret poorly done reviews. I am concerned unless

External 5/21/15 IRB Protocol Review process effectiveness (Section 5) See response to comment 4.1. The plan is to purchase and implement an electronic IRB process system that should facilitate the flow of information throughout the IRB application and review process.
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<td>real infrastructure support is provided, adding additional staff to train them on a broken system will lead to a bigger mess rather provide a way to move forward in a positive way.</td>
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<td>12</td>
<td>I am very concerned about the ability to provide meaningful scientific review if the proposal eliminates or significantly hinders review by those within the department of the investigator or who have previously collaborated with the investigator--for many of the studies that is going to be the only pool of people from within the institution with the appropriate expertise to actually provide the appropriate review. While we certainly can draw from external sources, I am skeptical that we can get a meaningful and particularly timely review if we need to make frequent use of external reviewers. Within the cancer realm, we are required by our NCI Cancer center designation to provide separate scientific review of all cancer related studies, and the draft doesn't seem to address if these same standards apply to the CPRC. I assume that is the intention and if so that should be made quite clear, as well addressing that we aren't going to start duplicating scientific review between the CPRC and the IRB.</td>
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<td>I think the proposed plan needs some revision. I did not see any mention of using a central IRB. I think this is necessary. Our current IRB is overloaded and understaffed. The ability to get an email or phone call often takes weeks. While I know the cost of central IRB is immense one way to decrease the load on the current IRB is to have sponsored projects go to the central IRB as they pay a fee anyway and have the internal projects use our IRB. I don't think increasing meetings or staff will be enough to fix the current issues. One other area is in regards to conflicts of interest. I'm</td>
<td>Faculty</td>
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uncertain why one would not allow anyone with a conflict of interest to be a PI. While I know that is the stance at Mayo, I have email confirmation from over a dozen other major academic institutions who allow conflicts of interest hold a PI position as long as they have a COI plan with the COI committee or similar committee at said institution. COI does not prevent good research done with integrity. My current COI allows me to be able to teach anesthesiologists all over the world how to better manage patient's pain which has an impact on thousands of patients. My impact on humanity is likely higher with my COI than with my research. I think if you have a COI plan and abide by it good research can be done and I beg you to reconsider this stance. I think having a zero tolerance for breaking the COI plan is a better option.

There are other issues but those are minor compared to these two. I hope you consider these options. Thank you

*These additional comments were submitted on 5/26/25:*

After further thought I also think the plan to bring the scientific review to the IRB is troublesome. Currently it takes months to just get an IRB approval, bringing this to the IRB will further delay things. Furthermore, I'm not confident there is sufficient knowledge on the IRB to say whether certain studies are scientifically sound especially in the area of anesthesia/pain management. I suggest to keep these within the departments ensuring that each department does have a scientific committee. Thank you

I think we should follow the practices of the other top 10 research universities and the FDA and NIH. Many of the recs in this report are well beyond these standards.

The intent is that the University of Minnesota be a leader in the protection of human subjects. However, see response to comment 1 on undue burden. Moving ahead, benchmarking against peers will be part of the implementation process.
The phrase 'reinventing the wheel' comes to mind with such exercises. To what extent, for better or worse, do our new formulations compare with our nearby peers.

| 15 | The phrase 'reinventing the wheel' comes to mind with such exercises. To what extent, for better or worse, do our new formulations compare with our nearby peers. | Faculty | 5/21/15 | Policy - undue burden | See comment above for 14 |

I have four brief suggestions.

1. **IRB relationship to the researcher:** IRB solutions are often bureaucratic. Our current IRB functions through forms, and typically, with limited relationship to investigators. This often does not allow the IRB to adequately assess (a) unique ethical demands of a particular research context, and (b) the current knowledge base, skills, and attitudes of a particular researcher in match to this particular context. A pre-IRB review meeting interview between the applicant and an IRB staff person to review the application is a potential opportunity both to resolve questions and misunderstandings from the initial pre-review of the application, and to assess this match. This would require training and empowerment of IRB staff into a more active and sophisticated role. Relationships between the IRB and researchers can and should be collegial and supportive of the researcher (and I am happy to say, this has been my experience at UMN when I have called). In most all cases, adversarial and even antagonistic relationships with the IRB do not advance research participant protections.

2. **Personalized Ethics Training:** The IRB process offers an opportunity to provide ethical decision making training that is individualized to the outcomes of an assessment of (a) the research context of the IRB proposal, and (b) the knowledge base, skills, and attitudes of the investigator. This has far greater likelihood of protecting research participants; in some cases, a focused and highly relevant training curriculum

| 16 | I have four brief suggestions. | Faculty | 5/22/15 | IRB Protocol review process (Section 5) Education (Section 13) Community Engagement (Section 16 and Executive Summary: Engaging Research Subjects) | 16.1 thru 16.3 Thank you for these excellent suggestions. After this implementation plan is formally approved by the regents there will be a process to create a detailed plan for how each part of the proposal will be implemented. We will include these suggestions in this process. 16.4 We agree that the CTSI Community Engagement Core will play a central role in the implementation of many of these recommendations. |
might both be more in depth and briefer than a bureaucratic, one size fits all, broad, exhaustive training model that uses a uniform research ethics curriculum. The later approach assumes one curriculum can address every context.

(3) Research Ethics Lectures and Seminars: One positive outcome of recent events is opportunity for a stimulating University-wide lecture series on contemporary issues in research ethics with human participants. A peer-reviewed program funding invitations to research ethics speakers in interest areas of faculty and students could provide topics and speakers. There is also a similar opportunity to augment seminars of traineeships at the undergraduate, graduate, and postdoctoral level with research ethics trainings by prominent scholars in these areas.

(4) Community Engagement Model: Use of the CTSI Community Engagement Core, and a community engagement model plays to our existing institutional strengths. Elements of community engagement approaches suggest promising models for enhancing protections of our research participants.

| 17 | My clinical research career at the University of Minnesota began in 1976, and having lived through the creation and growth of IRBs (there were none in 1976), I would like to share a few thoughts regarding the proposed changes. The best clinical research, from both an ethical and outcomes perspective, is done by investigators who have respect and compassion for the volunteers. In addition, the investigators should be respected and not unduly burdened by administrative requirements that have become increasingly complex and often counterproductive. In reading both the Auditor's and AAHRPP report, I |
| Faculty | 5/23/15 | Policy - undue burden |
| Education (Section 13) |
| Engaging research subjects (Section 12) |
| FUROC (Section 7) |
| We agree that we must find the appropriate balance such that research participants are protected without excessive burden on the investigator and without unnecessary regulation. The committee recognizes that this may take some time to sort out. The clarifications we have made to the report based on public comments should help to explain our intent that while some of the changes apply broadly, others are targeted at |
believe that we are responding with a plan that is too expensive, too cumbersome, and will not meet the goals intended. The two major conclusions from the AAHRPP report that we need to address are excerpted from their executive summary, and my suggestions follow.

"While there is no explicit requirement for ethics education for investigators imposed by the federal research regulations, such education is a requirement of NIH and NSF supported research and is widely considered to be a valuable element of a research protection program. The external review team noted the University’s recent introduction of policy changes that mandate additional training of IRB members. However, the broader educational policies and practices at the University fulfill minimal standards but represent a missed opportunity for a richer and more sophisticated institution-wide.

In my opinion, the training programs I have been required to take are inadequate and in some ways counterproductive. Being required to listen to lectures about shortcomings of research done many years ago, as if the standards of those days are still in practice, and working through an Internet program detailing regulatory minutia is not helpful. To foster respect and compassion for the volunteers, I suggest that we establish forums in which senior researchers discuss the hopes and fears of participating in a research trial with subjects who have experienced this. I believe that young investigators would develop the needed respect and compassion for those who sacrifice their time and literally blood to aid in translating research into clinical use from these interactions. These may be much more productive than lectures.

"Some research subjects, by virtue of impairment or incapacity, may be unable to fully protect their own interests at the point of study enrollment and during the course of research participation. The external review

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<td>specific types of studies that require more attention to ensure participant protection. Any new policies and practices will review administrative burden as a part of their implementation.</td>
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<td>We appreciate this excellent suggestion. In this plan we recommend that we use the current infrastructure of the CTSI around curriculum development and have that group partner with HRPP and OVPR to create a comprehensive, modern curriculum that addresses the needs of the research community (across the entire spectrum of clinical research). We recommend they review training programs already in place at other institutions to see what could be imported for our use as well as develop new curricula where needed. These suggestions will be made available to the group tasked with this activity along with our recommendation that they be strongly considered for implementation.</td>
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team observed that inadequate attention has been paid in IRB review and in University, hospital, and IRB policies to research with these subjects. One opportunity the University could consider in order to enhance subjects protection would require the involvement of clinical staff and others who are independent of the research team in formal gatekeeping roles. Such individuals may serve to mitigate or eliminate the conflict inherent in procedures related to recruitment, consent, and study exit. At Fairview Health Systems, where the relationship between research and clinical priorities in Psychiatry is strained and mistrust of researchers is widespread, the involvement of clinical staff in research functions as independent gatekeepers may help resolve this longstanding problem.

Although the intent is good, I believe that gatekeepers will be overly costly and burdensome, and again, if paid by the University, be subjected to criticisms of conflict of interest. More useful would be to establish and “ombudsman” independent of the U to whom research subjects and their close ones could turn to for concerns. In addition, the IRB could establish a system of randomly contacting research subjects to enquire about their comfort level with the team of clinical investigators.

In addition, I have concerns about returning scientific review back to the IRB. It was relegated to departments some years ago because it was felt that IRB members may not have always had the expertise to judge the scientific merits of some proposals. Sometimes overlooked in judging scientific merit in clinical research is that some studies are not major breakthroughs, but may improve the care and quality of life of patients.

