



OFFICE OF THE LEGISLATIVE AUDITOR
STATE OF MINNESOTA

A Clinical Drug Study at the University of Minnesota Department of Psychiatry: The Dan Markingson Case

Special Review

March 19, 2015

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OFFICE OF THE LEGISLATIVE AUDITOR

STATE OF MINNESOTA • James Nobles, Legislative Auditor

March 19, 2015

Members of the Legislative Audit Commission:

The Office of the Legislative Auditor conducted a review of the Dan Markingson case at the request of the chairs of the House and Senate Higher Education Committees.

Dan Markingson was a young man who committed suicide in 2004 while participating in a University of Minnesota Department of Psychiatry drug study. The case was the subject of a civil lawsuit and several regulatory reviews, but it still remains controversial.

While we think it is impossible to make a causal connection between Markingson's death and his participation in the drug study, we concluded that the case involves serious ethical issues and numerous conflicts of interest.

We are especially troubled by the response of University leaders to the case; they have made misleading statements about previous reviews and been consistently unwilling to discuss or even acknowledge that serious ethical issues and conflicts are involved.

We make two recommendations for legislative action to better ensure that human subjects are protected when they participate in drug studies conducted by the University of Minnesota Department of Psychiatry.

This review was conducted by Elizabeth Stawicki, Joel Alter, and Jim Nobles.

Sincerely,

A handwritten signature in black ink that reads "Jim Nobles".

James Nobles
Legislative Auditor

cc: Members of the House Higher Education Policy and Finance Committee
Members of the Senate Higher Education and Workforce Development Budget Division

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INTRODUCTION

On May 8, 2004, Dan Markingson violently killed himself while participating in a University of Minnesota Department of Psychiatry drug study.¹ Dr. Stephen Olson, a psychiatrist and associate professor in the department, managed the study. Drug manufacturer AstraZeneca funded the research, which is commonly referred to as the CAFÉ study.²

Markingson's death sparked a lawsuit against the University, Dr. Olson, and others; several state and federal reviews; and a national debate about the ethics of recruiting mentally ill patients into industry-sponsored drug research.

In recent months, the debate about the Markingson case—and how university officials have responded to it—has intensified. Criticism of the University and calls for an independent reexamination of the Markingson case have come not only from Markingson's family but also from medical professionals, bioethicists, law professors, and others within the academic community, including some University of Minnesota faculty. In an open letter to the Minnesota Legislature, former Minnesota Governor Arne Carlson recently joined in that criticism and called for further review.³

University officials have, however, repeatedly insisted that the Markingson case has been fully reviewed, with University personnel cleared of any wrongdoing, and that further examination is unnecessary. For example, in a 2011 letter, the then Board of Regents chair said that the University's General Counsel had provided the Board with the "extensive reviews" previously conducted of the Markingson case, and "we do not believe further University resources should be expended re-reviewing a matter such as this...."⁴ In a 2013 letter, University President Eric Kaler repeated that position; he said, "I do not believe additional review [of the Markingson case] is warranted."⁵

University leaders did, however, respond recently to a University Faculty Senate resolution that called for an outside panel of experts to review the University's current "policies, practices, and oversight of clinical research on human subjects at the University, in particular clinical research involving adult participants with diminished functional abilities."⁶

¹ The violent nature of Markingson's suicide (he slashed open his neck and abdomen with a knife) is cited by some as evidence of his continued psychotic condition despite having been in the University drug study and under the care of Dr. Olson for approximately five months.

² The study's full name was Comparison of Atypicals in First Episode (CAFÉ). It was simultaneously conducted at 26 sites around the United States and Canada. At each site, the medical person in charge, such as Dr. Olson in Minnesota, is referred to as the "principal investigator." We provide more details about the CAFÉ study throughout this report.

³ Arne H. Carlson, former Governor of Minnesota et al., An Open Letter to Legislators, February 2015.

⁴ Clyde E. Allen, Jr., Chair, Board of Regents, University of Minnesota, letter to Carl Elliot (and seven other professors at the Center for Bioethics, University of Minnesota), February 7, 2011.

⁵ Eric W. Kaler, President, University of Minnesota, letter to Leigh Turner, Ph.D., Associate Professor, Center for Bioethics & School of Public Health, University of Minnesota, May 29, 2013.

⁶ Resolution, Meeting of the Faculty Senate, Issues Arising from the CAFÉ Study and the Suicide of Dan Markingson Action by the Faculty Senate, December 5, 2013.

University officials hired the Association for the Accreditation of Human Research Protection Programs, Inc. (AAHRPP) to select members of the expert panel and manage the review's logistics.⁷ The panel released its report in late February 2015, and we note several of its findings and recommendations in this report, particularly in Finding 9.⁸

Because the external panel was not expected to examine the Markingson case, legislators and others asked the Office of the Legislative Auditor (OLA) to become involved. We agreed to focus our review on the Markingson case.

To conduct our review, we examined thousands of pages of documents from *Weiss v. Board of Regents et al.*, 27-CV-07-1679, as well as documents from all of the regulatory reviews related to the Markingson case. We also interviewed people knowledgeable about the Markingson case, psychiatry, and clinical drug studies.

CONCLUSION

We do not think it is possible to know whether Dan Markingson's suicide was connected to his participation in the University clinical drug study; the suicide of a person with serious mental illness may involve many contributing factors. However, the Markingson case raises serious ethical issues and numerous conflicts of interest, which University leaders have been consistently unwilling to acknowledge. They have repeatedly claimed that clinical research at the University meets the highest ethical standards and dismissed the need for further consideration of the Markingson case by making misleading statements about past reviews. This insular and inaccurate response has seriously harmed the University of Minnesota's credibility and reputation.

⁷ The members selected were: Anne Donahue, JD, Vermont state representative, mental health consumer advocate, and member of the former Subcommittee on the Inclusion of Individuals with Impaired Decision-Making in Research of the Secretary of Health and Human Services Advisory Committee on Human Research Protections; Melissa Frumin, MD, MS, Neuropsychiatrist and General Psychiatrist at Brigham and Women's Hospital, and Assistant Professor of Psychiatry at Harvard Medical School; Joan Rachlin, JD, MPH, former executive director of Public Responsibility in Medicine and Research (PRIM&R) from 1975 to 2014, and developer of an educational organization for those conducting and reviewing human subjects and animal research around the world; Megan Kasimatis Singleton, JD, MBE, CIP, associate director, Human Research Protections at the University of Pennsylvania Institutional Review Board; David Strauss, MD, Associate Professor of Psychiatry and vice-chair for research administration, ethics, and policy at the Columbia University Department of Psychiatry and director of psychiatric research at the New York State Psychiatric Institute; and Jeremy Sugarman, MD, MPH, MA, Harvey M. Meyerhoff Professor of Bioethics and Medicine, Professor of Medicine, Professor of Health Policy and Management, and deputy director for medicine of the Berman Institute of Bioethics at the Johns Hopkins University.

⁸ Association for the Accreditation of Human Research Protection Programs, *An External Review of the Protection of Human Research Participants at the University of Minnesota with Special Attention to Research with Adults Who May Lack Decision-Making Capacity*, February 23, 2015.

PREVIEW OF FINDINGS

1. Dan Markingson was extraordinarily vulnerable when Dr. Olson recruited him into a drug study; Markingson was mentally ill and faced commitment to a state psychiatric hospital if he did not cooperate with the Fairview University Medical Center treatment plan and his treatment team's aftercare recommendations following discharge. In 2009, the Legislature passed a law restricting the enrollment into drug trials of persons under a stay of commitment. See [pages 10-15](#).
2. AstraZeneca, the financial sponsor of the CAFÉ drug study, prorated its payments to the University based on the number of subjects Dr. Olson enrolled in the study and the number of follow-up meetings the subjects completed. Dr. Olson's goal was to enroll 30 people, and he had difficulty meeting that goal. This created an incentive to enroll and keep Dan Markingson in the CAFÉ drug study in November 2003. See [pages 15-17](#).
3. Markingson's mother, Mary Weiss, expressed strong concerns about her son's participation in the drug study and continually warned that he was not improving. There is little evidence that the study team adequately followed up with her about her concerns. See [pages 17-18](#).
4. Dr. Olson told the University's Institutional Review Board (IRB)⁹ that drug study participants would each have an advocate, but Markingson did not have an advocate with him at the time he signed the informed consent to participate in the CAFÉ drug study. See [pages 19-20](#).
5. The University of Minnesota's Institutional Review Board conducted a superficial review of Dan Markingson's suicide. The IRB did not review medical records, did not seek information from anyone other than Dr. Olson, and did not review information about Markingson's suicide. See [pages 20-22](#).
6. The Minnesota Board of Social Work investigated CAFÉ study coordinator Jean Kenney, a licensed independent clinical social worker.¹⁰ The Board found that she performed tasks beyond her competency and made significant errors. As a result, the Board entered into an Agreement for Corrective Action with Kenney. While the Board only had jurisdiction over Kenney, we believe its findings suggest that Dr. Olson inappropriately delegated tasks to Kenney and failed to provide her with adequate supervision. See [pages 23-24](#).

⁹ Institutional Review Boards are the groups within institutions that are required to approve proposals to conduct biomedical and behavioral health research that involve human subjects. The primary purpose of an IRB is to protect human subjects from physical or psychological harm by establishing research protocols and periodically reviewing ongoing research projects.

¹⁰ Minnesota has four levels of social work licenses based on academic degree and experience: (1) Licensed Social Worker (LSW) – Bachelor's License; (2) Licensed Graduate Social Worker (LGSW) – Graduate License; (3) Licensed Independent Social Worker (LISW) – Graduate license requiring 4,000 hours of non-clinical supervised practice; and (4) Licensed Independent Clinical Social Worker (LICSW) – Graduate license requiring 4,000 hours of clinical supervised practice. See <http://mn.gov/health-licensing-boards/social-work/applicant/>.

7. The Minnesota Board of Medical Practice's review of Dr. Stephen Olson was compromised because the expert consultant the Board hired to analyze the case had numerous conflicts of interests. See [pages 24-26](#).
8. University leaders—both administrators and regents—have responded to the Markingson case by dismissing the need for further review and ignoring serious ethical issues. See [pages 27-29](#).
9. An external panel of experts that recently reviewed the University's current human subjects protection program found significant and troubling problems. See [pages 29-31](#).

BACKGROUND

In 2003, Dan Markingson was a 26-year-old aspiring screenwriter living in Los Angeles, California, after having earned a B.A. in English from the University of Michigan. When his mother, Mary Weiss, visited in July, she noticed disturbing changes in her son's behavior. For example, Markingson had set up wooden posts around his bed to create an "astral field," and he thought an alien had burned a spot on his carpet.

