Final IRB Investigation Report into Fairview Concerns
Regarding Psychiatry Research Studies at the University of Minnesota

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INTRODUCTION

This report presents findings pursuant to the 10 March 2014 determination of the University of Minnesota (UMN) Institutional Review Board (IRB) to conduct an investigation into possible serious or continuing non-compliance affecting human research subjects by UMN Department of Psychiatry researchers, specifically studies on schizophrenia and bipolar disorder involving the following principal investigators and studies:

Beginning in late March 2014, the IRB investigation panel followed UMN IRB Policy 408A (Investigation Process) and reviewed all available study materials and obtained written responses from the four principal investigators. Further, so as to better understand facts and the subtle nuances of the psychiatric research environment, the panel conducted extensive in-person interviews. Additionally, so as to better understand the research environment, the panel also toured the relevant hospital clinics. By taking the extraordinary step of conducting numerous interviews, the investigation committee aimed to give voice to any person with information relevant to the protection of human research subjects in psychiatric research and to unearth any information that might be useful to the IRB as it pursues the same goal. Upon completion, this investigation conducted in-person, private interviews with 14 members of the Behavioral Health clinic of the University of Minnesota Medical Center, Fairview (i.e., Fairview employees), and 30 members of the UMN psychiatric research community (UMN employees), for a total of 44 interviews. Interviewees included Fairview caregivers (e.g., nurses, social workers, psych techs, physicians) and leaders, as well as UMN principal investigators, other faculty, and research staff, including student assistants.

The selection of potential interviewees was based on a list of persons generated from IRB study records and a list of all study personnel (current and past) provided by study principal investigators (PIs) at the request of the IRB. Additionally, an invitation email was sent to all potentially relevant Fairview staff. As their work proceeded, the panel invited other persons to be interviewed in order to learn more and/or clarify and confirm facts raised in prior interviews. All persons invited to be interviewed agreed to do so. All interviewees appeared to fully cooperate with the investigation; no one refused to answer questions. Interviews typically lasted one hour; there was minimal variation in the length of time for the interviews.

No interviews were conducted with research subjects. The panel was prepared to invite research subjects for interviews if such information was deemed necessary. Given the purpose and scope of the investigation, such information was deemed not needed.

All interviewees were asked similar questions unless they were not applicable due to job duties or related constraints. However, the panel also followed the lead of interviewees who wished to expand on topics they deemed important. Additionally, the panel pursued topics learned from one interview into the next (appropriate) one. In sum, the panel conducted exploratory work in order to assess the adequacy of the protection of human subjects in the identified studies and those related to them.
Given its wide scope and the nature of the academic calendar, this investigation has taken many months to complete. During the course of the investigation the panel routinely discussed whether there was any information suggesting human research subjects were at undue risk and additional IRB action (e.g., study suspension) was necessary. From start to finish, the answer was always no, current subjects were not at undue risk. At one point the panel did hold the approval of a treatment study using ketamine. This was because of a concern about the use of the drug in an unmonitored setting. But after further investigation and work with a willing investigator, all the concerns were satisfied and the study was approved.

This report reflects the distillation of a vast amount of information from extensive document reviews and forty four interviews conducted over four months into a focused document. The aim is to answer the investigation charge questions as clearly as possible and to summarize statements and opinions that are directly related to the IRB’s mission. This report is organized into sections following the IRB Executive Committee’s charge to the investigation panel. Apart from directions to the investigative team, the substantive questions posed were as follows:

Examine any and all aspects of the conduct of each study as necessary to determine compliance by the Principal Investigator and study staff, including but not limited to the following:

a. Were there adequate mechanisms in place to evaluate whether potential subjects had the capacity to consent to participation? Is there evidence that subjects were consented who lacked the capacity to consent?
b. Were proper recruitment strategies followed? Is there evidence that potential subjects were pressured or coerced to participate in the studies?
c. Were participants freely allowed to withdraw from participation? Is there evidence that participants’ rights to withdraw from a study were not respected?
d. Were the privacy rights of potential subjects respected? Is there evidence that research recruitment practices violated HIPAA?
FINDINGS

Examine any and all aspects of the conduct of each study as necessary to determine compliance by the principal investigators and study staff.

The investigation panel found no evidence of non-compliance by the named principal investigators or their study staff. The IRB study files and written responses submitted by the four principal investigators demonstrated regulatory compliance for recruitment, consent, study withdrawal and confidentiality. No evidence was produced during the interviews to show non-compliance. However, a number of concerns were expressed during the interviews as discussed below.

(a) Were there adequate mechanisms in place to evaluate whether potential subjects had the capacity to consent to participation? Is there evidence that subjects were consented who lacked the capacity to consent?

Document and interview evidence suggests that all subjects had the capacity to consent in research; no evidence of subjects lacking capacity to consent was identified. Nevertheless, several interviewees expressed great concern that consent procedures were insufficient.