Unfortunately, we live in an era where experts are often mistrusted and perceived as being biased. This often leads to persons with little knowledge of a field, such as the intricacies of clinical research, making reports and
recommends that may have little evidence of effectiveness and may be counterproductive. I hope that pressure from some individuals who have their own biases, such as beliefs that university faculty should not work with industry, do not lead to rapid implementation of policies that are more of a response to criticism than evidence based solutions. We should take seriously the criticism in the reports, but act only after fully determining if the proposed solutions will truly enhance the clinical investigator’s respect and compassion for volunteers.

I submit my feedback on behalf of my family who also had issues within the Fairview - Riverside - UMN - Department of Psychiatry research program.

Having read through the draft plan and also having attended the open public forum hosted by Dr. Brooks Jackson, I personally feel an initial first step towards resurrecting the research program and human subjects protection is being presented.

However, that is a small first step until I see and accept that the U of M fully understands and truthfully acknowledges that there were and are still major obstacles to clear as far as credibility is concerned. You don’t exonerate yourself and make false and misleading statements for a decade and then when exposed expect the public to pat you on the back.

The chair of the department stepping down should have been forced on the him years ago, and whether or not the Markingson treating physician was able to convince everyone that he does not coerce his patients is highly questionable since the Legislative Auditor's report states the opposite, and that very abusive and aggressive behavior has been his trademark.

Eliminating the Peer Review should have taken place years ago, as well as the proposed moratorium on accepting industry money for speaking etc while

| 18 | I submit my feedback on behalf of my family who also had issues within the Fairview - Riverside - UMN - Department of Psychiatry research program. Having read through the draft plan and also having attended the open public forum hosted by Dr. Brooks Jackson, I personally feel an initial first step towards resurrecting the research program and human subjects protection is being presented. However, that is a small first step until I see and accept that the U of M fully understands and truthfully acknowledges that there were and are still major obstacles to clear as far as credibility is concerned. You don’t exonerate yourself and make false and misleading statements for a decade and then when exposed expect the public to pat you on the back. The chair of the department stepping down should have been forced on the him years ago, and whether or not the Markingson treating physician was able to convince everyone that he does not coerce his patients is highly questionable since the Legislative Auditor's report states the opposite, and that very abusive and aggressive behavior has been his trademark. Eliminating the Peer Review should have taken place years ago, as well as the proposed moratorium on accepting industry money for speaking etc while | External | 5/24/15 | Engage Research Subjects (Section 12) Psychiatry (Section 11) Scientific Review (Section 6) Community engagement (Section 16) | The committee was keenly aware of the circumstances and history of the Markingson case. The 2013 Faculty Senate resolution calling for an examination of current human subjects protection was a result of the Markingson case and led to the external review of the University human subjects protection program. The committee hopes that the forward-looking actions presented in the report will change the culture at the University and that the University will embrace a human subjects protection program that meets the highest ethical standards. |
conducting a research trial for that very same company. Long overdue.

Soliciting help or advice from the community stands out as a very strong idea, and I don't mean from advocacy groups such as NAMI etc, I mean actual past patients or their family members that might be willing to offer advice in areas that were of concern while they participated in a trial.

The Markingson case at the U of M has brought to light so many issues for so many others that had been afraid or lacked the stamina that it must have taken for the Markingson family, to have carried the fight for so long.

Please listen to the family, listen to the patient, and just don't assume your research staff have their priorities always in place. That's the real issue.

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<th>19</th>
<th>I have comments regarding two topics:</th>
<th>External</th>
<th>5/24/15</th>
<th>IRB Membership (Section 4) Post Approval Review/Monitoring (Section 8)</th>
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<td>IRB Community Member Reimbursement</td>
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<td>Thank you for your insightful comments and the work you do for the UMN IRB. Your current workload is excessive and the new plan, which quadruples the number of medical boards should decrease your workload substantially. As you point out, serving as a community member on an IRB is a community service activity. The proposed payment is to acknowledge the work and time and inconvenience that community members expend in service to the university and it is not intended as a salary. The budget in section 19 of the plan has been changed to include funds for community members. As you have recommended, the PAR will stay under the direction of the IRB.</td>
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Implementation, does not bolster one's sense that members of the Implementation Team fully understand nor appreciate the role of community members.

Membership on the IRB requires a time commitment that far surpasses most volunteer engagements. Meeting attendance is a small fraction of that time commitment. At present I spend a minimum of 20 hours and most often 30 or more hours of preparation prior to each meeting. While increasing the number of panels and members is intended to spread out the workload and decrease the time required of each member, weekly meetings with a 60% minimum attendance requirement coupled with the additional preparation time that will be required to fulfill the aim of increasing the scope of panel discussions may not decrease the overall time commitment significantly. Community members do not perform this service for the money. However, fair compensation does provide an incentive to select this alternative over the many other less demanding volunteer opportunities that are available in our communities.

Separate PAR from a reporting relationship to the IRB

The work plan does not acknowledge the fact that the PAR function was moved from OVPR to HRPP several years because it was creating confusion and friction nor does it indicate what changes will be made to ensure a successful operation this time around. If one of the main foci of this work plan is to strengthen the role, recognition and effectiveness of the IRB, then moving the PAR out of HRPP seems to me to be a move in the opposite direction.

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| 20 | Thank you for your draft of a Work Plan for Implementing the Recommendations of the External Review of the University of Minnesota Human Research Protection Program. Not being an academic or engaged in academic External | 5/27/15 | Culture (Section 3) | Thank you for sharing your perspective. Your comments get to the need to change the culture at the U of MN regarding human studies research. You are correct that this plan alone will not change the |
research, I know little about the mechanisms involved or the adequacy of the numerous protections included in your plan. But as a concerned citizen, your plan seems to address the issues raised both by the report of the external review panel and by critics of prior U of M research practices.

However, one issue not addressed -- and it probably was not part of your mandate -- is how to ensure that University administrators at the highest levels, whether in the Medical School, the Office of the President, or the Regents, will respond appropriately to critics when and if redress through the mechanisms you recommend prove insufficient.

As you no doubt know, the report of Minnesota Legislative Auditor James Nobles claimed that University administrators at these highest levels responded in an insular and defensive manner to critiques of the U of M practices in and response to the Dan Markingson case, and that those administrators ignored "serious ethical issues."

I would suggest that so many such high-level administrators were involved that it is unlikely the response -- or lack of one -- was due to who they personally were. More likely, something within the institution produced such a consistent response from so many individuals. I am not at all confident that the external review panel and your subsequent report address this concern.

Whether this concern was covered by your mandate or not, it may well need to be further addressed by someone or some committee such as yours.

Thank you for your work on what seems to be an otherwise thorough report.

You raise some valid concerns and some reasonable suggestions
| Page | 35 | Just a couple of comments about the IRB draft  
1) I like the plan to have multiple IRBs to review proposals, so that applications can be reviewed more quickly. At one of my former institutions, which is smaller than UMN, we had 3 IRBs.  
2) If IRB members are going to be given salary support or paid in some way, there must be accountability regarding participation. Attendance at meetings must be recorded, and if a member misses more than a set percent of meetings, e.g., 20%, then they should be removed from the IRB or have a percentage of their support decreased.  
3) Having shorter weekly meetings for each IRB may be difficult for many faculty. Longer, less frequent meetings may be more desirable for at least some faculty.  
4) How do we reconcile the idea that we need, e.g., more heme/onc physicians on the IRB for their expertise, yet at the same time, reviewing the protocol of a division colleague is viewed as a conflict of interest? | Faculty | 5/27/15 | IRB Membership (Section 4)  
IRB Protocol Review Process (Section 5) | At IRB meetings those with a COI for a particular protocol must recuse from the vote. If necessary, ad hoc reviewers can be recruited for specific protocols. |
| 36 | I am writing as an alumni, former employee of the UMN IRB, past Research Compliance Officer in the short lived Office of Regulatory Affairs, Masters student in Regulatory Affairs and recent hire to the department of Psychiatry. | Faculty | 5/27/15 | Psychiatry (Section 11)  
Culture (Section 3) | The committee agrees, and with the exception of Section 11, the report is directed towards the entire university. |
I have worked in clinical research in every role I could think of, with "Investigators", at a "Sponsor", at an "IRB". I have volunteered to be a research subject. I have enrolled research subjects. I have monitored research. I believe in it. I live it.

I am concerned that the department of Psychiatry has been singularly identified. They most certainly do enroll vulnerable subjects, as defined on pages 37-39 of the Implementation Plan ("IP"), however, I believe most subjects enrolled would fit into this category based upon the definition. Why are other departments who also routinely function with this patient population not also identified? As the IP states, "In one sense, one failure adversely affects the particular study, all present studies, all future studies and even the broader community".

I understand that while the IP was a reaction to reports released that were directly tied to the department of Psychiatry, it would be remiss to not use this opportunity to create process improvement with all human subject research within the ENTIRE University of Minnesota.

First of all, thank you for the extensive effort and obvious dedication that has gone into development of this plan. I think that you have identified many of the issues that need to be addressed. I do have one overarching comment that I think is not adequately addressed, and that is the concept of "arm's length."

For research subjects to be adequately protected, there must be a firewall between the physician who is making medical decisions for the patient and the individuals and the entity that is conducting and profiting from the research. It must be recognized that a researcher and an institution profit in many non-financial ways from research that enrolls human subjects. The University of Minnesota receives significant research funding that adds to its stature as a research institution, and also

| 37 | First of all, thank you for the extensive effort and obvious dedication that has gone into development of this plan. I think that you have identified many of the issues that need to be addressed. I do have one overarching comment that I think is not adequately addressed, and that is the concept of "arm's length." For research subjects to be adequately protected, there must be a firewall between the physician who is making medical decisions for the patient and the individuals and the entity that is conducting and profiting from the research. It must be recognized that a researcher and an institution profit in many non-financial ways from research that enrolls human subjects. The University of Minnesota receives significant research funding that adds to its stature as a research institution, and also |
| Faculty 5/28/15 | Research and Vulnerable Populations (Section 10) COI (Section 15) External IRB (Section 5) | We agree that the plan should include information about Central IRB and it has been included in section 4. |
receives significant recognition for working at the frontiers of medicine. Without research, no advances will be made in patient care. Research is a fundamental part of our mission, but it also raises our stature locally and nationally.