While back in Minnesota on November 12, 2003, Markingson talked about participating in a satanic ritual in which he might be required to kill people, including his mother. In response, Markingson's mother called police, who took him to Regions Medical Center in St. Paul. Medical staff determined that Markingson was mentally ill and posed a danger to himself or others. They placed Markingson under a "72-hour-hold."¹¹

Due to a lack of available beds, Markingson was transferred that same day to Fairview University Medical Center (FUMC) hospital and placed under Dr. Stephen Olson's care. Dr. Olson is a psychiatrist and an associate professor in the University of Minnesota Department of Psychiatry.

Civil Commitment of Markingson

Dr. Olson started Markingson on an anti-psychotic drug on November 14, 2003.¹² The following day, Dr. Olson wrote in support of FUMC's court petition to commit Markingson to Anoka Metropolitan Regional Treatment Center, a long-term, state psychiatric hospital. Three days later, on November 17, a judge signed an initial commitment order, which confined Markingson to FUMC for additional "observation, evaluation, [and] diagnosis."

On November 20, a judge put Markingson's commitment on hold for six months on the condition that Markingson agree to comply with FUMC's treatment plan.¹³ Although the court found Markingson "mentally ill and in need of treatment," the judge did not find that Markingson was incompetent or needed a legal guardian to handle his affairs.

Markingson's Drug Study Participation

When Dr. Olson became Markingson's treating physician at FUMC, he was also leading a clinical drug study funded by AstraZeneca. The University of Minnesota was one of 26 sites in the U.S. and Canada conducting the three-year drug study known as the CAFÉ study.¹⁴ The study compared an AstraZeneca antipsychotic drug with two other similar drugs¹⁵ on individuals

¹¹ *Minnesota Statutes* 2014, 253B.05, authorizes and establishes the conditions for these "emergency holds."

¹² Dr. Olson prescribed Risperdal, a drug manufactured by Janssen Pharmaceuticals, Inc., a subsidiary of Johnson and Johnson.

¹³ The legal term is known as a "stay of commitment."

¹⁴ For the complete list, see https://clinicaltrials.gov/ct2/show/study/NCT00034892?show_locs=Y#locn.

¹⁵ AstraZeneca's drug is known as Seroquel (Quetiapine); the other drugs were Zyprexa (Olanzapine) produced by Eli Lilly and Risperdal (Risperidone) produced by Janssen Pharmaceuticals, Inc., a subsidiary of Johnson and Johnson.

experiencing their first “psychosis.”¹⁶ The U.S. Food and Drug Administration had already approved the three drugs as “safe and effective” treatments for schizophrenia; the study did not involve a new experimental treatment.¹⁷ The “double-blind” study randomly assigned one of the three medications to the patients.¹⁸ A double-blind study is one where both the subjects (in this case Markingson) and the research investigator (Dr. Olson and staff) do not know which study drug a patient is taking.¹⁹

On November 19, 2003, two days after FUMC started commitment proceedings against Markingson, Dr. Olson said he first talked with Markingson and Mary Weiss about Markingson participating in the CAFÉ study. Two days later, Markingson agreed to take part. The CAFÉ study’s coordinator, Jean Kenney, took Markingson’s psychiatric and medical history and obtained his “informed consent.”²⁰

The CAFÉ study was funded by AstraZeneca Pharmaceuticals, and the study was subject to an agreement between AstraZeneca and the University of Minnesota. A Columbia University professor designed the study, but AstraZeneca had authority in the agreement to make changes to the study’s protocols, duration, or number of participants. Dr. Olson also took on a dual role: he was not only Markingson’s treating physician but also the principal investigator of the research study into which Markingson had enrolled. Markingson’s participation in the CAFÉ study meant that his principal contacts with the study would be Dr. Olson and the study coordinator, Jean Kenney.

Markingson was assigned a CAFÉ study drug three days before Dr. Olson discharged him on December 8, 2003, to a state-licensed group home for people with mental illness. The discharge plan reminded Markingson to follow the aftercare agreement, which said: “Consequences for not following this plan could result in court commitment to the hospital.”

Markingson’s Group Home Experience

When FUMC discharged Markingson to a group home, he interacted with a significant number of people who were able to observe his behavior. They included the following:

- Staff at an FUMC day treatment program, which Markingson attended three times a week.

¹⁶ Individuals suffering from psychosis may lose touch with reality, for example, through delusions or hallucinations. In addition, psychotic individuals may lose motivation, have diminished expression of emotion, and exhibit poor grooming, anxiety, depression, aggression, or cognitive impairments.

¹⁷ Request For The Approval For The Use of Human Subjects in Research Health and Biological Sciences, Institutional Review Board, *Efficacy and Tolerability of Olanzapine, Quetiapine and Risperidone in the Treatment of First Episode Psychosis: A Randomized Double Blind 52-Week Comparison* (February 11, 2002).

¹⁸ *Ibid.*

¹⁹ Office of Training and Communication, Guidance for Industry, E 10 *Choice of Control Group and Related Issues in Clinical Trials*, Food and Drug Administration (2001), 4.

²⁰ In general, no investigator (researcher) may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative; 21 *CFR*, sec. 50b (2014).

- A Dakota County case worker, David Pettit, who was assigned to work with Markingson on November 24, 2003.²¹ Pettit first met Markingson on November 26, 2003, five days after Markingson consented to participate in the drug study.²²
- A psychologist in Eagan, who Markingson visited monthly.
- Staff at the group home.
- Dr. Olson and Jean Kenney in follow-up visits at FUMC.
- Markingson's mother, Mary Weiss, and a family friend, Mike Howard. Mary Weiss drove her son to and from appointments at least three days a week from April 11, 2004, until his death.

Mary Weiss and Markingson's treatment team sharply disagreed over the state of Markingson's mental health. Mary Weiss frequently reported to Dr. Olson, Kenney, and Pettit that her son was deteriorating and needed help. Generally, Pettit, the medical team, and group home staff reported Markingson was doing well, at least for the first few months after he came to the group home.

In the month before Markingson died, however, more observers reported some decline in his condition. One report found that Markingson appeared very inattentive in his group therapy; he sat smiling to himself. Two days later, Markingson said he had never heard of the Easter holiday even though he said he was raised Catholic. Other observers noted that he looked more disheveled and had a mildly "wilder" look in his eyes but still in contact with reality.

At the same time, Pettit, Kenney, and Dr. Olson were discussing the possibility of Markingson moving into his apartment in Minnesota. Dr. Olson recommended that Dakota County seek an extension of Markingson's commitment, primarily as a way to keep him from returning to California. Just a few days before Markingson killed himself, his social worker wrote the court to extend Markingson's stay of commitment for another six months. The next day, Markingson successfully completed the FUMC day treatment program.

During the early morning hours of May 8, 2004, Markingson went into a bathroom at the group home and slashed open his neck and abdomen with a knife. A coroner's report in 2004 showed Markingson had no drugs in his system; four years later, a toxicology test conducted by a private laboratory showed Markingson had a CAFÉ study drug (Seroquel) in his system at the time of his death.

²¹ David Pettit was not a licensed social worker during the time he was Dan Markingson's case manager, according to the Minnesota Board of Social Work. He was licensed in 1990 but his license expired in 2001. Minnesota law does not require county social workers to be licensed. *Minnesota Statutes* 2014, 148.065, subs. 4 and 4a. As a result, the Board of Social Work has no jurisdiction to investigate complaints regarding unlicensed social workers or discipline them. *Minnesota Statutes* 2014, 148E.185.

²² David Pettit Deposition, June 14, 2007, p. 37, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

Lawsuit Brought Against the University of Minnesota and Others

In January 2007, Dan Markingson's mother filed a lawsuit in Hennepin County District Court in response to her son's death. Her claims ranged from medical malpractice to negligence to product liability against the following defendants:

- The University of Minnesota Board of Regents and the University's Institutional Review Board (IRB)
- Dr. Stephen Olson and Dr. Charles Schulz (head of the University's Department of Psychiatry)
- Drug manufacturer AstraZeneca²³

In pretrial motions, the University argued that neither the Board of Regents nor the University's IRB could be held liable for Markingson's death or any of the actions alleged by Mary Weiss because the University had "statutory immunity" (or what is also known as "discretionary immunity").²⁴ Judge John Holahan agreed. He also dismissed claims against AstraZeneca.

The judge also dismissed one claim filed against both Dr. Olson and Dr. Schulz on the issue of Markingson's informed consent. The judge said Weiss offered no evidence that Markingson was legally incompetent to sign the form. Markingson signed the document, which informed him that the study was voluntary and about "any conflicting interests of the researcher, and the risks associated with the study."

The judge did allow a medical malpractice claim for failing to provide Markingson "proper care and treatment" to go forward against Dr. Olson. The issue never went to trial. Dr. Olson paid Mary Weiss \$75,000 to settle her claims against him. The University filed a motion seeking court costs from Weiss but agreed to waive those costs in exchange for her forgoing an appeal.²⁵

²³ Weiss' attorney filed an amended complaint seeking punitive damages, November 27, 2007, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

²⁴ *Minnesota Statutes* 2014, 3.736, subd. 3(b). The State of Minnesota, which includes the University of Minnesota, has generally been subject to tort liability since 1976 when the Legislature abolished the state's immunity through the Tort Claims Act. Before that, the state had to consent to be sued. But the Legislature also carved out numerous exceptions to that act. One is known as the discretionary function exception, which provides immunity to the state and its employees when performing or failing to perform a discretionary duty. *Dunnell Minnesota Digest*, vol. 43, sec. 1.07(b).

²⁵ An external panel's report made special mention that the University of Minnesota sought court costs from Markingson's mother, Mary Weiss. It said, "The University's motion to seek court costs from Mary Weiss...certainly did not create the impression of a humane response, and the [panel members were] told that the public perception is that she never received an expression of regret or apology in the aftermath of her son's death." Association for the Accreditation of Human Research Protection Programs, *An External Review of the Protection of Human Research Participants at the University of Minnesota with Special Attention to Research with Adults Who May Lack Decision-Making Capacity*, February 23, 2015, 89. University of Minnesota officials told us they remain deeply sorry to Dan Markingson's family for its loss, and they said the study team sent a sympathy card and flowers to the family in the week following Markingson's death.

Reviews of Markingson's Treatment and Suicide

Markingson's death also touched off several regulatory inquiries, some automatic and others that Mary Weiss initiated as formal complaints. Dr. Olson reported a "Serious Adverse Event" to the University's IRB. The University then notified the U.S. Food and Drug Administration (FDA) and the U.S. Department of Health and Human Services, Office for Human Research Protections, which it is required to do.