Though no specific cases were identified, concern was repeatedly expressed about the consent process and procedures for obtaining and maintaining informed consent of research subjects who were also patients in the Fairview hospital and clinics. Several interviewees indicated that they did not trust some psychiatric researchers to obtain and maintain consent. Interviewees also described potential problems with relying on parents or family members to provide consent for minor or subjects with greatly diminished cognitive capacities. Whereas some research investigators (and perhaps the IRB) might assume a family-member consent was adequate, some interviewees believed that parents, for example, do not always have the best interest of their minor child in mind when giving consent, and parents and family member themselves may suffer diminished capacity due to illness or mind-altering substances such as alcohol. Further, several interviewees expressed concern that some investigators did not sufficiently consult with hospital caregivers, who are often in position to best know a particular patient (or family member’s) cognitive abilities at any given time. As a result, there was concern about a researcher’s ability to obtain and maintain informed consent of research subjects.

(b) Were proper recruitment strategies followed? Is there evidence that potential subjects were pressured or coerced to participate in the studies?

Document and interview evidence suggests that proper recruitment strategies were followed; no evidence of improper recruitment was identified. Nevertheless, several interviewees expressed great concern that recruitment procedures were insufficient to protect vulnerable subjects.

Several interviewees expressed concern about the lack of transparency, consultation, and scientific motivation for psychiatric studies run by some PIs. Such concerns are directly related to the recruitment
of patients for psychiatric research. Fairview staff, especially, expressed concern that UMN researchers
did not fully appreciate the vulnerable state of many patients, or their family caregivers. Accordingly,
several interviewees expressed concern that recruitment procedures, while perhaps technically
compliant with regulations, were not sufficiently protecting (potential) human research subjects.
Concern was expressed regarding the recruitment and enrollment of study subjects in the inpatient
setting and the impact it may have on the safety other patients and caregivers. This was of particular
concern for placebo controlled trials as unmedicated patients may become unruly or even violent.
Concern was expressed regarding patient status. Some caregivers stated that it was not in the patient’s
best interest to be recruited for a research study if stable on a regimen.

(c) Were participants freely allowed to withdraw from participation? Is there evidence that
participants’ rights to withdraw from a study were not respected?

Document and interview evidence suggests that subjects were allowed to withdraw from participation
(as medically appropriate) at any time; no evidence of violations of withdrawal rights was identified.
Nevertheless, several interviewees expressed great concern that the consent process (on which the right
to withdraw rests) was insufficient to protect vulnerable research subjects. Readers are referred to
question (a) above, and the reports conclusion below. Additionally, some interviewees expressed
concern about the hyper-diligence of some research staff to almost befriend if not temporarily adopt
research subjects. The dimly lit line between advocating for and protecting subjects versus coercing
them to not withdraw concerned some interviewees.

(d) Were the privacy rights of potential subjects respected? Is there evidence that research
recruitment practices violated HIPAA?

Document and interview evidence suggests that subject privacy was respected; no evidence of HIPAA
violations was identified. No concerns about privacy violation were expressed.
CONCLUSION

This report’s findings are based on extensive research by an IRB committee tasked with determining whether specified psychiatric research studies were compliant with policy and regulations. The focus on psychiatric research is understandable given the history of UMN psychiatric researchers, current controversies surrounding past cases (e.g., the death of Dan Markingson), concerns raised by anonymous persons in the Fairview system, and the recognized vulnerability of persons who, due to their illnesses, have various degrees of diminished capacity to understand their rights and responsibilities as research subjects. When it comes to the protection of human research subjects, the vulnerability of persons with diminished capacity, especially due to mental illness, cannot be over emphasized. Yet there is a great need for better medication and treatments for such persons, and such activities require rigorous research with human research subjects. Consequently, there is a necessary tension between the need for more research and the protection of human research subjects, whose dignity and safety must be paramount.

This IRB investigation uncovered no evidence of non-compliance by psychiatric researchers. Not a single case of a subject being improperly recruited, consented, or otherwise not protected was reported or found. Many that were interviewed have engaged in rigorous and exemplary practices to assure that individuals or their representative are appropriate to consent and appreciate the vulnerability of their population. They have had well established practices in their studies and have recognized their responsibility as investigators to ensure the protection of subjects. That said, there are evident concerns about the culture of psychiatric research at the University.

In the main, this investigation found that there is a great deal of mistrust and misunderstanding within and between UMN researchers and Fairview caregivers. Fairview caregivers do not trust some UMN researchers to protect human research subjects; for some, the level of distrust is profound. In addition, some UMN researchers did not trust other UMN researchers to protect human research subjects. A handful of principal investigators and some research staff were implicated. What is more, many interviewees expressed strong negative opinions about the motivation for certain studies (e.g., science versus money? Placebo control needed?) directed by a few investigators and their associated efforts to recruit and obtain informed consent from cognitively diminished (potential) subjects under such circumstances.