But the rewards of research, whether financial or in reputation, to the individual or the institution, create tremendous bias that is difficult to manage, even when aware of it. The Implementation Team has recognized this within a department (Psychiatry) and addresses it, but fails to recognize that the same bias extends beyond a department to a school and to the full university. The school of medicine AND the university as a whole have an equal conflict of interest that is not addressed in any way in the workplan - only the conflict of the individual researcher and the individual's department.

The only truly objective review of the appropriateness of research comes from outside, from a body that does not stand to profit, which exists as an external or centralized IRB. There are a number of laudable academic institutions that have contracted their review process to these IRBs, primarily to address the inherent conflict of interest of reviewing research within an institution. At first blush one would think that this would be a terrible way to go - by distancing itself, it appears that the institution is abrogating its responsibility to ensure the safety of patients. In actuality, these institutions are taking the highest ethical and moral stance, making sure that a group with no immediate reward reviews all research that involves human subjects.

The centralized IRB can be one that exists as a separate entity with no ties to an individual institution; it can also exist as a "pool" of institutional IRBs that share the work of reviews (Emory is in one such pool), and ensure that each review is conducted by a group not affiliated with the institution enrolling the patients.
The FDA has recognized the enhanced objectivity of having external, centralized review boards, and has long accepted their review in sponsored trials. We believe that the FDA is moving to mandate that outside, centralized IRBs manage all sponsored studies, and that institutions that do not permit use of a centralized IRB will not be allowed to participate in these studies. At present, a researcher cannot participate in many large drug trials unless through a centralized review board; we know personally of 10 over the last 3 years that we could not participate in because the UMN IRB refused to allow external IRB review. It seems the UMN IRB felt they had a superior process, which we now see was not true.

I would urge the Implementation Team to strongly consider implementing an external review process. As put forward in the workplan, inherent bias continues to exist although perhaps somewhat diluted. The only way to maximally manage bias and conflict of interest is to utilize a centralized IRB.

This would not, of course, eliminate the IRB at the University of Minnesota. It would continue to perform a vital regulatory role, providing strong oversight and direction, education and management of ongoing trials. But the final, overarching decision about the ethics and morality of the research would be done by individuals with no personal gain. If an external IRB is not to be employed, it should at least be made available for those trials where the FDA has mandated this approach. To insist that approval must be internal only eliminates opportunities for our patients and researchers to participate in important trials.

I hope that this comment will raise some other possibilities for managing the very difficult questions of conflict of interest and bias, not within an individual or department, but within an entire school and a university.
Finally, I would ask the Implementation Team to very clearly state that the physician making medical decisions for a patient CANNOT BE the individual who is a named investigator in study. This is a critically important protection that I did not see specifically called out (although I may have missed it in the extensive document).

Thank you for the opportunity to comment, and best wishes as you move forward.

| 38  | I appreciate the tremendous amount of work done in a short time by the “implementation team” and the opportunity to comment on the proposed plan. Most of my concerns relate to the recommendations for scientific review. As background, I have a long history of NIH- and pharmaceutical company-funded clinical and translational research at the University and, as a result, a long history of working with the University of Minnesota IRB.  

I have a few comments regarding the draft plan.  

First, I notice that the only (internal) clinically-oriented physicians and the (outside) chair on the committee are from Departments of Medicine. Is there a reason physician-researchers from other departments were not included in discussion and development of the plan?  

Second, regarding, “Management of Conflict of Interest,” there are two issues that I feel need to be specifically addressed:  
a) Payment for subject enrollment. This can occur in both sponsor-created and investigator-initiated trials. (One can understand a sponsor’s perspective - providing a large grant and having zero enrollment would not be acceptable.) Prohibiting such trials at the University would limit clinical research. Consequently, guidelines should be developed. Obviously, physician payment per subject enrolled is a conflict. What other | Faculty | 5/28/15 | Scientific Review (Section 6)  
COI (Section 15) | Committee members included representation from many groups within the university. To be sure, some groups were not included, but there is a trade-off between having a committee that is highly representative but unwieldy and a committee that is less representative but of a feasible size to function effectively. The COI section has been clarified. |
guidelines can be developed without limiting investigators’ participation in these trials?
b) The guidelines that are developed for both scientific and human subject protection should include time limits on the review. University of Minnesota participation in multi-center studies is currently limited by extended IRB review and stipulations, followed by re-review and new stipulations, etc. (e.g., we have an application that was submitted in November and after responses to stipulations was sent back and returned with new stipulations, etc. By the time this protocol is IRB-approved [if ever], the multicenter study will have completed [or nearly completed] enrollment and we will have lost the opportunity to learn if the protocol is of benefit to our patient population). This entire process could be streamlined (e.g., a separate group available to review and turn around resubmitted applications.) If there is going to be an additional step in the process - i.e., scientific review - similar streamlining and efficiencies must be included in the plan.

Third, regarding “Scientific Review.” I am concerned about how the “scientific review” process will be designed and implemented. If Departmental Review is eliminated, then, unlike the makeup of the implementation team, the scientific review group should be multidisciplinary. I am strongly opposed to the statement “HRPP managed” process (for scientific review) could be done through the CTSA Translational Research Portal (as stated in recommendation B.8, page 24). The heavily Department of Medicine-directed CTSI already has considerable power and influence at the University. In my opinion, giving the CTSI additional power would be a mistake. No one small group should have that much control over the University’s Medical School research agenda. If moved outside of the Departments, the scientific review should be done by an independent committee (which should have strict, and tight, time limits for review and response).
In fact, considering that one recommendation is to pay reviewers, wasn’t it a conflict of interest for the Department of Medicine loaded “implementation team” to consider recommending that the scientific review be done by the Department of Medicine-loaded CTSI?

39 The draft work plan from the President’s external review panel offers a number of important and excellent suggestions for improving the conduct of clinical research at the University of Minnesota and it’s clinical partner, Fairview.

While I support the majority of these recommendations, there are two which I find unacceptable.

The first of these is the suggestion of compensation for members of the IRBs, particularly faculty. I certainly agree that the number and composition of the IRBs be expanded and that guidelines for workload be developed. These are important and necessary changes as is the recommendation of targeted participation by specific faculty groups. However committee service is an expected role for faculty and there are many essential committees of the University (Admissions committees, Promotion and Tenure Committees for example) where service of faculty is required but not compensated. To select out one committee function for University payment to the departments for faculty time serves to diminish the importance of service on other vital committees. Rather the workload and term of service on the IRB should be crafted so that it is in line with service on other committees. I strongly disagree with this recommendation.

The second recommendation with which I disagree is that all of the clinical research of the Department of Psychiatry be placed under the direction of the CTSI. To single out one clinical department for this regulation is extraordinary and it is extremely punitive. In fact it

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<th>IRB Membership (Section 4) Psychiatry (Section 11)</th>
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Thanks for your comments. The COI and Psychiatry sections have been modified.
ensures that the department of Psychiatry will never be able to succeed in recruiting an outstanding Department leader now that the current Departmental Chair has resigned. This department is essential for the medical school. It educates our students and residents in a specialty which is badly needed by the state and the nation. Psychiatrists are in short supply locally and nationally and we seem to have forgotten the outstanding job in education and training that our Psychiatry department and its faculty have done in what appears to be a frenzy to “punish” the department for what are perceived as lapses in clinical research procedures. We seem to have forgotten the hundreds of important research studies conducted over the years by faculty of this department which have enhanced our scientific knowledge and the treatments for patients. If all clinical research across all departments is to be put under the umbrella oversight of the CTSI, I would question the feasibility but not object. However I strongly oppose the overreaction which has led to this recommendation for the Psychiatry department. If enacted, the consequences will be serious and longlasting.

Finally the suggestions about a new position of Ethics coordinator seem unnecessary given the other substantive changes and the recommendation for no personal compensation from a research sponsor to an investigator, while not unreasonable, requires more clarification. I assume that the investigator is allowed to receive reimbursement for their role in the research study as is any other PI and I am confused by the “EXCEPTION CLAUSE” which weakens this section considerably.

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<th>Research Involving Vulnerable Populations (Section 10)</th>
<th>Engaging Research Subjects (Section 12)</th>
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<td>have department-based review processes. Under the new process, PIs and department committees are allowed and encouraged to recommend experts from within and outside their department to serve as reviewers. We appreciate this comment and have language in this report that strongly recommends that we use existing resources to help with engaging research participants.</td>
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41 Having reviewed the managing conflict of interest section pages 52-53 I have significant concern over the suggested change in policy stating ".....individuals who seek approval from the IRB as study staff on a protocol may not receive any personal compensation (other than supported thorough research grants) from a company during the time that investigator participates in any new research study funded by that industry sponsor."

This policy will prevent faculty from work with industry that is outside the purview of being the site PI for industry sponsored trials; examples include being the National PI for a multisite trial where consulting fees are provided rather than %effort and the site PI for a different study, it would prevent consulting on unrelated studies, i.e. consulting on work such as device development or other technology that has nothing to do with the trial they may be the site PI for, one would be prevented from serving on a DSMB for that company, another example would be the inability for a site PI of an industry sponsored study to participate in studies that are developed by industry in partnership with the NIH. There are numerous examples like this that would significantly limit industry interactions and potentially compromise our ability to compete for dual sponsored |

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<td>Thanks for your perspective. The COI section has been modified for clarity.</td>
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grants/studies. The unforeseen restrictions to such a policy can be and will likely significantly compromise our ability to expand collaborations and research programs which depend in part on collaborations with our industry partners.