We will discuss some of the inquiries in more detail in our findings. The following is a brief summary of each inquiry:

1. The University's IRB, which oversees research involving human subjects, performed what it called a "routine, full-board" review of Markingson's death. It found no irregularities or noted further follow up performed. We discuss the inadequacy of the IRB's review in Finding 4.
2. The Minnesota Department of Human Services investigated the group home where Markingson lived for five months and where he died. It was alleged that the home violated Minnesota law by neglecting a vulnerable adult (Markingson) prior to his suicide.²⁶ The investigator disagreed.
3. The Minnesota Office of the Ombudsman for Mental Health and Mental Retardation investigated Markingson's death and issued recommendations in eight areas of concern.²⁷ We think the recommendations are particularly relevant to two of our findings and discuss them in Findings 1 and 5.
4. The FDA, which regulates drugs and drug studies, investigated five allegations filed against Dr. Olson by Mary Weiss. An FDA investigator found no evidence of misconduct or significant violation of the protocol or regulations.²⁸ But the review never discussed the potential coerciveness of obtaining consent from an individual under a stay of commitment. The reviewer never asked to talk to Mary Weiss, and the reviewer did not talk to David Pettit, group home staff, or FUMC's day treatment psychotherapist.²⁹

²⁶ State law defines neglect as: "The failure or omission by a caregiver to supply a vulnerable adult with care or services, including but not limited to, food, clothing, shelter, health care, or supervision which is: (1) reasonable and necessary to obtain or maintain the vulnerable adult's physical or mental health or safety, considering the physical and mental capacity or dysfunction of the vulnerable adult and (2) ...not the result of an accident or therapeutic conduct." *Minnesota Statutes* 2014, 626.5572, subd. 17(a).

²⁷ *Minnesota Statutes* 2014, 245.97, subd. 5. The office is now called the Ombudsman for Mental Health and Developmental Disabilities.

²⁸ U.S. Department of Health and Human Services, Food and Drug Administration, *Establishment Inspection Report* (Minneapolis, 2005), 1.

²⁹ The reviewer attempted to talk to David Pettit, group home staff, and the FUMC day treatment psychotherapist but was told they could not speak to her without a signed consent from a Markingson relative. The FDA did not pursue obtaining the consent.

5. The Minnesota Board of Medical Practice investigated Dr. Olson in response to allegations filed by Mary Weiss. The Board hired a psychiatrist to review the case and dismissed Weiss' complaint. We think the Board's review was seriously compromised because the psychiatrist the Board hired had significant conflicts of interest, as we discuss in Finding 7.
6. The Minnesota Board of Social Work investigated CAFÉ study coordinator Jean Kenney, a licensed independent clinical social worker.³⁰ The Board found that she performed tasks beyond her competency and made significant errors. As a result, the Board entered into an Agreement for Corrective Action with Kenney. Although the Board had jurisdiction over Kenney only, we believe its findings also suggest Dr. Olson inappropriately delegated tasks to Kenney and failed to provide her with adequate supervision. We will discuss the Board's finding and their implication for Dr. Olson's supervision of Kenney in Finding 5.

FINDINGS

Finding 1. Dan Markingson was extraordinarily vulnerable when Dr. Olson recruited him into a drug study; Markingson was mentally ill and faced commitment to a state psychiatric hospital if he did not cooperate with the Fairview University Medical Center treatment plan and his treatment team's aftercare recommendations following discharge. In 2009, the Legislature passed a law restricting the enrollment into drug trials of persons under a stay of commitment.

Dan Markingson was vulnerable in several ways: (1) For the first time in his life, he was confined to a locked psychiatric unit; (2) he had arrived in a serious state of psychosis; (3) he started taking a powerful drug; and (4) he was highly dependent on Dr. Olson as his treating physician not only for care but also in deciding whether he would live independently again. In an effort to explain the chain of key observations that took place leading up to Markingson's consent to participate in the study, we provide a brief timeline beginning with his arrival at Fairview University Medical Center (FUMC).

³⁰ Minnesota has four levels of social work licenses based on academic degree and experience: (1) Licensed Social Worker (LSW) – Bachelor's License; (2) Licensed Graduate Social Worker (LGSW) – Graduate License; (3) Licensed Independent Social Worker (LISW) – Graduate license requiring 4,000 hours of nonclinical supervised practice; and (4) Licensed Independent Clinical Social Worker (LICSW) – Graduate license requiring 4,000 hours of clinical supervised practice. See <http://mn.gov/health-licensing-boards/social-work/applicant/>.

TIMELINE

- Nov. 12, 2003** Dan Markingson arrives at FUMC with delusions that his role in a satanic cult may require him to kill people, including his mother. Due to indications of mental illness and dangerousness to self and others, Markingson is placed under Dr. Stephen Olson's care.³¹
- Nov. 14, 2003** Markingson begins taking Risperdal, an antipsychotic medication.
- A court-appointed social worker³² interviews Markingson and finds Markingson "is believed not to have the capacity to make decisions regarding neuroleptic medications."³³
- Dr. Olson writes to the court that Markingson is mentally ill and lacks the capacity to make decisions regarding his medical treatment. Commitment proceedings begin.
- Nov. 17, 2003** A Dakota County judge orders that Markingson continue to be held at FUMC.
- Nov. 18, 2003** A neuropsychologist evaluates Markingson and estimates his "overall intellectual functioning...in the superior range." She reports that he seemed to understand instructions except "on a somewhat complex task when he repeatedly asked for instructions even after they had been given."
- Nov. 19, 2003** A court-appointed psychologist examines Markingson and reports Markingson has a "gross impairment of judgment, behavior, capacity to recognize reality, [or] capacity to reason or understand."³⁴ But at the same time, the psychologist says Markingson's "thinking was logical and goal oriented" and "did not appear to be delusional."
- Dr. Olson first discusses CAFÉ study with Markingson and Mary Weiss.
- Nov. 20, 2003** Dan Markingson appears for his commitment hearing in Dakota County. A district court judge "stays" (puts on hold) his commitment to Anoka Metro Regional Treatment Center on the condition that he "remain hospitalized, cooperate with the treatment plan at Fairview University Medical Center until medically discharged, and follow all of the aftercare recommendations of the treatment team."³⁵
- Nov. 21, 2003** CAFÉ study coordinator Jean Kenney and another CAFÉ study researcher perform an evaluation of Markingson, which indicates that he is competent to give informed consent.
- Markingson agrees to participate in the CAFÉ study and signs the ten-page informed consent document.

³¹ During his short stay at Regions Hospital, Markingson was deemed mentally ill and in danger of causing injury to self or others if not immediately detained. Under *Minnesota Statutes*, 253B.05, he was placed under an emergency 72-hour hold.

³² The social worker for this examination was Ken Geister. The court appointed social worker David Pettit as Dan Markingson's case manager on November 24, 2003. Pettit met with Markingson for the first time on November 26, 2003.

³³ Neuroleptic medications are a type of antipsychotic drug that has a tranquilizing effect.

³⁴ Report of Examiner, James L. Jacobson, Ph.D., LP, submitted to Dakota County District Court, filed November 20, 2003.

³⁵ The court order staying Markingson's commitment to Anoka Regional Treatment Center did not require Markingson to participate in the drug study; it simply required Markingson to comply with Fairview's treatment plan, among other things. There is no evidence that the court was ever aware that Markingson's treatment under Dr. Olson included participation in a drug study. Dr. Olson said in a deposition that he did not inform the court directly that Dan was participating in a drug study but that the county case manager was required to report to the court that Dan was meeting the terms of the commitment that he seek appropriate care. Dr. Stephen Olson, MD, Deposition, May 1, 2007, pp. 78-79, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

Rather than continue to treat Markingson with the antipsychotic medication he initially prescribed (and later claimed had been effective), Dr. Olson discussed with Markingson the idea of participating in the CAFÉ study, which meant Markingson would be randomly assigned one of the three study medications. Dr. Olson now had two potentially conflicting roles in Markingson's life—researcher and treating physician. As with any researcher or physician involved with a “double-blind” study, Dr. Olson did not know what medication Markingson was taking.

Concern about Coercion

In 2005, the state's Office of the Ombudsman for Mental Health and Mental Retardation, Medical Review Subcommittee, reviewed Markingson's death. Unlike the other agencies that conducted reviews, the Ombudsman's office does not have regulatory powers; it conducts reviews and makes recommendations to improve how people with mental illness or mental disabilities are treated.

After reviewing “the circumstances surrounding the death of Daniel Markingson,” the office's Medical Review Subcommittee made recommendations in eight areas.³⁶ It based its recommendation to the University's Institutional Review Board on two concerns:

1. Markingson was recruited into the CAFÉ study while he was under a stay of commitment.
2. Dr. Olson served as both Markingson's treating physician and the principal investigator of the study into which he recruited Markingson.

In a June 2005 letter, the Ombudsman's medical review coordinator stated the following:

People under a stay of commitment for mental illness may require special protection to ensure that their voluntary informed consent is indeed voluntary and not intentionally or unintentionally coerced. The client [Dan Markingson] signed the “Adult Consent Form” for the CAFÉ study on 11/21/2003, the day after the hearing that resulted in the client's stay of commitment. The client's stay of commitment included eleven “terms and conditions” enumerated by the judge, including “that the Respondent [Markingson] remain hospitalized, cooperate with the treatment plan at [the hospital] until medically discharged, and follow all of the aftercare recommendations of the treatment team.”

The IRB's own web-based tutorial “Informed Consent Overview—Selecting Participants” states, “Doctor-patient relationships between the investigator and [study] participants should be avoided, when possible, to eliminate any power-based coercion. Patients can say no to someone they do not expect to see in the

³⁶ Jo Zillhardt, Medical Review Coordinator, Office of the Ombudsman for Mental Health and Mental Retardation, letter to Mary Jones, Dakota County, June 17, 2005. The office is now called the Ombudsman for Mental Health and Developmental Disabilities.

future, but it is very difficult for people to say no when they rely on someone for ongoing medical care.³⁷

Similar concern about recruiting vulnerable subjects into drug studies is contained in guidance from the U.S. Department of Health and Human Services. That guidance states:

The predominant ethical concern in research involving individuals with psychiatric, cognitive, or developmental disorders, or who are substance abusers is that their disorders may compromise their capacity to understand the information presented and their ability to make a reasoned decision about participation.

Many individuals with disabilities affecting their reasoning powers may be residents of institutions responsible for their total care and treatment. The impact of institutionalization may further compromise their ability to exercise free choice (voluntariness). (These concerns apply both to voluntary patients and those committed involuntarily.) The eagerness for release may induce an institutionalized person, especially one who is involuntarily confined, to participate in research out of a desire to appear “rational” and “cooperative” to those who will make decisions about his or her release.³⁸

In addition, we learned that although the Minnesota Board of Medical Practice dismissed allegations against Dr. Olson, it received an independent assessment that said the circumstances under which Markingson was enrolled in the CAFÉ study could be seen as “highly coercive.”³⁹ Even the consultant who recommended that the Board dismiss the allegations against Dr. Olson said the fact that Dr. Olson was both Markingson’s treating psychiatrist and the CAFÉ study principal investigator was “not ideal” and “open to criticism as possibly constituting coercion. This is particularly true when the patient is under a Stay of Commitment.”