Our interpretation of the expressed opinions of interviewees is that some psychiatric researchers fail to appreciate the difference between patient care and research; the so-called therapeutic misconception wherein research practices are tangled up in patient care did not seem fully appreciated. Data suggest this is true for researchers at all levels, from some faculty researchers to their research assistants. In addition, it appeared that not all UMN researchers appreciated the full range of risks of psychiatric studies on quite vulnerable subjects, subject’s families, other patients in the in-patient clinics, and caregiving staff, especially nurses. There is a gap between how some UMN researchers understand the sufficiency of their own efforts to protect human research subjects and the perception of other stakeholders, especially Fairview caregivers. Importantly, many UMN researchers do fully grasp the
nuances of protecting human subjects and enjoy a strong reputation across institutions. On the other hand, many Fairview staff did not understand the basic risk-reward aspects of research; for them, patient care was the only ethical objective. Fairview staff uniformly reported comfort with research in general, but few appeared comfortable with commonly accepted recruitment and consent procedures, or the occasional need for riskier investigations when potential benefits to subjects — if not medical science more generally — was great.

It is difficult to know exactly why Fairview caregivers mistrust some UMN researchers. No clearly inappropriate acts were identified that would justify strong feelings. Instead, research conducted for this report suggests the attitude stems from a seemingly psychic-cultural wound associated with the death of Dan Markingson over ten years ago. Despite findings of previous investigations, many interviewees reported concerns about the how the Markingson case was handled and communicated to caregivers, then and now. Interviewees expressed several unanswered questions about the details of the Markingson case, and subsequent cases, and some drew conclusions, justified or not, through a lens of mistrust if not cynicism. In addition, mistrust of certain researchers and associated research staff seemed to be based on the actions that, while technically compliant, were perceived as less than optimal in an ethical care framework. Some expressed deep anxieties about recent psychiatric research studies and/or proposals. Such concern appears to stem from (1) a framework of past violations, real or perceived, (2) a failure to consult and work with caregiving staff, (3) professional disagreements over the optimality and monitoring of care for non-research patients by some physician PIs, and (4) a sense, however real, that UMN and Fairview leadership valued research more than patient care and that persons raising concerns about the protection of human research subjects were, at best, unwelcome if not targeted for dismissal. Of concern is that research for this report suggests that leaders in both the Department of Psychiatry and the Fairview hospital system do not seem to appreciate the level of distrust or the reasons (whatever they are) for it. Absent a better term, UMN and Fairview leadership appears insensitive to the cultural tensions and the causes of it. In short, UMN and Fairview leadership appears to be exacerbating the tension by not understanding and/or addressing the issues at hand, real or perceived.

At one level, cultural divides within and across organizations may be of no concern to the protection of human research subjects or the IRB. After all, this investigation found no evidence of non-compliance. Yet at another level, this investigation has not only uncovered great tension between Fairview caregivers and some UMN psychiatric researchers, but leadership that appears unaware if not disinterested in tension. These facts would appear important to an IRB aiming to fully understand the research environment, too often minimally described in IRB applications, in which especially vulnerable subjects are invited to participate in, at times, risky research. Knowing that Fairview caregivers do not trust some UMN Psychiatrists, that some UMN psychiatric researchers do not think highly of Fairview caregivers, that past psychic wounds from long ago continue to fester, and that organizational leaders appear tone-deaf to the situation should compel the IRB to pay greater attention to psychiatric research studies. With respect to protecting some of the most vulnerable among us, it would seem prudent for the IRB to increase situational awareness and extend vigilant monitoring of some psychiatric investigations.
APPENDIX – CHARGE LETTER FROM IRB EXECUTIVE COMMITTEE TO INVESTIGATION PANEL

1. Conduct an investigation to determine whether serious or continuing non-compliance has occurred in active Department of Psychiatry studies on schizophrenia and bipolar disorder involving the following Principal Investigators and studies:

   i. Follow the procedures outlined under IRB Policy 408A: Investigation Process in conducting the investigation.

2. Examine any and all aspects of the conduct of each study as necessary to determine compliance by the Principal Investigator and study staff, including but not limited to the following:
   a. Were there adequate mechanisms in place to evaluate whether potential subjects had the capacity to consent to participation? Is there evidence that subjects were consented who lacked the capacity to consent?
   b. Were proper recruitment strategies followed? Is there evidence that potential subjects were pressured or coerced to participate in the studies?
   c. Were participants freely allowed to withdraw from participation? Is there evidence that participants’ rights to withdraw from a study were not respected?
   d. Were the privacy rights of potential subjects respected? Is there evidence that research recruitment practices violated HIPAA?

3. If additional Psychiatry Department studies on schizophrenia or bipolar disorder become active during the course of the investigation, consider expanding the scope of the investigation to encompass the new studies and potentially new investigators.

4. Review all materials, reports and responses generated earlier in the review process. Obtain and review any additional materials that may be needed, including IRB files, researcher records, medical charts, and any other necessary documentation.

5. Give the researchers under review an opportunity to provide input through written comments. Interview as needed the researchers, study staff, Fairview staff, research participants, and any other witnesses the panel deems relevant to the investigation. Summarize or audio record any witness interviews.

6. Prepare a report at the end of the investigation that summarizes the information the panel considered and outlines the panel’s conclusions and recommended actions. Send the report to the IRB Executive Committee and the researcher under review.

7. Complete the investigation within three months. Request an extension for good cause if additional time is needed.