I believe we will find that this policy is going to be too restrictive and will hurt research at this University. I appreciate the need for the community outside and for many inside the University to feel we are doing the things we need to do to address concerns that have been raised, but I truly hope we can do so without compromising the future of research at the institution by instituting the above policy.

| 42-44 | https://drive.google.com/file/d/0B20cWO6w77sPMHbGboRmUTJCYWc/view?usp=sharing | Faculty (3 co-signers) | 5/29/15 | Policy – undue burden |

Thank you for your (always) thoughtful and substantive comments on the draft implementation team’s report. As you might expect, we have received other comments on the draft plan, some of which are echoed in your letter. From my perspective, it is absolutely understood that our institution has done exceptional clinical research both historically and currently, and through that research has contributed tremendously to the better health and wellbeing of our society. Thus, our commitment to clinical research is unassailable, and we believe strongly in the need to continue our excellence in this area. I would also state that both the implementation team and the RCAC (as well as many of the comments), have made it clear that whatever changes are made through this process, it should not add inappropriate new burdens on
the investigator and the hope is that we can make things easier and faster as we implement the electronic IRB process as recommended by the implementation team.

You also comment on the insufficient detail about exactly how some of the recommendations will be operationalized. Given the time frame available to the team to produce a report in response to the charge from the President, and the scope of the charge, it was not possible to fully work out the operational aspects of every recommendation. Having said that, I want to assure you that as the recommendations are adopted, significant input from the clinical researcher community will be sought to make sure that they are done thoughtfully and appropriately.

I look forward to continual engagement with you and your colleagues as we move this process forward.

<p>| 45 | <a href="https://drive.google.com/file/d/0B20cWO6w77sPVUdua21QUHNfcVE/view?usp=sharing">https://drive.google.com/file/d/0B20cWO6w77sPVUdua21QUHNfcVE/view?usp=sharing</a> | Faculty | 5/29/15 | Community Engagement (Section 16 and Executive Summary: Engaging Research Subjects) | This comment emphasizes the importance of community member involvement at all steps in the approval and oversight of human research oversight. We agree and the current plan includes provisions to recruit community members for these roles. We agree that the CTSI Community Engagement Core will be an important resource as we implement the recommendations of this plan. |</p>
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<td>Faculty</td>
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<td>Thank you for your comments. Several of the sections of the plan to which you refer have been modified for clarity.</td>
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<td>47-48</td>
<td>Faculty</td>
<td>5/31/15</td>
<td>We agree that the CTSI will only oversee Psychiatry studies that involve vulnerable participants or are interventional. In addition, these comments question the changes in the COI policy and the potential adverse effects on the ability of investigators to participate in consulting for innovations in medical research. These are good points and the COI plan has been modified to clarify that researchers may continue to consult for industry and at the same time conduct research sponsored by the same company. The change is that the investigator may not get personal income from consulting or from educational activities while participating in research sponsored by the same company.</td>
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<td>49</td>
<td>Faculty</td>
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<td>The plans to compensate IRB members will also apply to the behavioral boards, so the proposed changes will be harmonized for all the iRBs.</td>
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<td>IRB Protocol Process Review (Section 5)</td>
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interacted with the IRB for many years as a principal investigator, primarily the Social and Behavioral IRB.

I realize that the External Review committee did not analyze the operations of the Social and Behavioral IRB, and that, accordingly, your committee focused almost exclusively on the biomedical IRB. My suggestion is that once the implementation plan is adopted for the biomedical IRB, a panel should examine the procedures of the Social and Behavioral IRB in the light of this plan. I have no specific issues to raise concerning the Social and Behavioral IRB. But in order to protect its integrity and harmonize its procedures with the updated biomedical IRB, I think such a review would be valuable. Would your committee consider making a recommendation along these lines?

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<th>Faculty</th>
<th>5/31/15</th>
<th>Policy - undue burden</th>
<th>To comment on where 10% compensation for IRB comes from: See response to #3.</th>
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| 51 | A. Background. | Faculty | 5/31/15 | Post Approval Review/eIRB (Section 8) | We agree with recommendation #4, and the implementation of an electronic IRB (which is recommended in the draft report), will allow us to accomplish the goals you outlined.

With respect to recommendations #1-3, we also agree that these recommendations are important and are good suggestions, but feel that they are beyond the specific charge
full audiotape of the Minnesota Senate Hearing with the Legislative Auditor. In addition, I attended the Town Forum May 4 and the Board of Regents Meeting on May 7.

On April 30, 2015, I served as substitute senator for Albert Marden in the UM Faculty Senate and, there, made an important suggestion to President Kaler concerning the Markingson family.

B. Abbreviations.

[AAH] = the AAHRPP Report (2/26/15)
[OLA] = the Legislative Auditor Report (3/19/15)
[P] = the current draft work plan

C. My Overview of the Workplan.

This Workplan clearly represents a serious attempt at methodical implementation of the specific recommendations in [AAH]. It is laudable for the checks-and-balances which permeate the plan. Likewise for adhering to basic common sense.

As a whole, however, the plan's emphasis is largely reactive rather than being pro-active. It is analogous to boiling down a (high quality) 1000 page treatise on bio-ethics in an uninspired way into a new 'executive' sub-bureaucracy at UM.

Though the plan is intended to be impressive ("beyond reproach"), it is decidedly less so given certain areas of silence in regard to issues raised explicitly in [AAH] and [OLA]. Likewise in regard to awareness of a gap in existing Minnesota Law.

D. My Main Suggestions.

There will be 4. Suggestions #1 and #3 are the most important.
(1) Do Not Ignore the Past.

Why does it seem that this plan [P] is fundamentally disconnected from the past? I.e., that the past is 'finessed'.

No statement is ever made that errors were made. Is UM perfect? Pages 86-89 in [AAH] are some of the MOST important in that document, even if the innocuous sounding recommendations on pp.89-90 do not enunciate that. One needs to read between the lines.

UM's "defensive posture" was highlighted as NOT being wise (pp.87,88) and it is suggested virtually explicitly that apologies are essential to move forward. I am reminded of the quote in [OLA,p.29] by Dr David Strauss: "The regulations are only the floor. Any institution that aims that low is likely not going to be doing a terribly good job."

Lines 4-9 on p.89 of [AAH] concerning UM seeking court costs [$57000] from Mary Weiss are particularly shocking. See also sentence #1 in [AAH, p.89, Section 3.6.3] -- the meaning of which is clear (cf. the word humane).

Though UM has publicly apologized for Dan Markingson's CARE, there has been silence (as far as my most recent knowledge goes) about the UM court cost matter highlighted on lines 4-9.

This plan should recommend that a _full and sincere_ apology be made as a clear demonstration of institutional culture change starting at the top. This is completely in line with [AAH].

(A big new, corrective, mini-bureaucracy is fine to point to, but, please, pay attention to what started all this.)
(2) A Gap in Minnesota Law regarding Psychiatric Patients.

[P, section 11, pp.40-44] gives special attention to the Department of Psychiatry. [AAH, p.66, last paragraph] raised serious questions about awareness ‘there’ as to Minnesota law regarding vulnerable patients and perceptions of coercion in clinical drug studies. Cf. also [AAH, pp.82 (final paragraph), 84 (recommendation 4)].

It is commonly said that Dan’s Law, from 2009 [Mn Stat 253B.095 Subd 1 (d4) and (e)] now protects FUMC patients under stays of commitment or in the process of civil commitment vis a vis drug trials.

This is NOT quite correct. There is still a serious concern --very pertinent for [P] -- as to the protection afforded patients at FUMC under 72-hour involuntary holds. See Mn Stat 253B.05 Subd 3(a)(e), especially (e).

Patients in such a status can very definitely **perceive** coercion to comply with suggestions of an attending psychiatrist, eg, as to medicines, lest action be taken by the facility itself -- for instance, via ‘MD spin’ -- to extend the involuntary confinement period.

To be more specific: clause (e) states the period is 72 hrs UNLESS a court order to hold the person is obtained. How might that order be obtained in the mind of an impaired patient?

I quote here from a NAMI document:
"An initial hold lasts for only 72 hours. However, there will be a hearing before the 72-hour period is over. The judge can then order the person with mental illness to be confined until the end of the commitment process.

(But: regarding the civil commitment process)
"The petitioner is _often the head of a treatment facility_ (emphasis mine!) where the person with mental illness is being treated, but the petitioner can also be a family member, friend or someone in the community. However, we recommend that family NOT be the petitioner." {Thus: who is?? And note the word 'often'.}

SEE: http://www.namihelps.org/assets/PDFs/civilcommitmentSinglePg102108.pdf

It would be good to see some attention paid in [P] to the matter of 72 hr holds and appropriate patient protections. And, EQUALLY IMPORTANTLY, to gauging the prevalence of any potentially 72 hr coercive situations ***in the past***.

(Federal Guidelines presumably also say something about this matter, i.e. clinical drug study recruitment in a potentially coerced state, but these may not be codified into law.)

(3) State Oversight for a Probationary Period.

President Kaler's statement "trust but verify" should mean something. Moreover, to be beyond reproach, is it not wise for people "driven to discover" to be prepared to think OUTSIDE the box??

The plans detailed in [P] frankly tend to be an uninspired implementation of the recommendations in [AAH]; very much common sense and "in the box".

Picking up on the idea raised in [P, p.8 (External Advisor) and p.56 section 17], I would like to propose that the University of Minnesota INVITE official State oversight of itself for _several_ years (via some sort of State ombudsman + expert deputy helper(s)) at least in regard to the plan's implementation in psychiatry vis a
This oversight ombudsman should ideally have subpoena power.

This action would be consistent with [P, p.5 (last line), 7 (metrics), 20 (final paragraph), 42 (lines 5-8), 54 (paragraph 1)] and would, at the same time, represent an alternate time-limited form of [OLA, p.31, recommendation 2].

If one thinks about it, I believe this action has MUCH to recommend it. And it exemplifies a true "trust but verify".

(This oversight can, of course, be extended outside of psychiatry, but, in the interest of feasibility and reasonable workload, it is natural to draw the line of demarcation there.)

(4) Database for Easy Tracking of Serious Adverse Event Reports.

[AAH, p.53, line 12] laments, re: monitoring, the lack of a centralized database for reporting and tracking adverse events -- as well as unanticipated problems and subject complaints.