More recently, the panel that conducted the outside review of the University’s human subjects protection program added its voice to concern about possible coercion. It said, “The fear of being subjected to an involuntary legal process for perceived noncooperation, even if there is no *direct* threat of such legal compulsion, is an overwhelming barrier to voluntariness.”⁴⁰

³⁷ *Ibid.*, 4-5.

³⁸ U.S. Department of Health and Human Services, Office for Human Research Protections, *Institutional Review Board Guidebook, Cognitively Impaired Persons*, Chapter 6(D), 1993, http://www.hhs.gov/ohrp/archive/irb/irb_chapter6.htm.

³⁹ The identity of the person who provided the independent assessment referenced here is not public information. However, it is worth noting that this individual is not the psychiatrist hired by the Board to provide advice on its investigation into a complaint filed against Dr. Olson. As discussed in Finding 7, we think the Board of Medical Practice review was compromised because that psychiatrist was a colleague of Dr. Olson at the University Department of Psychiatry, where he had participated in industry-sponsored clinical drug studies.

⁴⁰ Association for the Accreditation of Human Research Protection Programs, *An External Review of the Protection of Human Research Participants at the University of Minnesota with Special Attention to Research with Adults Who May Lack Decision-Making Capacity*, February 23, 2015, 67.

Finally, we note that in 2009, the Minnesota Legislature enacted legislation that, with some exceptions, prohibits a person under a civil commitment order from participating in a psychiatric drug study.⁴¹ If a court is asked to allow an exception, the law prohibits the person's treating psychiatrist from also being the psychiatrist conducting the drug study. The law is commonly referred to as "Dan's Law" because it reflected concerns about the conditions under which Dr. Olson recruited Dan Markingson into the University's CAFÉ drug study.

Markingson's mother, Mary Weiss, testified in support of the legislation and said:

I spent the summer [of 2003] getting Dan home to Minnesota and finally in the fall into a hospital to hopefully be treated for his mental illness. Instead, Dan was put into a clinical study. He was taken to court, given a stay of civil commitment and ordered by the court to get treatment for his mental illness. The doctor involved signed a statement indicating that Dan did not have the capacity to make a decision regarding neuroleptic medication, but yet, one week later Dan was signed into a study....

Had this bill been law five years ago, Dan would be alive. And I am hoping that you will approve it because of all of the people who fall into the same situation as my son. Dan was not an anomaly. There are many others who are ordered to get treatment and find themselves in a study. A study is in no way treatment.... I hope that you will understand the importance of this bill and the lives that it will save in the future.

Response from University Officials and Dr. Olson

University officials and Dr. Olson have denied that there was anything inappropriate about Markingson's recruitment into the CAFÉ drug study. Dr. Olson noted that Markingson signed the "Adult Consent Form" for the CAFÉ study that the IRB had approved.⁴²

Dr. Olson has also emphasized that because Markingson began taking the antipsychotic drug Risperdal on November 14, 2003, by November 21, 2003, he was mentally competent to provide "informed consent" to participate in the CAFÉ drug study. Dr. Olson supports his position by citing examinations Markingson underwent at FUMC by a neuropsychologist and a court-appointed psychologist.

Dr. Olson also rejected the suggestion that Markingson was coerced into participating in the drug study because his stay of commitment to Anoka Metro Regional Treatment Center was conditioned on his cooperation with Dr. Olson's treatment plan. In documents we reviewed,

⁴¹ *Laws of Minnesota* 2009, chapter 58; codified as *Minnesota Statutes*, 253B.095, subdivision 1(d)(4) and (e). The initial version of the legislation called for an outright ban on using patients under stayed commitment orders to participate in clinical trials, but the National Alliance on Mental Illness Minnesota objected. According to a press account, the organization contended that "mentally ill patients benefit from experimental drugs or treatments when traditional therapy fails them." Jeremy Olson, "Minnesota House, Senate Unanimously Pass Limits on Researchers' Use of Mentally Ill Patients," *St. Paul Pioneer Press*, May 8, 2009.

⁴² Adult Consent Form, *Efficacy and Tolerability of Olanzapine, Quetiapine and Risperidone in the Treatment of First Episode Psychosis: A Randomized Double Blind 52 Week Comparison*, The CAFÉ Study, November 21, 2003.

Dr. Olson said he first presented information about the drug study to Markingson on November 19, 2003. On November 21, study coordinator Jean Kenney read him the ten-page “informed consent” document (as Markingson followed along with his own copy). Dr. Olson noted several times that Markingson was told that he did not have to participate in the drug study and that he had a right to alternative treatment. It is not clear what Dr. Olson or Ms. Kenney said or implied about what that alternative might be.

Dr. Olson also has noted that the social worker Dakota County appointed to manage Markingson’s case agreed that Markingson’s participation in the drug study was acceptable. However, that case manager was not present when Markingson signed the drug study informed consent document. The social worker’s first in-person contact with Markingson was on November 26, 2003.⁴³ In fact, given his confinement and isolation at FUMC, Markingson had no one to provide him with independent advice about agreeing to participate in the drug study; all of the information and advice he was given came from Dr. Olson and Jean Kenney. We discuss this lack of a neutral person—or advocate—in Finding 4.

Finding 2. AstraZeneca, the financial sponsor of the CAFÉ drug study, prorated its payments to the University based on the number of subjects Dr. Olson enrolled in the study and the number of follow-up meetings the subjects completed. Dr. Olson’s goal was to enroll 30 people, and he had difficulty meeting that goal. This created an incentive to enroll and keep Dan Markingson in the CAFÉ drug study in November 2003.

Dr. Olson’s goal—as established in his agreement with AstraZeneca and application to the IRB—was to enroll 30 people in the CAFÉ study. According to Dr. Olson’s written responses to our questions, 20 individuals signed CAFÉ consent forms, 3 of whom did not continue for various reasons. Seventeen were given one of the three CAFÉ study drugs, and nine completed the study. Dan Markingson was enrolled in the CAFÉ study by Kenney and Dr. Olson on November 21, 2003. He was the 13th person they enrolled in the study.

AstraZeneca paid the University \$15,648 for each patient who completed the study. AstraZeneca prorated the payments for patients who left the study. For example, Dan Markingson completed 11 of 19 visits with the treatment team. According to the agreement, AstraZeneca would pay \$9,546 for this number of visits. The drug maker would also pay \$100 to the University of Minnesota for “psycho-educational interventions”⁴⁴ that were completed for five specified visits per patient.⁴⁵

In January 2003, CAFÉ study coordinator Jean Kenney e-mailed the organization that was managing the study for AstraZeneca, expressing worry about being able to recruit enough people

⁴³ David Pettit Deposition, June 14, 2007, p. 37, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

⁴⁴ The informed consent offers the human subject five sessions of “supportive and psychoeducational therapy that will provide you with information about your illness, and provide some emotional support during your recovery.”

⁴⁵ The agreement specified that the \$100 per patient payment would be based on completing visits 1, 3, 5, 8, and 10.

into the study.⁴⁶ Kenney expressed frustration that parents were intervening to dissuade potential enrollees. She said:

Have had another person show interest from inpatient and then the parent put the pressure on and said, “NO.” (3rd time this has happened) Have tried to ask about concerns, etc. but usually just get a NO. So, some frustration here b/c we really need to get more enrollees. We’ve had none for January and that concerns me a lot.

Kenney received the following response:

Hopefully your hard work will start to pay off soon! The specialty inpatient unit sounds like it will help out a lot with recruitment!! Take care and try not to get too frustrated!

In a written response to our questions, Dr. Olson rejected the inference that either he or Jean Kenney had any financial incentive to enroll people in the CAFÉ study or to keep them in the study. He said:

The salary payments from the University of Minnesota to the FUMC CAFÉ study research team—including salary payments to me and Jean Kenney—were not affected by the number [of] subjects enrolled in the CAFÉ study or the number of visits each subject completed. My salary and Jean Kenney’s salary were determined by the Department of Psychiatry, and were not affected by the amount of support provided by the CAFÉ study or for any other study.

In my experience, sponsored support for clinical trials is almost always based upon the number of subjects enrolled and the number of visits completed for each subject; this is a standard arrangement for sponsored research—whether sponsored by a government agency or by industry. Sponsor payments in this case and in all sponsored research at the University, are made to the University’s Sponsored Project Administration for the purpose of funding the study, and are not made to any individual, department, or college.

In a later statement to us, Dr. Olson said Dan Markingson “remained in the study because his case worker and care providers involved in his case believed that he was doing well and not because of any research incentives.” Dr. Olson said he had several subjects in the CAFÉ study who did not do well on their assigned medication and were dropped from the study and treated with alternative care.

Even though payments from AstraZeneca did not go directly to Dr. Olson or Jean Kenney, University officials told us—and have said publicly many times—that the University’s budget depends on faculty bringing in outside revenue from research grants. Nevertheless, we cannot be certain what role obtaining outside revenue played in Dan Markingson’s recruitment and

⁴⁶ We obtained the e-mail from Hennepin County District Court records in the civil case, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

retention in the CAFÉ study. But we do know that AstraZeneca set a goal for Dr. Olson and prorated its payments to the University in a way that clearly created an incentive to enroll and keep subjects enrolled in the CAFÉ study. We also know that Dr. Olson kept Markingson in the study despite Mary Weiss' repeated warnings that Dan was not well and the study medication was not working.

Finding 3. Markingson's mother, Mary Weiss, expressed strong concerns about her son's participation in the drug study and continually warned that he was not improving. There is little evidence that the study team adequately followed up with her about her concerns.

Although Dan Markingson was an adult, he authorized and signed a release that allowed Dr. Stephen Olson and the CAFÉ study staff to verbally share his medical information with his mother. Weiss repeatedly questioned her son's treatment team about his care and health. She wrote letters and telephoned her concerns. She told the treatment team that Markingson said people were speaking to him through the television; his medicine was not working; she saw a rage in him; and that he had told her he had "fooled the doctors."

While progress notes show Weiss' calls and their content, there is little documented evidence that the study team followed up with her, particularly in a timely way. In one incident on April 11, 2004, Weiss, who had seen her son that day and reported he was out of control, left an alarming message on Jean Kenney's phone: "Do we have to wait until he kills himself or anyone else before anyone does anything?"

Weiss' call on April 11 is not documented in Markingson's progress notes until four days later, April 15. There is no documented evidence that anyone on the treatment team followed up with her until at least a week later. Throughout Markingson's time in the CAFÉ study, Weiss also wrote letters and telephoned Dr. Olson but she said that he never responded. She then wrote a letter to the head of the psychiatry department, Dr. Charles Schulz, in early March of 2004.⁴⁷ Receiving no reply, she sent Dr. Schulz another letter, this time by certified mail.⁴⁸ She asked Dr. Schulz who she should go to if Dr. Olson would not talk to her.

At the end of April, less than two weeks before Markingson died, Weiss sent Dr. Schulz another letter.⁴⁹ She worried that the treatment team was pressuring her son to move into an apartment rather than the group home, and that he simply was not ready to live independently. She also asked, "If this were your son, would you allow him to be placed into a study where you did not know what medication he was on? And what action would you take if you knew he was not doing better?"

⁴⁷ Dr. Schulz was a co-investigator in Dr. Olson's CAFÉ study and a paid consultant for AstraZeneca, the drug manufacturer that funded the CAFÉ study. Mary Weiss, letter to Dr. Charles Schulz, Professor and Head, Department of Psychiatry, University of Minnesota Medical School, March 4, 2004.

⁴⁸ Mary Weiss, letter to Dr. Charles Schulz, Professor and Head, Department of Psychiatry, University of Minnesota Medical School, March 15, 2004.

⁴⁹ Mary Weiss, letter to Dr. Charles Schulz, Professor and Head, Department of Psychiatry, University of Minnesota Medical School, April 26, 2004.

Dr. Schulz replied, “I would have to answer that I would be very interested in my son receiving treatment in a well organized treatment trial that has been run by such effective staff as Dr. Olson and Jeannie Kenney.”⁵⁰ What Weiss did not know at the time was that Dr. Olson helped write Schulz’s response. In addition, Schulz was a co-investigator in the CAFÉ study and a paid AstraZeneca consultant, the same drug company that funded the CAFÉ study.

We think Weiss’ observations should have been taken more seriously. When a family member takes the time to compose a letter to the treating physician and the head of the department, common courtesy requires an acknowledgement that the letter was received and a response, even if brief. The study team should have built a more open and collaborative relationship with Mary Weiss. While she was not a medical professional schooled in psychiatry, she was Dan’s mother and knew her son’s history from birth. She was also in a position to offer an outside perspective given that she drove him to and from his appointments. Even if the team ultimately ruled out her concerns, it should have explained the reasons why so that she knew that those caring for her son had heard her and considered her observations.

This was also the view of the Medical Review Subcommittee of the Ombudsman for Mental Health and Mental Retardation when it reviewed the Markingson case.⁵¹ The Ombudsman’s report said the study team should have taken additional time and effort to educate Mary Weiss about her son’s illness. Instead, Weiss ultimately reached the conclusion no one could help her or her son. She said, “I was watching my son deteriorate and there was absolutely no one that I could go to.”⁵²

We asked the current IRB Chair, Dr. Susan Berry, about where family members could go to register concerns or complaints and she said the informed consent form that study participants such as Markingson signed included that information. The consent form said to direct any questions or concerns to Fairview’s Patient Relations Department.⁵³ Dr. Berry said very likely Fairview would have said “that’s not a Fairview concern but we can pass it on to the IRB.”

But Weiss and a family friend, Mike Howard, said they never saw the informed consent form or knew that the University had an IRB until after Markingson died.⁵⁴ They also said no one from the University nor the CAFÉ study ever offered to help them file a complaint. Given Weiss and Howard’s persistence to convey concerns with the members of the treatment team and the head of the department, it seems logical that they would have also contacted the IRB if they knew it was an avenue to pursue.

⁵⁰ Dr. Charles Schulz, Professor and Head, Department of Psychiatry, University of Minnesota Medical School, letter to Mary Weiss, April 28, 2004.

⁵¹ The office is now called the Ombudsman for Mental Health and Developmental Disabilities.

⁵² Mary Weiss Deposition, July 5, 2007, p. 71, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

⁵³ The informed consent form language said: “This research has been reviewed and approved by the IRB at the University of Minnesota. If you have any questions or concerns regarding your rights as a research subject, you may contact the Patient Relations Department at Fairview University Hospital.... The phone number is 612 273-5050.”

⁵⁴ Mike Howard says he found the signed consent form in the trash of the group home the morning of Markingson’s death when Howard was looking for some of Markingson’s personal items that were missing from his room.

Finding 4. Dr. Olson told the University’s Institutional Review Board (IRB) that drug study participants would each have an advocate, but Markingson did not have an advocate with him at the time he signed the informed consent to participate in the CAFÉ drug study.

Dr. Stephen Olson’s application to the IRB for CAFÉ study approval described the precautions he would take to minimize risk to the human subjects. One of those precautions was “Subjects will have an advocate. This person will typically be a case manager, nurse, family member or friend....”

Patient advocates can help patients make informed decisions in several ways. They can help the patient weigh the risks and benefits of participating (or continuing) in a study. In Markingson’s case, an advocate could have considered his special circumstances—including the potential coerciveness of being under a stay of commitment—and discussed those issues with Markingson *before* he signed the consent form. There is no documentation that anyone discussed those issues with Markingson.

We asked Dr. Olson who Markingson’s advocate was and he told us that it was Dakota County social worker David Pettit. Markingson signed the informed consent on November 21, 2003, but Dakota County had not assigned Pettit to Markingson’s case until *three days later* (November 24, 2003). Pettit did not meet Markingson in person until November 26, 2003.⁵⁵ In addition, we learned during our review that at the time he was assigned to Dan Markingson, David Pettit’s state license as a social worker had expired.⁵⁶

When we submitted a draft of this report to Dr. Olson, he then said that there were two other social workers assigned to Markingson before signing the consent form. Nonetheless, there is no documentation that either of the two social workers was present when Markingson signed the informed consent.

Dr. Olson has told other reviewers that Markingson was still in a screening period until he began taking the study medication December 5, 2003. Pettit had been assigned as Markingson’s case manager by then, and Dr. Olson would have dropped Markingson from the study if Pettit objected. Pettit did not object. Pettit also said in a deposition that he never discussed with Dr. Olson whether Markingson was competent to consent to the CAFÉ study.

A neuropsychologist evaluated Markingson on November 18, 2003, and determined that Markingson’s “overall intellectual functioning was estimated to be in the superior range.” The same evaluator said Markingson seemed to understand instructions except “on a somewhat complex task when he repeatedly asked for instructions even after they had been given.” But the neuropsychologist evaluated Markingson for cognitive problems, not whether he understood the potential coercion of taking part in the study while under a stay of commitment.

⁵⁵ David Pettit Deposition, June 14, 2007, p. 37, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

⁵⁶ According to the Minnesota Board of Social Work, David Pettit was licensed in 1990 but his license expired in 2001. Minnesota law does not require county social workers to be licensed. *Minnesota Statutes* 2014, 148.065, subs. 4 and 4a. As a result, the Board of Social Work has no jurisdiction to investigate complaints regarding unlicensed social workers or discipline them. *Minnesota Statutes* 2014, 148E.185.

Dr. Olson noted that Markingson underwent another evaluation before he signed the consent document, an evaluation by CAFÉ study staff Jean Kenney and Elizabeth Lemke. Both had inherent conflicts of interest in evaluating Markingson’s ability to consent and later in obtaining his written consent.

One person who could have served as Markingson’s advocate was his mother, Mary Weiss. As Dr. Olson told the IRB in his application, an advocate could be a family member. Moreover, a University of Minnesota CAFÉ study recruiting document said: “Everyone in the study will be offered an educational program about psychotic disorders and family members will be encouraged to participate.”

Because there was no one independent of the CAFÉ study present when Dan Markingson signed the consent form, it is impossible to be certain that he comprehended the study’s ten-page informed consent form. It is also impossible to know—again from an independent source—what impact being locked up under a stay of commitment had on his ability to freely consent to participate in the CAFÉ study.

Finding 5. The University of Minnesota’s Institutional Review Board (IRB) conducted a superficial review of Dan Markingson’s suicide. The IRB did not review medical records, did not seek information from anyone other than Dr. Olson, and did not review information about Markingson’s suicide.

In a May 16, 2014, statement, the University’s Academic Health Center said the IRB performed a “full-board review” of Dan Markingson’s suicide. It also asserted that “our IRB fulfills its obligation to rigorously evaluate serious adverse events.”⁵⁷

Dan Markingson’s suicide was clearly one of the most serious “adverse events” the University of Minnesota has experienced in a clinical drug study. Based on our review of University documents, we found that the IRB review of Dan Markingson’s suicide was far from a “rigorous evaluation.” Here is what actually occurred:

- May 12, 2004: Dr. Olson notifies the IRB of Markingson’s death.
- May 13, 2004: The IRB sends Dr. Olson a letter requesting more information about the process Dr. Olson used to obtain Markingson’s consent to participate in the CAFÉ study and Markingson’s participation in the follow-up study visits.
- May 13, 2004: The IRB notifies the Food and Drug Administration’s Minneapolis office of Markingson’s suicide.

⁵⁷ Academic Health Center Communications, University of Minnesota, *Statement in response to calls for further inquiry into the Dan Markingson case*, May 16, 2014.

- May 17, 2004: Dr. Olson responds with a one-and-a-half page letter to the IRB's May 13, 2004, request for more information about Markingson's consent to participate in the CAFÉ study and his participation in the follow-up study visits.
- May 26, 2004: The IRB reviews Dr. Olson's May 12 notification of Markingson's death.
- June 23, 2004: The IRB reviews Dr. Olson's May 17 letter.
- June 25, 2004: The IRB notifies Dr. Olson its review was concluded. The letter notice said:

The IRB Human Subjects Committee received your response to its stipulations on May 13, 2004. Since this information satisfies the requirements set by the IRB, review of the recent unanticipated problem and serious adverse event report involving Subject 00100013 [Dan Markingson] is concluded. The committee reviewed and noted the additional information regarding the consent process and interim clinic visits for study Subject 00100013.

The IRB documents do not indicate how much time or substantive discussion was involved in the Board's review of Dr. Olson's submissions. According to Dr. Susan Berry, the current IRB Chair:

No interviews were requested or conducted by the IRB as part of its review of this event [Markingson's suicide]. It was not at that time and is not now the practice of the IRB to seek interviews unless an event or issue has been referred by the IRB for formal investigation by a three-person investigation panel of IRB members per our standing policies, then and now. The IRB did not at any point in its review of this event determine that this matter should be referred for a formal investigation.

The IRB chair at the time was designated to be the Board's "primary reviewer" of Dr. Olson's submissions about Markingson's death and participation in the CAFÉ drug study. We found this concerning because the IRB chair and Dr. Olson were colleagues in the Department of Psychiatry. This raised at least the perception of a conflict.

We asked Dr. Berry about a possible conflict, and she dismissed the concern. She said having colleagues in the same department review each other's work happens "all the time." She added:

So what I'd say is that, again, in some cases the very people who can give you the most useful and helpful answer may be a colleague. We don't regard being in the same department as a conflict of interest, and so we would not have thought [it was a conflict]...in this situation.

However, the IRB chair was not being asked to review a draft research paper or other academic work prepared by his colleague, Dr. Olson, but the suicide of a person in a drug study overseen by Dr. Olson. We think the IRB's decision was inappropriate.