Though [P, p.59, item 12] seemingly addresses this, the connection to the lament in [AAH, p.53, line 12] needs to be made much clearer.

Right now, the link is largely opaque. See, eg, [P, p.51, lines 3-6, for Cause]. UM General Counsel Donohue effectively stated in a 2014 letter to Arne Carlson that UM is basically a 19th century institution in NOT having available any type of (even very primitive) centralized database of this kind -- and that it would extremely cumbersome, if not impossible, to create such.
Had time permitted me to speak, my comment to the Board of Regents on May 7 would simply have been: "As a Fellow in the Minnesota Supercomputer Institute, I do NOT believe this at all. Creating such a database cannot be very hard, particularly if a graph-based record input is employed. This is not the 19th century."

I hope that this input can help in making UM's response to this year mess truly beyond reproach.

| 52 | Thank you for the opportunity to offer a suggestion towards strengthening the Panels Human Subject Protection Plan. One glaring shortcoming that seems to be missing from the proposal is the way potential study enrollees are being screened and enrolled by the department of psychiatry researchers and their staff. Having witnessed Dan Markingson being in a locked ward for thirty days, and then reading the take from the AAHRPP panel that in itself being confined and restricted can cause patients with already diminished capacity to not fully understand exactly what they are consenting to if they choose to enroll into a study. I realize that an advocate is being suggested, which is a good idea, but I would guess that over 90% of the patients being pushed to consent into psych studies while in Fairview are there on a 72 hour hold, or some type of involuntary commitment. These are the patients that are most vulnerable and susceptible to coercion or misunderstanding about the nature of the study. Perhaps a moratorium needs to be enforced that prohibits these patients from being approached during the first days they are hospitalized and locked in a ward. The attached link may be of some additional value, I would recommend reading it before the draft becomes final. | External | 5/31/15 | Vulnerable Subjects (Section 10) | COI (Section 15) | Your comments will be available for review by those who implement this plan. Thanks for your perspective. |
Thank you.
[http://repository.jmls.edu/cgi/viewcontent.cgi?article=10&context=lawreview]

53  I fully agree with the comments that Dennis Hejhal has made earlier today. For your convenience I attach these as a pdf file.

https://drive.google.com/file/d/0B20cWO6w77sPYTNVd2w4SWVZYTQ/view?usp=sharing

Between November, 2003 when Dan Markingson was enrolled in the experimental drug trial and the present, the University of Minnesota's administration, as represented by Bruininks, Kaler, the University attorneys' office headed by Rotenberg, Donohue, Vice President for Research Herman, the Academic Health Center headed by Cerra, Friedman, Jackson, more generally the Board of Regents and Morrill Hall, have not dealt in an honest and forthright manner with regard to the ongoing scandal associated with Dan Markingson, Robert Huber as the VICTIMS, but also in the treatment of all faculty and staff (both at the University and at Fairview) who have attempted to shine the light of integrity on the ethical breaches and, simply put, indecent behavior towards Dan Markingson, Mary Weiss, Robert Huber.

The highly critical external review would never have occurred, had not Professors Carl Elliott and Leigh Turner invested considerable effort to bring into the open what Morrill Hall was doing all it could to conceal. In December, 2013, I together with seven other members of the Faculty Senate introduced a resolution calling for an external investigation with particular attention to the Psychiatry Department and the circumstances of Dan Markingson's suicide in May, 2004. This resolution which was illegitimately modified by the Faculty Consultative Committee, formed the basis for the solicitation of the external review.

| Faculty | 5/31/15 | Hejhal see above & Post Approval Review |

These comments underscore the reality that this implementation plan alone cannot be a blueprint to change the culture of human studies research at the UMN: such a change will require additional collegial discussions and planning by the University community.
Following the external review’s damning report, following the Legislative Auditor’s damning report, the implementation task force released on May 18 its recommendations and held a self-congratulatory media briefing. Why their recommendations could not have been issued in September, 2004, why more than a decade had to pass, why the University attempted to obtain $57,000 from Mary Weiss, goes undisussed and unanswered in the sixty-eight page draft document they produced.

To add insult to injury, Kaler publishes today, May 31, a counterpoint op-ed piece in the Star-Tribune in which university public relations sinks to a new low by invoking Miles’ quip, "Markingson's legacy" and writes "Critics are important voices, but there comes a point at which criticism of past actions stops being a catalyst for reform and, instead, becomes a barrier to necessary change in the future.” Chutzpah unbound!

If the implementation task force wants to make a lasting impact beyond its "forward looking" (since it is too painful to look back honestly) recommendations, let it call for the immediate changing of the name of the newly christened Bruininks Hall, to a more justified name Dan Markingson Hall. May his memory be a blessing.

| 54 | https://drive.google.com/file/d/0B20cWO6w77sPS291aElzUjAxb2c/view?usp=sharing | Faculty | 5/31/15 | Language change recommendations  
IRB Protocol Review Process (Section 5)  
Scientific Review (Section 6)  
A previous commenter also suggested changing from the word “subject” and throughout the document “subject” has been changed to “research participant.” Institutional Review Board is the term used in the U.S. Code of Federal Regulations and to avoid confusion we’ll continue to use it in this document. The draft plan has been modified to clarify several points noted in these comments, including the protocol review process and |
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| 55 | https://drive.google.com/file/d/0B20cWO6w77sPWWQ0cUtmcTdrTEE/view?usp=sharing | Engaged Community Members (Section 16) | conflict of interest issues.
Currently and moving forward, for studies involving minimal risk, scientific review is conducted by the IRB (see revised Section 6 of the report.) |
|   |   | COI (Section 15) |   |
|   |   | Engaging Research Subjects (Section 12) |   |
|   |   |   |   |
| 56 | I commend the team for their commitment to advancing the care of our human research subjects. I believe everyone desires a system that protects our research participants, while simultaneously supporting the advancement of clinical research at UMN and avoiding imposing any excessive burdens on research participants. In response to the public comment period, I am including responses to the working document in the email text below. | Faculty 6/1/15 | Thank you for your comments and suggestions. We agree that the plan should address the role of Central IRBs and we have added this to the plan. We agree that minimal risk studies will not require pre-review and can be reviewed directly at the IRB. We agree that minimal risk studies will not require routine monitoring. Patients who have just had sedation for an elective procedure should not be enrolled in a study. Using a web-based survey tools is a good suggestion and can be considered. We agree that some research may not require a plan to |
|   |   |   |   |
|   |   | Section 4: IRB membership |   |
|   |   | Section 6: Scientific Review of Studies |   |
|   |   | Section 8: Monitoring of Studies |   |
|   |   | Section 10: Research with Human Subjects who |   |
|   |   |   |   |
|   |   |   |   |
There is a compelling rationale for increasing IRB size to accommodate workload, and certainly both monetary and academic compensation are warranted. Recommendation: However, given the amount of (challenging) time commitment needed from faculty and the great expense incurred with the new proposal, I would pose to the committee whether use of a centralized IRB might be a cost-effective option here, and free up faculty time for conducting research.

Section 6: Scientific Review of Studies.

This includes a proposal to eliminate departmental peer review as an option for scientific review, and move this to a HRPP managed review procedures. Studies that are minimal risk will not require scientific review other than by the IRB reviewer (as is the case currently). The IRB has traditionally considered studies with a simple blood draw or other minor procedure as above minimal risk. These studies (such as a serum draw from a healthy control patient) differ greatly in intensity and participant risk from more complex testing or intervention studies. Recommendation: Consider offering a rapid scientific review mechanism, or even continued departmental review for studies in which: (1) risk represent a minor increased over minimal risk; and/or (2) the test or study procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations.

Section 8: Monitoring of Studies

Included in this section is a proposal that live consent monitoring should be performed, including video documentation of informed consent and/or monitoring the process (unclear if both or one or the other). While it is somewhat vague, my interpretation in reading this section is that the proposal is for consent monitoring to

have impaired or fluctuating capacity to consent.

Section 12: Engaging Research Subjects

share results and an investigator could request an exemption during the protocol application process.
be performed in every study. This seems quite logistically challenging and also an extra burden on subjects, many of whom may be uncomfortable with being filmed. Recommendation: Monitoring the informed consent process is a reasonable proposal for high risk studies (ie particularly those under an IND or IDE). However, for low risk studies (blood testing, an imaging study, or interview/questionnaires, for example), this seems unnecessary in every study and could be done in a small sample for auditing.

Section 10: Research with Human Subjects who Have Impaired or Fluctuating Capacity to Consent

This section includes guidance for subjects who have normal consent capacity at the time of the informed consent process but have a fluctuating ability to consent during the study. I assume this section was drafted primarily with mental health disorders in mind, but the definition of fluctuating consent is unclear. Would this include a surgical patient, who is temporarily sedated but is expected to fully gain consciousness after a number of hours and has in advance consented to the procedures/interventions? Recommendation: Since the extra procedures to obtain durable power of attorney or representative for patient with expected potential fluctuating consent capacity could be an extra burden to both patients and investigators, and could potentially prohibit opportunities for patients to participate in studies, I would recommend very careful definition, including statement about whether this includes (or specifically excludes) patients with short period of impairment expected for a procedure with sedation.

Section 12: Engaging Research Subjects

Point 1: The workplan proposes to better assess research subject experiences, including creating a research subject satisfaction survey that is distributed to subjects and surrogate decision-makers to evaluate
their research experiences. I welcome the opportunity and mechanisms for subjects to provide feedback on their research experience. I am attentive, however, to not increasing burdens on our study subjects. Recommendation: Any satisfaction survey should be brief, and not mandatory for subjects to complete (which I assume would be the case). A web-based mechanism might be considered to provide opportunities for feedback independent of study visits.