After completing its review of Markingson's suicide, the IRB received a recommendation from the Minnesota Ombudsman for Mental Health and Mental Retardation based on the Ombudsman's review of Dan Markingson's suicide.⁵⁸ The recommendation said:

People under a stay of commitment for mental illness may require special protection to ensure that their voluntary informed consent is indeed voluntary and not intentionally or unintentionally coerced.

The recommendation was referred to the IRB's executive committee and the committee asked Dr. Olson for his opinion. According to Dr. Berry, at a September 12, 2005, meeting, Dr. Olson said "appropriate measures were taken to assure competency when consenting a mentally ill subject." The Ombudsman's office said it never heard back from the IRB about any action taken in response to its recommendation.

When asked what changes the IRB made in response to its review of Dan Markingson's suicide, Dr. Berry said:

There is no documentation clearly linking IRB changes to its review of Dan Markingson's suicide. It is thought, however, that this event may have led the IRB...[to ask] investigators...to provide justification of a plan to target or include mentally, emotionally or developmentally disabled persons. In addition, investigators were asked to explain how competency to provide consent would be determined and any plan for obtaining surrogate consent.⁵⁹

Dr. Berry told us that the IRB pays close attention to research policies, procedures, and guidance but cannot ensure that a researcher is following the strict letter of the law or ethical principles. According to the chair, the University's IRB trusts that its research investigators will follow the rules. The chair told us, "If you don't trust your investigators, then the whole system doesn't work." Asked whether the IRB ever applies the axiom "trust but verify," she said it would be applied infrequently because, again, "the general consensus is really trust your investigators."

This view of an IRB's responsibility is in sharp contrast to guidance from the U.S. Department of Health and Human Services. It says that IRBs are administrative bodies "established to protect the rights and welfare of human research subjects recruited to participate in research activities conducted under the auspices" of the affiliated institution.⁶⁰

Given this responsibility, we think Dan Markingson's suicide should have triggered a heightened response from the University's IRB. We are troubled by the IRB's limited response and by University officials' misleading statements about the IRB review of the Markingson case.

⁵⁸ The office is now called the Ombudsman for Mental Health and Developmental Disabilities.

⁵⁹ Susan A. Berry, M.D., Chair, Institutional Review Board Executive Committee, letter to James Nobles, Legislative Auditor, February 5, 2015.

⁶⁰ U.S. Department of Health and Human Services, Office for Human Research Protections, *Institutional Review Board Guidebook, Jurisdiction of the Institutional Review Board*, Chapter 1(A), 1993, http://www.hhs.gov/ohrp/archive/irb/irb_chapter1.htm.

Finding 6. The Minnesota Board of Social Work investigated CAFÉ study coordinator Jean Kenney, a licensed independent clinical social worker.⁶¹ The Board found that she performed tasks beyond her competency and made significant errors. As a result, the Board entered into an Agreement for Corrective Action with Kenney. Although the Board only had jurisdiction over Kenney, we believe its findings suggest that Dr. Olson inappropriately delegated tasks to Kenney and failed to provide her with adequate supervision.

The University's IRB guidance to researchers says principal investigators are ultimately responsible for the conduct of their research teams. According to the IRB, "Though research responsibility may be delegated to research staff, researchers must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility."⁶²

When asked in a sworn deposition in *Weiss v. Board of Regents et al.*,: "So Dr. Olson was the individual at the University of Minnesota who decided what tasks you were to perform [in the CAFÉ study]?" Jean Kenney said, "Yes."⁶³

The Board found that in her work on the CAFÉ study, Kenney performed medical tasks that she was not qualified to perform, and that her performance on those and other tasks was often substandard. The Board said:

- Kenney had no formal medical training but regularly performed tasks which were beyond her competence and scope of practice as a licensed independent clinical social worker. Those included dispensing prescription drugs without authorization and in violation of the University's policy.⁶⁴
- Kenney routinely initialed clinical documents with a physician's initials.
- Kenney failed to adequately address family concerns in a timely and effective manner, document critical information regarding interventions and plans, and maintain interagency communications.
- Kenney's documentation consistently fell below minimum standards of practice for a licensed independent clinical social worker.

⁶¹ Minnesota has four levels of social work licenses based on academic degree and experience: (1) Licensed Social Worker (LSW) – Bachelor's License; (2) Licensed Graduate Social Worker (LGSW) – Graduate License; (3) Licensed Independent Social Worker (LISW) – Graduate license requiring 4,000 hours of non-clinical supervised practice; and (4) Licensed Independent Clinical Social Worker (LICSW) – Graduate license requiring 4,000 hours of clinical supervised practice. See <http://mn.gov/health-licensing-boards/social-work/applicant/>.

⁶² University of Minnesota, Institutional Review Board, Guidance and FAQs, *What Every Researcher Needs to Know, Principal Investigator Responsibilities*, <http://www.research.umn.edu/irb/guidance/pir.html#VOe--hE5DIU>.

⁶³ Jean Kenney Deposition, May 8, 2007, p. 26, *Weiss v. Board of Regents et al.*, 27-CV-07-1679.

⁶⁴ The University contends that Kenney's role of handing out and counting pills did not constitute the dispensing of prescription drugs and was neither unauthorized nor in violation of University policy. It says that Dr. Olson was responsible for modifying the dose of any medications for study participants.

- Kenney failed to communicate a new medication risk to Markingson, and to modify and resubmit the informed consent form to the IRB.⁶⁵

The Board determined that Kenney violated the Minnesota Social Work Practices Act.⁶⁶ However, the Board did not discipline Kenney but entered into a public Agreement for Corrective Action.⁶⁷ The corrective action included that she: complete 18 hours of continuing education; hire a Board-approved licensed independent clinical social worker as a consultant who would report Kenney's progress to the Board and; prepare a report to the Board about what she learned from the continuing education.

As part of the settlement agreement, Kenney made no admissions and claimed that many of the allegations against her were inaccurate and did not fully describe her work as a study coordinator on the CAFÉ study. She also noted that the CAFÉ study was supervised by a national sponsor and approved by the University of Minnesota through its Institutional Review Board, and that she worked under that supervision and in accordance with approved protocols. In addition, the University disputes the Board's findings, suggesting to us that Kenney acted as a study coordinator on the CAFÉ study, not as a social worker.

The Board's findings are troubling because they show serious problems with Kenney's performance and in the way Dr. Olson and others at the University administered the CAFÉ study. They are also troubling because they show yet again that University officials have made misleading and even inaccurate statements about past reviews of the Markingson case.

Finding 7. The Minnesota Board of Medical Practice's review of Dr. Stephen Olson was compromised because the expert consultant the Board hired to analyze the case had numerous conflicts of interests.⁶⁸

In October 2008, Mary Weiss filed a complaint with the Minnesota Board of Medical Practice against her son's treating physician, Dr. Stephen Olson. The Board regulates physicians and

⁶⁵ AstraZeneca had sent a warning to CAFÉ study sites about an increased risk of diabetes and hyperglycemia on March 15, 2004, arguably invalidating the consent form Dan Markingson signed on November 21, 2003. Dr. Olson notified the IRB of the updated version of the consent form in a letter to Patrice Webster, Assistant Director, IRB, on May 10, 2004. The letter contained a note that said "the revised consent form is to be used to re-consent enrolled subjects only...."

⁶⁶ *Minnesota Statutes* 2014, chapter 148E.

⁶⁷ https://www.hlb.state.mn.us/bosw/docs/SO-ACA/ACA_Kenney-13622-11082012.pdf.

⁶⁸ According to the Board's executive director, because the Board dismissed the allegations against Dr. Olson, the Board cannot make public any documents related to the case. In fact, she told us the Board cannot even confirm or deny there ever was a case. However, we concluded that it is lawful and even necessary for us to discuss the case in this report for two reasons. First, many documents related to the case have been made public by the principal parties in the case—Mary Weiss and Dr. Olson. Second, the University has repeatedly cited the Board of Medical Practice review when it has claimed that the Markingson case has been thoroughly reviewed by several government agencies and nothing inappropriate has ever been found. For these reasons, we discuss the Board's review, but we decided not to disclose the name of the consultant the Board hired. Some commentaries about the Markingson case have speculated who the consultant was, but, to our knowledge, documents from the case have not officially confirmed the consultant's name.

other medical professionals; its purpose is to protect the public.⁶⁹

Weiss contended that Dr. Olson violated Minnesota laws that regulate physician ethical conduct.⁷⁰

But the Board disagreed. In a letter to Mary Weiss, the Board announced it had dismissed her complaint after it had conducted a thorough investigation.⁷¹ It said an “independent expert consultant” had reviewed all the investigative data.⁷² However, we found that the consultant had numerous conflicts of interests, conflicts the consultant had alerted the Board to *before* it hired him to review the Markingson case. The consultant acknowledged being very familiar with Dr. Olson and the Markingson case.

- The consultant was a member of the University’s IRB when the IRB approved Dr. Olson’s CAFÉ study in which Markingson participated.
- The consultant chaired the IRB five-person Human Subjects Committee on May 26, 2004, when the committee reviewed Markingson’s death. Although the consultant served as one of the committee’s two “primary reviewers,” he told the Board that he was not involved in the decisions regarding the case because of IRB conflict of interest policies.
- Although not specifically involved in the CAFÉ study, as a faculty member at the Department of Psychiatry, the consultant conducted research on medications for people diagnosed with schizophrenia.
- The consultant was director of the Ambulatory Research Center where Dr. Olson’s drug trial took place.⁷³ In fact, the consultant had research space at the center and interacted with Dr. Olson’s research assistants.
- The consultant had extensive contacts with the pharmaceutical industry, including AstraZeneca, the sponsor of the CAFÉ trial. Minnesota Board of Pharmacy records indicate that the consultant received more than \$83,000 in payments from AstraZeneca in 2006 alone.

⁶⁹ According to *Minnesota Statutes* 2014, 147.001, subd. 2: “The primary responsibility and obligation of the Board of Medical Practice is to protect the public. In the interest of public health, safety, and welfare, and to protect the public from the unprofessional, improper, incompetent, and unlawful practice of medicine, it is necessary to provide laws and regulations to govern the granting and subsequent use of the license to practice medicine.”

⁷⁰ *Minnesota Statutes* 2014, 147.091, subd. 1(g), prohibits individuals licensed by the Board of Medical Practice from: “Engaging in any unethical conduct; conduct likely to deceive, defraud, or harm the public, or demonstrating a willful or careless disregard for the health, welfare or safety of a patient; or medical practice which is professionally incompetent, in that it may create unnecessary danger to any patient’s life, health, or safety, in any of which cases, proof of actual injury need not be established.”

⁷¹ Helen Patrikus, Medical Regulations Analyst, Minnesota Board of Medical Practice, letter to Mary Weiss, June 15, 2010.

⁷² *Ibid.*

⁷³ The Ambulatory Research Center is part of the Department of Psychiatry. Its website says its mission is to “increase our understanding and improve the treatment of mental disorders.” See <http://www.psychiatry.umn.edu/research/arc/home.html>.

- The expert's resume showed that he was holding positions at the University of Minnesota as vice-chair of the Department of Psychiatry Research Committee and a member of the Department of Psychiatry Research Council.

Rather than look for another consultant, a Board staff person sent the prospective consultant the following message:

I was able to discuss your possible conflict on the Dr. Olson case and the conclusion here is that as long as you feel you can review the materials objectively, then we are comfortable having you do the review.⁷⁴

Representatives of the Board told us that ideally they look for an expert consultant who has no conflicts of interest. But in specialties such as psychiatry, they said there is a small pool from which to choose. They also said, as a government agency, the Board can only hire consultants through the Request for Proposals process or posting requests on its website. In addition, they said that physicians generally are not interested in serving as consultants to the Board, and those that are willing often have time constraints or balk at the pay.⁷⁵ The Board's policy is to limit its expert consultants to physicians who are licensed by the Board. Only rarely does it go out of state for a consultant.

The Board representatives said they chose the consultant for the Olson case because he had written about ethics, had turned down previous cases when he thought he could not be impartial, and had experience with academic drug studies.

Nonetheless, we believe the Board erred in its choice of an expert consultant to review Dr. Olson's conduct. Even one of the conflicts we identified above should have been enough for a disqualification, particularly in a case where a person died. The idea that there was a small pool of experts to choose from within the state should not have been a factor. The Board should have suspended its policy of relying on Minnesota physicians to review the case because that policy ultimately led to a compromised and suspect review. In a case this serious, the Board should have looked outside the state if necessary for a truly independent reviewer who possessed no conflicts in the case.

It is worth clarifying that the University of Minnesota did not play a role in the Board of Medical Practice's selection of a consultant in the Board's review of Dr. Olson. In fact, University officials told us they were not aware of who the Board of Medical Practice hired as a consultant until informed of this by our office.

⁷⁴ To avoid disclosing the name of the consultant the Board hired, we do not cite the source of this message.

⁷⁵ The Board representatives told us the average payment is about \$250 per hour.

Finding 8. University leaders—both administrators and regents—have responded to the Markingson case by dismissing the need for further review and ignoring serious ethical issues.

At the beginning of this report, we quoted a 2011 letter from the then chair of the University Board of Regents and a 2013 letter from University President Kaler saying that further review of the Markingson case was not needed.

More recently, in a statement issued on May 16, 2014, the University’s Academic Health Center again rejected the need for “further inquiry into the Markingson case.” According to the statement:

The facts clearly demonstrate that this matter has been thoroughly reviewed by appropriate internal and external oversight authorities, and in all of those reviews there has never been any finding of research abuse or a causal connection between Mr. Markingson’s death and his participation in the study.⁷⁶

In addition, we recently asked the executive director of the Board of Regents a series of questions about how the Board has responded to the Markingson case. We asked, for example, whether the Board, or a committee or subcommittee of the Board, had ever held a public meeting to discuss the Markingson case, and received the following answer:

No, the Board of Regents has not publicly discussed the Markingson matter. It is not the role or custom of the Board to publicly debate or otherwise publicly air individual disputes. In a \$3.5 billion organization with more than 23,000 faculty and staff, such a practice would quickly make Board meetings impractical and unwieldy.⁷⁷

In a letter to former Governor Carlson dated May 9, 2014, the current Board chair said the following:

...this matter has been extensively reviewed by independent governmental agencies and courts, as well as by the University, and all reviews result in the same conclusion: there was no improper care provided to Mr. Markingson, nor was there research misconduct or violation of any applicable laws or regulations, nor was there any causal connection between Mr. Markingson’s death and his participation in the research study.⁷⁸

The University has disregarded some past reviews of the Markingson case that had negative findings, such as the Board of Social Work and Ombudsman for Mental Health and Mental Retardation reviews we discussed earlier. In addition, we disagree with the University’s

⁷⁶ University of Minnesota, Academic Health Center Communications, *Statement in response to calls for further inquiry into the Dan Markingson case*, May 16, 2014.

⁷⁷ Brian Steeves, Executive Director and Corporate Secretary, University of Minnesota Board of Regents, letter to James Nobles, Legislative Auditor, March 5, 2015.

⁷⁸ Richard Beeson, Chair, University of Minnesota Board of Regents, letter to The Honorable Arne H. Carlson, May 9, 2014.

conclusion that the Markingson matter has been fully reviewed by independent governmental agencies and courts. We have expressed concerns about the adequacy of some reviews, such as the IRB and Board of Medical Practice reviews. We would like to briefly discuss two other reviews: the civil lawsuit against the University and the FDA review.

In Mary Weiss' civil lawsuit, *Weiss v. University of Minnesota et al.*, the court dismissed Weiss' claims against the University based on "discretionary immunity."⁷⁹ The judge also dismissed one claim filed against both Dr. Olson and Dr. Schulz on the issue of Markingson's informed consent. The court, however, allowed to go forward Mary Weiss' medical malpractice claim for failing to provide Markingson "proper care and treatment" against Dr. Olson. The issue never went to trial. Dr. Olson settled out of court.

The FDA report found no evidence of misconduct or significant violation of the research protocol or regulations.⁸⁰ But the review never discussed the potential coerciveness of obtaining consent from an individual under a stay of commitment. The FDA said: "There was nothing different about this subject [Markingson] than others enrolled to indicate he couldn't provide voluntary, informed consent per review of his medical records or the approved study protocol." But there was something different—Markingson, unlike others, was under a stay of commitment. That order required him to "cooperate with the treatment plan at [FUMC] until medically discharged and follow all the aftercare recommendations of the treatment team." The FDA did not explicitly discuss how the stay of commitment might have influenced Markingson's ability to freely consent. Markingson consented, but the FDA report did not provide convincing evidence that he was given sufficient information about his options.

In addition, statements from University officials, like the recent statement from the Academic Health Center, often narrowly frame concerns about the Markingson case as "research abuse" and "a causal connection between Mr. Markingson's death and his participation in the study." While those are certainly important issues, there are others:

- The potentially coercive circumstances under which Dan Markingson was recruited into the CAFÉ study.
- Dr. Olson's inappropriate delegation of medical tasks to a person unqualified to perform them.
- The IRB's superficial review of Dan Markingson's suicide.

⁷⁹ *Minnesota Statutes* 2014, 3.736, subd. 3(b). The State of Minnesota, which includes the University of Minnesota, has generally been subject to tort liability since 1976 when the Legislature abolished the state's immunity through the Tort Claims Act. Before that, the state had to consent to be sued. But the Legislature also carved out numerous exceptions to that act. One is known as the discretionary function exception, which provides immunity to the state and its employees when performing or failing to perform a discretionary duty. *Dunnell Minnesota Digest*, vol. 43, sec. 1.07(b).

⁸⁰ U.S. Department of Health and Human Services, Food and Drug Administration, *Establishment Inspection Report* (Minneapolis, 2005), 1. It is worth noting some general issues with the scope of the FDA review. The FDA reviewer never asked to talk with Mary Weiss. Also, the reviewer did not talk to social worker David Pettit, group home staff, or FUMC's day treatment psychotherapist because she was told they could not speak to her without a signed consent by a Markingson relative; the FDA did not pursue obtaining the consent.

We raised these concerns based on our independent review. But medical and bioethics professionals both inside the University of Minnesota and in other academic institutions have voiced similar concerns. University officials' unwillingness to acknowledge and address this wider range of ethical problems is troubling. Rather than acknowledge the concerns, University officials have dismissed them and essentially said there is nothing to talk about.

This kind of insularity is particularly troubling because it comes from University officials with an obligation to foster open discussion and debate about complex issues and societal concerns. It leaves us wondering why the University of Minnesota has a Center for Bioethics when University officials will not meet with the center's faculty to discuss the very real and important bioethical questions the Markingson case raised.

We understand that the University of Minnesota has been and should continue to be an institution that delivers not only high quality medical care but also engages in cutting edge medical research—research that does pose risks to human subjects. In addition, we do not question the appropriateness of the University obtaining money from pharmaceutical and other medical companies to support that research. However, in every medical research study—whether supported with public or private money—the University must always make the protection of human subjects its paramount responsibility.

University officials have often said that protecting human subjects and conducting ethical clinical research is of primary importance. As one former University President said: “It is the commitment of this institution and of the governance overseeing this institution that all research will be conducted following strict ethical standards, as well as within all federal, state, and local regulations and procedures.”⁸¹

We do not think the University fulfilled that promise in the way it treated Dan Markingson and his family. As one of the external panel reviewers, Dr. David Strauss, said at a meeting of the University's Faculty Senate: “The regulations are only the floor. Any institution that aims that low is likely not going to be doing a terribly good job.”⁸²

Finding 9. An external panel of experts that recently reviewed the University's current human subjects protection program found significant and troubling problems.

We received a copy of the external panel's report on February 27, 2015, and were impressed with its thoroughness and frankness, and disturbed by its findings. In our view, it is a damning report. For example, the report states the following:

⁸¹ Robert H. Bruininks, *A letter from University President Robert H. Bruininks on the importance of subject protection in research*, appeared on the University of Minnesota's website at <https://web.archive.org/web/20100609215633/http://cflgacy.research.umn.edu/subjects/presletter.cfm>.

⁸² Dr. David Strauss, Presentation of Association for the Accreditation of Human Research Protection Programs report to the University of Minnesota Faculty Senate Hearing, March 6, 2015. Dr. Strauss is Associate Professor of Psychiatry and Vice Chair for Research Administration, Ethics, and Policy at the Columbia University Department of Psychiatry. He is also Director of Psychiatric Research at the New York State Psychiatric Institute and oversees its 23 research divisions and 10 research centers, core research programs, and research compliance functions, including IRB, Institutional Animal Care and Use Committee, conflict of interest, and research integrity.

In the context of nearly continuous negative attention, the University has not persuaded its critics (from within and outside the University) that it is interested in more than protecting its reputation and that it is instead open to feedback, able to acknowledge its errors, and will take responsibility for deficiencies and their consequences.⁸³

On the day the Association for the Accreditation of Human Research Protection Programs (AAHRPP) released its report, President Kaler issued a statement in response that was disappointing because it again tried to diminish the importance of the problem. While President Kaler said he would ask the Vice President for Research and Dean of the Medical School to “lead implementation of the recommendations,” his statement also included this:

While their [AAHRPP] recommendations are sound, it is important to put the review team’s work in context. They looked at a narrow slice of our research enterprise: human subjects research related to people with diminished decision making capacity. This represents a small fraction of our clinical research enterprise. Clearly, and consistent with our charge to them, the panel’s view and subsequent analysis was limited.⁸⁴

Even if people with diminished decision-making capacity are a “small fraction” of the University’s “clinical research enterprise,” the external panel’s findings were far-reaching and substantive. Furthermore, the Markingson case shows that one death can create not only a personal and family tragedy but also a public controversy that can seriously damage the University’s reputation.