Point 2: This section also contains reference to requiring investigators to have a plan for data sharing with subjects, and other plans for expressing appreciation. In our research, we do currently distribute trinkets at study end, birthday cards, and share the manuscript with final results. However, I recognize the spectrum of clinical research. Some studies are long-term, with no immediate results available. Some may be very early translational or mechanistic studies which use human blood or tissue but are not directly relevant to the healthy volunteer participant. Recommendation: Some consideration should be given to the spectrum of clinical research. Some studies may not be appropriate or feasible to communicate results back to participants. A results communication plan should be a part of any intervention trial; other studies might be subject to individual consideration.

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<th>Every section of the report.</th>
<th>To comment on scientific review: Under current IRB process for review, experts cannot review a study where their department head is the PI. The committee feels that should continue to be the case, and is an example where outside experts may need to be retained to review studies where a department head is the PI.</th>
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<td>58</td>
<td>These standards look fine, but in the end it is about clinical results, too.</td>
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This is important to doctors in our area when deciding about where we wish to refer our patients. Psychiatry is especially an unpredictable field, as some well-intentioned changes have worse outcomes—especially when it comes to suicide prevention endeavors.

Thus, one addition to: 14. Accountability Metrics on page 49 to include outcome data before and after these changes.

Since suicide events are a sad but easily measured outcome these suicide events should be an important PUBLIC disclosure of the success or failures in these program changes: trend University research program suicide events by department from 2005-14 versus suicide events from 2015-24.

It could be adjusted for the number of participants as well, – a rate dividing events by total number of research subjects.

**Response to #2 on scientific review:**
Agreed. Scientific reviewers must have the appropriate expertise as is pointed out in Section 6 of the report.

Thank you for your extensive and responsive work in creating the Implementation Plan for the Recommendations related to our Human Research Protection Program.

I strongly encourage increased involvement by community members in your plan. I find in my work at the CTSI that they bring such great value and insight.

Indeed, community members unaffiliated with the UMN are included in the plan.

We agree that scientific review is an important part of the IRB approval process. The intent of the draft plan was to suggest that the HRPP

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Research with Human Subjects who Have Impaired or Fluctuating Capacity to Consent (Section 10)

COI (Section 15)

manage the review process and use whatever approach it deems appropriate. With respect to the issue of consent, the report proposes significant new approaches that represent state-of-the-art standards for interacting with research participants and as such, we believe will protect the participant interests maximally. The draft report also suggests that involvement of personnel that are not part of the research team to maintain objectivity and to make sure that all parts of the clinical research and care team are engaged is an important step. We agree with recommendation 10. Current thinking with respect to COI is to require investigators performing clinical research to report all relevant income from the first dollar, and with approval of the Conflict of Interest Committee an investigator may concurrently consult for a company and conduct research sponsored by that company if the payments for the consulting are directed by the company to the University and not to the investigator.

I offer comment on two specific areas of the plan.

The first is in relation to the “enhanced research compliance office” which is mentioned frequently in the report and will potentially have responsibility for post-approval monitoring and “for cause” investigations among other things.

A research compliance office currently exists in the OVPR. The staff, while few in number, have extensive experience resolving issues across all

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Staff 6/1/15

Post Approval Monitoring (Section 8 and 9)

Education (Section 13)

We agree that the most appropriate path forward to increase compliance oversight of the UMN's human participant research program is to build on the expertise that already exists in the OVPR Research, Education and Oversight Office (REO). Additional resources will be made available for this office to conduct inquiries/investigations about human participant research
levels of the institution. They have formed strong bonds with central offices such as Audits, the Controller’s Office, Sponsored Financial Reporting and other research related offices. It is not clear from the report what the intent of the Implementation Team is with respect to this unit. It would seem more expeditious to build on this team’s experience and provide sufficient staff and resources to take on additional responsibilities such as the PAR and investigational activities. A well-considered structuring and hiring would result in a compliance unit that has the broadest experience and could provide a much more rounded and robust approach to managing and mitigating risk. This approach is similar to the model which was in place some years ago and which would serve the institution well moving forward. The intent behind moving the PAR function into the IRB was well considered, but it must also be recognized that the objectivity of either type of review was reduced when the reviewers report up to the IRB Executive Committee. In addition, the ability to move investigations forward quickly is severely hampered when the investigation must rely on action by the IRB Exec which meets only monthly. The current research compliance group has extensive experience with conducting various types of investigations – collecting and analyzing the data, developing recommendations and resolving issues. I urge the team to take the time to adequately assess what is already in place, as they begin to develop an enhanced research compliance office.

My second comment has to do with the research education aspects of the report. For several years it has been a goal of the OVPR to streamline and facilitate researchers’ access to and completion of high quality research-related education. I am gratified that the Implementation Team calls for a activities at the UMN. At present, the PAR function will remain in the IRB, clinical trial monitoring will occur in the CTSI and REO will oversee investigational activities.

We appreciate the thoughtful comments about administrative oversight of the education components of the implementation plan. We want to ensure that we have the highest quality, most modern and up to date training opportunities available across the entire spectrum of the clinical and translational workforce (investigators, coordinators, project managers, etc). We have recommended the point person for this task be administratively housed in the CTSI with strong collaborative relationships with the Center for Bioethics and OVPR. The reason to house this individual in CTSI is because of the established infrastructure they have for curriculum development and assessment. In addition, the University of Minnesota CTSI is part of a network of CTSI’s across the country that have many different courses and programs already developed and tested. We can tap into those resources and implement successful training programs here in a more efficient manner. See response to comment #17 also.
cohesive plan for managing this important aspect. Currently there is little cohesiveness or consistency with respect to the quality or content of offerings. It is difficult for researchers and staff to identify and confirm completion of required training. Finally, the timing and frequency of educational offerings is not coordinated which results in gaps but also in researchers being overwhelmed.

I think it would be extremely beneficial to the researchers and to the institution to have research education continue to be housed in the OVPR and also to partner with CTSI, Bioethics, faculty, and others to develop clear and cohesive policies with respect to required education. We should build on this broad expertise to provide education that is relevant, timely and targeted to meet regulatory requirements, but which also aligns closely with our faculty’s research portfolios. This represents another return to a model that was in place within the OVPR previously. From its inception RCR was led by faculty. There existed a Faculty Advisory Committee which reviewed courses given by units external to OVPR to determine if the material presented met a standard which made it eligible for inclusion in the list of approved research ethics training. I would encourage the re-formation of such an advisory committee to provide guidance with respect to researcher education. I would also encourage the consolidation of research training to a single location within the OVPR, again with the charge and expectation that this unit collaborate widely. It will be critical that full cooperation, participation and support from faculty and units be clearly spelled out in the development of this program.

| 63 | We need more than just researchers on the IRBs. Would be nice to have involved community members | Staff | 6/1/15 | IRB Membership | Indeed, community members unaffiliated with the UMN are included as members on all IRBs. |
and practitioners with knowledge about the field working toward keeping the research grounded too.

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I am writing to respond to the Draft Work Plan that was submitted for public comment. I appreciate the time and thought that the team put into this document, especially given the tight timeframe. While I agree with many of the recommendations put forth by the team, there are a few that might need further consideration once they are delegated to people to implement.

1. Video recording: While I understand that there is an FDA information guidance that suggests using video-recording for some consent situations, I am not sure that mandating that all consent procedures for vulnerable subjects needs to be recorded. If this were to be implemented, it should be done by an objective group of consent monitors who report to OVPR rather than to departments or study teams. The video recording should be done with real cameras instead of smartphones, to avoid HIPAA compliance issues and breaches of confidentiality. Furthermore, the consent monitor should always first obtain consent from the subject or LAR to record. I am concerned that there may be a heightened observer effect from the act of recording, such that some potential subjects may feel more compelled to say yes. I do agree with the Implementation Team that consent monitors could be employed to act as third-party witnesses to the consent process, and should be available for any consent situation. It seems to me that consent monitors would be sufficient as a measure to prevent coercion and undue influence, and that recording is not necessary.

2. Metrics: A number of the metrics were focused on

Staff 6/1/15 Research with Human Subjects who Have Impaired or Fluctuating Capacity to Consent (Section 10) Accountability Metrics (Section 14) COI (Section 15)

Thanks for these comments. They will be shared with those who implement this plan.

Good idea to have non-research clinicians as well: we encourage those who are interested to discuss IRB participation with their departmental leaders.
counts of occurrences. Perhaps in the first year after implementation it is fine to have baseline absolute numbers. However, counts don't necessarily show any improvement or reduction over time for the effects one hopes to see. After the first year, consider using averages or percentages in defined timeframes to demonstrate the effectiveness of the process changes. This approach can help with holding people accountable to the process changes.

3. Sponsor compensation: I am not sure how all compensation to investigators from sponsors is going to be defined once this is recommendation is implemented. Based on what I have heard about the Sunshine Act's Open Payments database, I would caution against using this as the source of truth for determining compensation levels. It seems that there is still some confusion about what is reportable in that database. Perhaps in the interim, the REPA reporting process can be revised to ask additional questions about compensation. Once the Open Payments database has been underway for a while, and is being used consistently, then perhaps it would be a good source of truth.

| 65 | https://drive.google.com/file/d/0B20cWO6w77sPVnhWR20zVmxOWEU/view?usp=sharing | Staff | 6/1/15 | COI (Section 15) | Please note that the COI section of this plan has been modified for clarity. Thanks for sharing your perspective. |
| 66 | My only request is, I believe, vital to creating a research environment of which we can be proud: For changes to be accepted, meaningful, and based on all the relevant information, it is absolutely critical that research coordinators and other staff at the "boots on the ground" level be included in planning and shaping an ethical culture. Because: 1) If you want buy-in, a grassroots, cooperative approach is essential, and 2) These research team | Staff | 6/1/15 | Culture (Section 3) | We agree that the input and participation of research coordinators is critical to the success of implementing this plan. |
members very often have a much better idea than the PIs do of how studies play out on an everyday basis, and they spend more time with the subjects.