In fact, University officials, both the administration and the Board of Regents, continue to be sharply criticized for their repeated efforts to dismiss and diminish concerns about clinical drug studies at the University. We heard that criticism as recently as March 6, 2015, when members of the University Faculty Senate discussed the external panel’s report.⁸⁵ Several members noted that the administration brought in the external panel not at its initiative but in response to a Faculty Senate resolution. Members also noted the contradiction between the expert panel’s findings and repeated assurances by University officials that research at the University involving human subjects was conducted consistent with the highest ethical standards.

The external panel’s report was a clear contradiction to repeated statements by University officials that its human subject research meets the highest ethical standards. Both this report and the external panel’s report found that those statements are not credible.

⁸³ Association for the Accreditation of Human Research Protection Programs, *An External Review of the Protection of Human Research Participants at the University of Minnesota with Special Attention to Research with Adults Who May Lack Decision-Making Capacity*, February 23, 2015, p.87.

⁸⁴ Statement from President Kaler regarding the independent review of human subject research, February 27, 2015, <http://discover.umn.edu/news/vision-leadership/statement-president-kaler-regarding-independent-review-human-subject-research>.

⁸⁵ A video recording of the Senate Faculty meeting can be accessed at <http://www1.umn.edu/usenate>.

We are encouraged that President Kaler, in his statement on the external review, said: “It is my expectation and intent to review each [recommendation] carefully and take the steps necessary to become exceptional.” The external review has provided an important blueprint for the University to follow.

RECOMMENDATIONS

A primary problem uncovered by our review is past and current University leadership that is defensive, insular, and unwilling to accept criticism about the Markingson case either from within or outside the University. However, we do not have a recommendation that would change attitudes at the University about openness, accountability, and transparency. We can only suggest that the Legislature make the issue—and need for change—a more important consideration in selecting people to serve on the University Board of Regents.

To strengthen the protection of human subjects in University research, we make the following recommendations:

1. The Legislature should enact legislation that requires the University of Minnesota to fully implement the external review panel’s recommendations before the University’s Institutional Review Board approves additional Department of Psychiatry drug studies.⁸⁶
2. The Legislature should enact legislation that authorizes the state’s Office of the Ombudsman for Mental Health and Developmental Disabilities to monitor the participation of people in the University’s Department of Psychiatry drug studies. The Legislature should provide the office with adequate resources to effectively monitor psychiatric drug studies at the University.

⁸⁶ To ensure compliance, the Office of the Legislature Auditor will conduct a follow-up review in the fall of 2015.

March 18, 2015

James Nobles
Legislative Auditor
Room 140 Centennial Building
658 Cedar Street
Saint Paul MN 55155-1603

Dear Mr. Nobles:

The University of Minnesota is now and always has been committed to meeting, upholding and exceeding the highest ethical standards in research practices involving human subjects. While we believed that our current research program reflected this commitment, recent findings from a review by an external independent panel and an Office of the Legislative Auditor (OLA) report demonstrate that we can and must do better.

The loss of Dan Markingson's life is a tragedy. His care team was profoundly saddened by his death, and the University has great sympathy for those closest to him, especially his mother, who lost her son. We at the University have always been dedicated to finding cures and treatments for the most vexing diseases that plague our community, including mental illness. Our goal is to apply the highest standards of ethics and humanity to guide our every interaction with those who entrust themselves to our care.

The Board of Regents has closely followed the work of the external review panel and is aware of OLA's findings. Chair Beeson and Regent Simmons have already created a plan for the Board to take an active role in shaping the University's action plan. The Board will provide ongoing implementation oversight through its Audit Committee to ensure transparency and accountability. I look forward to demonstrating to the Regents our commitment to improve.

To that end we are taking immediate actions:

- Suspending enrollment in all Department of Psychiatry interventional drug studies currently active or awaiting approval, until they have been reviewed by an independent institutional review board (IRB), which will recommend to the University Institutional Official (Dr. Brian Herman) whether or not the suspension should be lifted.
- Creating an Implementation Team to review and prioritize the external panel's recommendations, develop a plan to implement them, and oversee the implementation. They will report action items and the implementation plan to President Kaler within 60 days (May 15, 2015).

- Using an independent IRB and the University's post approval monitoring process, we will sample additional interventional clinical studies targeting vulnerable populations to guarantee that ongoing activities are appropriate and consistent with approved protocols, and that interactions with human subjects are consistent with the recommendations of the external review panel.
- Appointing a Community Oversight Board, comprised of external experts in human subjects research and research ethics with special emphasis in the area of working with individuals with diminished mental capacity, to make sure that the University's approaches to human subject research are leading practice.
- Visiting leading institutions to learn the best practices followed by their IRBs.
- Implementing new IRB software to enhance the efficiency of the IRB review processes and oversight.

This work has already begun. Before we received the Legislative Auditor and external panel reports, the University committed significant new resources to its Human Research Protection Program (HRPP) and to hire more training and post-approval monitoring staff. We are actively adding more members with relevant expertise to the Institutional Review Board (IRB). We have also established a Research Compliance Advisory Committee that includes nationally recognized experts to consult on strategic risk management in research, including the conduct of human subjects research in individuals with diminished mental capacity.

The University has attempted to address numerous questions about how individuals with diminished mental capacity are engaged in human subjects research. We are sorry that, in particular related to the case of Mr. Markingson, our response has come across as defensive. We want to assure you that our only intent has been to be factual in our responses. The University has relied on the external agencies charged with investigating such matters (the FDA, the Minnesota Board of Medical Practice, and the Hennepin County District Court), to inform us of any deficiencies in our processes and practices and affirm our compliance with laws and regulations.

The University did not influence any of the external reviews and none of those previous reviews reported regulatory violations or alerted us to ethical breaches. If these external reviews were flawed, we were not aware of those shortcomings. We believe that the University's statements were not misleading, but in retrospect, with the recent broader review performed by the external panel and the Legislative Auditor's report, we are now aware that some of our practices have not been above reproach. We regret not identifying our own shortcomings ourselves, and are committed to being transparent and responsive as we move forward.

The independent panel review importantly notes that "the federal human subjects regulations that lie behind and most often animate institutional policy and procedure are all but silent with regard to the protection of individuals with impaired decision making and individuals from populations in which such impairment is lacking." This area of human subject research is continually evolving and the University is committed to improving our practices and serving as a national model of excellence.

continually evolving and the University is committed to improving our practices and serving as a national model of excellence.

As we move forward, we will use the independent panel's and Legislative Auditor's reports to improve. And we will take an introspective look at ourselves to improve our culture, enhance our policies and practices, make new investments, and reinvigorate our commitment to training, oversight and accountability.

As the independent panel report states there is "much strength in the University's human subjects program and the value of the newly implemented enhancements in policy and practice. The vast majority of faculty and staff demonstrated pride in their work, obvious dedication to the ethical conduct of research, and a desire to improve performance." We have an excellent foundation on which to build.

We appreciate the opportunity to discuss the Legislative Auditor's report with the Senate Higher Education and Workforce Development Committee. We look forward to using this report to improve our human subjects research program and ensure we are beyond reproach.

Sincerely



Eric W. Kaler
President

cc: Regent Richard Beeson, chair
Regent Dean Johnson, vice chair
Regent Thomas Anderson
Regent Laura Brod
Regent Linda Cohen
Regent Thomas Devine
Regent Michael Hsu
Regent Peggy Lucas
Regent David McMillan
Regent Abdul Omari
Regent Darrin Rosha
Regent Patricia Simmons
Brooks Jackson, dean of the Medical School & Vice President, Academic Health Sciences
Brian Herman, vice president, Research
William Donohue, general counsel
Gail Klatt, associate vice president, Internal Audits

March 18, 2015

OLA
OFFICE OF THE LEGISLATIVE AUDITOR
STATE OF MINNESOTA, JAMES NOBLES, LEGISLATIVE AUDITOR

On behalf of Mary Weiss and the rest of Dan's family, I would like to express our profound gratitude to the Office of the Legislative Auditor for this report. Not only do these findings confirm the research abuses that led to Dan's death, but they also bring to light the failures of transparency and honesty by university officials that prevented a genuine investigation for so long. Over the past eleven years the University of Minnesota has made us feel as if we have no voice, no rights, and absolutely nothing remotely called justice. This report is the first step towards accountability.

When Dan died in 2004, Mary and I began to look for answers. We naively thought that with all of the state and federal agencies supposedly charged with protecting vulnerable patients, not to mention all of the offices at the University of Minnesota itself, there had to be someone in authority who would see the wrong that had been done and would do something to help us. We were mistaken. Instead, we ran up against a monumental government bureaucracy indifferent to our situation, backed by an army of university attorneys and hospital risk managers who denied wrongdoing and had unlimited university funds available to help them avoid responsibility for their actions.

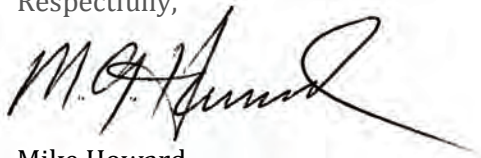
It was not until Carl Elliott and then Leigh Turner of the University's Center for Bioethics became involved in Dan's case that things began to change. Those two made it a personal mission to expose the wrongdoing at their own university, from the unethical actions of the clinical investigators in the Department of Psychiatry to the failings of the University's Institutional Review Board to the deceit of the Office of the General Counsel. This report corroborates everything they have been saying and writing for years, only to be ignored or even punished for saying it. Later, they were joined by Niki Gjere, a psychiatric nurse who risked her job by giving first-hand public testimony about the disgraceful way that Dan was treated by psychiatrists at University of Minnesota Medical Center – Fairview, and by former Governor Arne Carlson, whose conscience and determination led to the involvement of the legislature.

What this report does not mention is the physical toll that this ordeal has taken on Mary. For eleven years her efforts to get some measure of justice on behalf of her son have been met with nothing but false promises by government officials, and lies, bullying, and threats by University of Minnesota attorneys and administrators. I am convinced that the stress and anxiety of these constant, seemingly futile battles contributed to her current health problems, especially the strokes that have left her seriously disabled.

Mary is not alone in her struggle. There are many other victims of research abuse at the hands of psychiatrists at the University of Minnesota. Like us, the families of these victims have been bullied and harassed by university officials. As a result, they have been made to face their grief, anger and pain for the balance of their lives without any chance at closure.

We were always led to believe that physicians should observe the core values of their profession, which are centered in the duty to help the sick and infirm and to do no harm. Instead, at the University of Minnesota we found physicians who were neglectful, dishonest, and above all, arrogant. We also found university attorneys, public relations officers and administrators who would stop at nothing to insure these physicians were never punished for their actions. Until all of these people are held accountable, nothing at the University of Minnesota will change.

Respectfully,

A handwritten signature in black ink, appearing to read "M. Howard", with a long, sweeping underline that extends to the right.

Mike Howard