| 67 | [https://drive.google.com/file/d/0B20cWO6w77sPQ2t0TVoyTmNRd00/view?usp=sharing](https://drive.google.com/file/d/0B20cWO6w77sPQ2t0TVoyTmNRd00/view?usp=sharing) | Staff | 6/1/15 | All sections of the report | Thank you for these thoughtful constructive comments. The COI section of the report has been modified for clarity. Your comments will be shared with those who implement this plan. |
| 68 | Introducing myself: I have 16 years of experience as an RN in Emergency, Cardiac, and Intensive Care Nursing. I went to a Hospital School of Nursing in Minneapolis, a 3 year program and then back to school to obtain a BA in Organizational Management years later at Eastern University Degree Completion Program in PA. I worked at a pharmaceutical company, Wyeth, now Pfizer, for 12 years with my new degree. Prior to that, I worked as a study coordinator for an in-house trial at a Contract Research Organization for 5 years. I also worked in Data Quality and then obtained Clinical Research Associate training in order to monitor trials across the country. A device company moved me back to Minnesota in 2006. A small medical device company recruited me after 2.5 years because now I had pharma and device experience with clinical research. I was a program manager of 2 EU trials for a novel product for about 3 years. Now I am back working in the clinical setting with patients utilizing my nursing background and 23 years of experience with clinical trials, Phase I-IV as a Clinical Research Coordinator. Comment: With all of the Guidances, GCPs, SOPs, required CITI and HIPAA training, consent training and research knowledge gained through experience, I find it very awkward to be associated with a media blitz that invariably filters down to anyone working in FUROC (Section 7) Research with Human Subjects who Have Impaired or Fluctuating Capacity to Consent (Section 10) | Staff | 6/1/15 | FUROC (Section 7) Research with Human Subjects who Have Impaired or Fluctuating Capacity to Consent (Section 10) | We applaud your positive approach to move forward with high quality and safe clinical trials. Thanks for your perspective. Your insightful comments will be available to those who implement this plan. |
clinical research at UMN/Fairview locations. The impact will be felt by everyone currently conducting trials or for those considering trials due to the recommendations in this report. I would have liked the focus first to be on those who are responsible for the violations and inconsistencies started in the psychiatry group, rather than a broad approach outlined in this report. It feels like the original problem is now diluted by the trickle down effect of all of Clinical Research and the IRB. Oversight and checks and balances are very important, but what about all of the quality research completed with utmost integrity within the organization?

I am surprised that the Sponsor hasn't commented on the psychiatry trials. Typically, with monitoring and oversight, sites that are not doing the right thing are identified and are likely closed due to noncompliance. Is there any information available about the sponsor? Psychiatry trials are invariably difficult to sort out vulnerability. Black box warnings have been applied to the labeling for anxiety and depression drugs due to the fear of suicide in those taking the medications, other trials have been stopped due to similar situations (Lilly, for example).

The Implementation Team Members are distinguished in their degrees and positions, however, which of these is currently conducting clinical research? Was Fairview Research Administration (FRA) consulted? FRA provides oversight for Fairview Southdale trials and has an excellent working relationship with Research Coordinators who prepare all of the required documents, from startup to finish - the aim is to get it right the first time in order to not delay the clinical trial from approval by the IRB. I appreciate working with FRA and the IRB and thank them for all that they do to help at all points in the trial, start to finish.
Comments:
1. Both FRA and the IRB are short-staffed.
2. Scientific Review - If done by a new group it may impact the timeline for getting documents to the IRB. There need to be medical experts in the therapeutic area that review and comment and turn around time needs to be monitored.
3. When the term, "Fairview," is used, is that all inclusive for all of UMN/Fairview Research? Sometimes the term Fairview is used and in other places, University, is used.
4. The IRB application form contains a section on vulnerable adults. The IRB will be alerted if there is a vulnerable population ahead of time if the form is used correctly. This is Research 101.
5. Train Managers and Supervisors and VPs to follow ethical guidelines and have the fortitude to identify and work with abusers of any clinical research principle immediately.
6. Video Consenting? We will need a consent to videotape the patient first and then consent for the trial. Who will do the videotaping? Who can be spontaneous enough for videotaping in an emergent situation or if a patient comes in requiring a pacemaker in the near future? This idea is fine for on-occasion, but not for all trials.
7. Witnessing Consent - A nurse not involved with the trial would need some training about the protocol; this does not make for an entirely non-biased person then. Nurses need to know what they are witnessing, it is not the ideal for all protocols and will require more time to find someone willing to be a witness.

I am out of time! Let's get this sorted out in order to move forward. New drugs and new devices are not going to be approved without clinical trials, obviously. We can do it and do it well.
Thank you for considering my comments re: the implementation report. Despite all the comments, I believe the report is very comprehensive and helpful in highlighting the issues.

a) The budget must be allocated to the IRB to achieve the greatest impact on quality improvement. Allocating money to other organizations is not an efficient way to improve the IRB operations. This is due to: such arrangement further requires communication channels via a middleman, and thus is not as effective as additional tools and quality improvements within the IRB.

b) There is a balance between promoting research and protecting human subjects. Not having research would expose subjects to 0% risk. That, however, would deprive the subjects from potential new therapies. To that extent, I think the federal conflict of interest policy is sufficient for research. There are instances when receiving payments from the industry sponsors is justified, for example, in the case of an investigator training other investigators in the use of a complex and invasive medical device. In this case, it is likely that such training would be more effective and result in better patient outcomes than training from an uninvolved physician.

c) Scientific Review can be an advisory function, but the IRB is ultimately responsible for deciding if it's ethical to involve subjects in a particular research in a particular way. I think the IRB must have more direct consulting resources with the expertise at the meeting, as opposed to devoting more resources to "Scientific Committees". Scientific opinions must be advisory to the IRB discussion. To that extent, they must be more detailed for the IRB to review (some are sufficient by reputation of the associated grant, but some that don't have a published peer review

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Response 69a: We agree that sufficient funds must be allocated to the IRB to enable it to be effective and efficient. A comprehensive human subject protection program requires more than the IRB, which is why some funding must go to other entities as described in the report.

Response 69b: We agree that it is important to conduct research on new drugs and new devices while ensuring the highest protection for the subjects participating in such studies. As for conflict of interest, the Implementation Team feels that the new policy described in Section 15, which goes beyond the federal standard, is the right one for the University of Minnesota. We agree that there are narrow circumstances where consulting and conducting research for an industry sponsor is appropriate, which is why exceptions are allowed under the new policy.

Response 69c: We agree that the scientific review is an advisory function to IRB deliberations. It is important to have the right experts performing the scientific review, and Section 6 of the report describes changed procedures for ensuring this. It is equally important to have the right experts on or available to the IRB for its deliberations and Section 4 of the report describes new ways to ensure that expertise is present.

Response 69d: Unlike the IRB
type evaluation, need to be more descriptive than just check marks).

d) The community oversight committee sounds very similar to the function of the currently used "Executive IRB". Why not change/empower the current body instead of creating another committee? Seems very redundant.

e) Review response to the IRB application in 10 days is unreasonable (for non-emergency research). An acknowledgement is different than a response, and a response in 10 days is not a requirement in any standard, nor is it a good business practice. Perhaps with unlimited resources, but not with limited resources when the effort must focus on the sound and thorough evaluation of research. This is just a frivolous number.

Thank you for your consideration of the above, and for your effort to strive toward "Beyond Reproach". Have a great day.

Executive Committee, the new Community Oversight Board is intended to be separate from, and not connected to IRB operations.

Response 69e: We agree that a 10 day turnaround time from time of submission to review response is aggressive, but attainable given the increased number of IRBs described on the report and the focus at IRB meetings on significant issues. However, appropriate and meaningful review is paramount, which means some protocols many take longer than 10 days to review even under the new system.

Thank you for your careful review of the draft plan and for your suggestions. We agree that the positive aspects of the current excellent research program at the U of MN needs emphasis and we added a paragraph to the beginning of the document in which we paraphrased your comments.

Regarding the IRB, we are confident that increasing the number of boards and the variety of expertise on those boards will help address the issues you identified in having appropriate
expertise and reasonable turnaround times for reviews. Your proposal for review of cardiovascular studies by the Lillehei Heart Institute with operating procedures to insure scientific rigor without COI issues is very reasonable. We’ll share your proposal with the IRB administrator and this can model can be discussed and developed during the implementation period.

The proposed changes in the COI policy for research will not prevent any current industry related research activities. The change is the dollar threshold for reporting and the prohibition of receiving personal income from consulting and educational activities. We view the Fairview University Oversight Committee (FUROC) as being complementary to the IRB and not a replacement for the IRB. The primary aim of the FUROC will be to provide a forum for discussion and for concerns about research that is conducted collaboratively.

We would like to thank the Cultural Wellness Center (CWC) for their comments and generous offer. We will make the Community Engagement Core of CTSI (tasked with developing the community engagement piece of the plan) aware of the CWC and the opportunity to partner with them in these efforts.
This plan does not prohibit experts in rare disorders in children from working with the pharmaceutical industry to develop new therapies. The proposed policy would not allow an expert on a study team to receive personal income during the study from a company whose product was being evaluated in the study. However one could continue to consult for the company during the study provided any consulting payment was given to the University and not taken as personal income. Also study related travel expenses paid by the company would be allowed as a legitimate expense of the research study such as for study preparation training or presentation of results for example.

We are excited to participate in building an HRPP that can be looked upon as a model of excellence. We hope you will consider our feedback.

**Section 4 - Membership**

We tremendously appreciate that membership on the IRB will be promoted and tangibly supported by the institution. This has been a chief complaint and significant barrier to attracting and retaining the membership we require. We applaud the recommendation for more frequent meetings allowing for smaller agendas and shorter meetings. This directly aligns with feedback we received from members when we conducted our member evaluation in December 2014. Members were asked to indicate if the IRB meeting is running too long when it enters its 2nd, 3rd or 4th hour. 63% of members agreed three hours is too

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The thoughts presented here are in agreement with the recommendations of the implementation team. The recommendations of the implementation team are not meant to dictate how the IRB conducts its business, and if appropriate changes have already been instituted that meet the suggestions of the implementation team, that is positive.

With respect to the quality of protocol submissions, I agree that this is an area or opportunity and I am hopeful that increased education coupled with an electronic IRB (and for Psychiatry international drug and device trials, the involvement of the
long, 37% objected to meetings lasting four hours but no members objected to a meeting lasting two hours. We have heard, however, that weekly meetings for clinicians may not be an achievable expectation. The work plan noted that members assigned to one panel may serve as alternates for members on other panels. Though this is allowable, it may be more desirable to define both a member and an alternate from departments from which we receive a high volume of submissions. The central benefits of eliminating the rotational membership are allowing members to establish a rapport with one another and a familiarity with the PIs and research assigned to their committee. It is more likely these benefits would be realized by having a member and alternate with similar, required expertise sharing the assignment.

We agree that board members who are not fulfilling the attendance requirement should discontinue membership. We recommend that report include a statement that requires departments with a high volume of submission to the IRB to quickly identify that an underperforming member’s replacement.

Section 5 – IRB Review Process

The IRB has implemented important changes to meeting management and pre-review that will allow for more accurate documentation of committee decisions and more appropriate risk evaluation. Members are now required to identify the regulatory or policy basis for changes required, our minutes template has been revised and staff retrained to support more accurate documentation. We are confident that our current pre-review and triage process are more appropriately evaluating risk and assigning review accordingly. It is CTSI), will improve the quality of the applications and shorten the time for approval.

The implementation team recognizes that much of what is being proposed will require new resources and has made recommendations for an almost doubling of the current IRB budget. The intent of this new process is not that the IRB panels conduct the scientific review, but rather that HRPP manage the scientific review. The new process is intended to add no additional burden while at the same time ensuring that appropriate experts are performing the scientific review and that only those without conflict perform the review.

The implementation team recognized that the post approval review and monitoring of clinical trials are some of the most effective means to make sure the research is being conducted appropriately, and to catch any problems that may arise during the conduct of the trial with minimal delay. It debated where this activity should reside institutionally or remain with the HRPP program. As you have recommended, the PAR will stay under the direction of the IRB.

The implementation team agrees with your contention that greater collaboration and coordination of training efforts is needed at the institution. The rationale for potentially locating this activity in the
important to note that the independent inquiry panel’s period of agenda review included a period of staff transition and the number of minimal risk studies assigned to fully committee review was unusually and uncharacteristically high as a result.

A key component of committee burden not addressed by the inquiry panel or the work plan is the assignment of inadequately prepared submissions for committee review. Such submissions are often the most time consuming to review and document. These submissions frequently result in deferral and require re-review by the committee. Deferred submissions are slow to gain approval and require duplicate committee effort. The work plan notes that “The IRB will also have adequate administrative staff to provide pre-review of items to determine if it is necessary and required to bring them to full committee”. Evaluation of risk is one key component of pre-review but an equally significant outcome of pre-review process would be the opportunity identify and allow investigators to correct inconsistencies, errors or omissions. A robust pre-review process will allow for more focused and relevant committee discussion and will positively impact agenda size. The work plan’s proposed turn-around time of two weeks for a review response from date of submission could discourage a meaningful pre-review process. We recommend that the work plan statement related to turn around time be revised to “two weeks for review response from the date is a submission is determined to be review-ready”.

Section 6 – Scientific Review of Studies

The work plan recommends, “department review will be eliminated and that function will be combined into a CTSI is to leverage the national network of translational and clinical research education and training modules that have been developed and deployed by the CTSA network. This represents a much more comprehensive set of resources than any one institution can muster on its own, and more consistent training across a national clinical research network would allow more consistency and better trained investigators. As with other activities assigned to the CTSI by these recommendations, an assessment period will be in place to make sure that these functions are occurring properly and with efficiency. Should the CTSI approach not be feasible, the institution will examine other options.
new Method 4 called “HRPP Managed Scientific Review.” The current HRPP administered scientific review process receives approximately 8 submissions per month. The relatively low volume of submissions requires limited staff support and a small base of reviewers to maintain. It is recommended that the work plan acknowledge that a significant increase in the volume of submissions will require additional HRPP staff resources to support. A similar service expectation as IRB membership as well as appropriately scaled institutional support will be require if HRPP staff, not investigators, must identify reviewers. We recommend that we review the current tool to determine if additional functionality could be added to reduce staff burden.

**Section 8 – Monitoring of Studies**

The Post Approval Review (PAR) program was created as a component of the IRB at the end of 2011 due to concerns about the quality, effectiveness and relevance of reviews being conducted by the previous program. Over the last four years, the PAR program has become a highly valued and a respected component of the IRB. The IRB and the research community view the PAR review process as an important mechanism to assure the quality of the work being performed. The benefits of this program were further described in the report of the AAHRPP led inquiry panel, which indicated that PAR was well conceived and provided thorough, substantive, and meaningful reviews of human subjects research. The most significant criticism noted in this same report was that the program has been under resourced.

We are in support of the implementation team’s recommendations related to enhancement of the
communication strategy associated with PAR results to ensure higher accountability of the research community and IRB. We also support shifting responsibility to conduct formal investigations out of IRB authority, as these are often extremely resource intensive and require relevant expertise that may not be represented or available. However, both staff and members agree that retaining oversight of the PAR program is critical to enhancing the IRB’s mission and assuring the quality and safety of research conducted at this institution. A higher level of accountability and oversight can be achieved via communication strategies and does not require shifting this program from the very entity under which it has thrived.

One area not investigated by the AAHRPP led inquiry panel nor the implementation team was related to the work of other monitoring functions at this institution including the CTSI. Greater collaboration and communication across monitoring functions is needed when non-compliance is suspected. It should be the expectation that each monitoring function is appropriately reporting suspected research non-compliance regardless of the mission of the said monitoring agency. Communication expectations across programs should not differ when research non-compliance is suspected.

As noted above, the PAR program has been recognized as high functioning and effective. Shifting this critical resource out of the IRB will result in a net loss of resources. It is difficult to understand how removing resources from the IRB addresses the inquiry panel’s recommendations.

Section 13 – Education and Training of
Investigators

In section 3.3.1.4 of its report, the inquiry panel recommends the University “create opportunities for advanced training in human subjects protections for all individuals involved in human subjects protections including investigators, IRB members and staff, research personnel, and clinical staff on units that conduct research”. The panel recognized that the need for ongoing and advanced training in human subjects research protections extends well beyond the investigator. The significant expansion of IRB membership will result in a significant training need. It seems inefficient and potentially ineffective to house the new Human Research Procedures, Policies and Ethics Education Coordinator within the CTSI, not the IRB. Evidence that the IRB is best positioned to identify and implement relevant training related to human subjects protection is provided in the inquiry panel’s report. The report noted several positive steps in education and training, specifically:

Within the past year, the University has made a few significant changes to its requirements for education pertaining to human subjects research. In February 2014, the University refined its requirements for human subjects training to require that all individuals engaged in human subjects’ research at the University complete basic human subjects training through the CITI program. Accompanying this change was a new continuing education requirement: Specifically, all individuals engaged in human subjects research must now re-certify their training every three years. In addition, in January 2015, the University purchased a site license for PRIM&R’s E-ROC
online learning platform and plans to require this training for all IRB members. In addition to changes in these basic educational requirements, the University also instituted a new CITI course requirement in February 2014 for individuals who wish to serve as sponsor-investigators. Documentation of successful completion of this tailored training is required as part of the IRB submission process whenever a University researcher plans to serve as a sponsor-investigator.

It is notable that all of these revised requirements and training opportunities were identified and implemented by the IRB. As with monitoring, it seems curious to respond to criticism that the IRB is under resourced with a proposal to provide additional resources to the CTSI. It is true that we need greater collaboration and coordination of training efforts. Housing this position within the IRB, with an expectation of outreach, collaboration and coordination with CTSI and the Center for Medical Bioethics will ensure that the focus of this new resource remains on human subjects protections and the ethical conduct of research. It will also ensure that training offerings are inclusive of the various learning communities including medical and social researchers, IRB members, IRB staff and clinical staff on units. The IRB currently receives and responds to requests to provide training to research teams, classes and departments. These trainings focus on IRB and human subjects research basics, how-to prepare and submit applications and specialized topics by request. Having a dedicated resource within the IRB will allow the IRB to enhance and expand these offerings.
There has been growing awareness of the need for training and mentoring for researchers and research staff on topics extending beyond research ethics and human subjects protection. There are various groups and individuals working to close these gaps. CTSI may require additional, dedicated training resources but it may be most effective for these resources to focus on coordinated these efforts. The inquiry panel pointed to positive steps, led by the IRB, to enhance training. We ask that we be allowed to continue and expand on the base we have worked to develop.

Conclusion

Responsibly conducted, scientifically sound research may hold the potential to ease suffering, prolong life or expand the collective understanding of the human experience. The value of advancing knowledge must always be weighed against the risks of acquiring that knowledge. There are many considerations that shape the feasibility and desirability of pursuing a research question. The Institutional Review Board is the one entity charged with primarily representing those who may be harmed or unduly burdened by the pursuit of knowledge. An HRPP that adheres to best practices and creates an ethical climate that is beyond reproach requires an independent and appropriately resourced IRB. A well-functioning and appropriately resourced IRB is essential to maintaining the public trust. There is much in the implementation team’s work plan that moves us in this direction. We understand and embrace the need for greater collaboration and communication across and among the various components of the UMN HRPP and specifically with HRPP. Over the last two years the HRPP office has contributed to efforts that leveraged HRPP and
CTSI strengths to create more effective and efficient processes, most notably the HRPP scientific assessment process housed within the CTR portal and the clinicaltrials.gov review process. We are committed to continuing to identify and foster opportunities to collaborate with CTSI but these partnerships require that both entities are appropriately resourced. As noted above, members of the IRB staff and committee members are concerned that some recommendations in the draft work plan may result in reduced IRB resources and potentially diminish the IRB’s autonomy and ability to evaluate, monitor and educate.