Comparative Table: Overview of 'reviews' of the Markingson Case

Date: November 14, 2013

The University of Minnesota has taken the position that the suicide of Dan Markingson has been sufficiently reviewed by the University itself and various other agencies and units independent from the University, and that none of them found any problem with the University's role. More specifically, it has repeatedly claimed, most recently in its response letter to Trudo Lemmens dated 12 November 2013, that the Markingson case has been thoroughly "reviewed" by the FDA, the Hennepin County District Court, the Minnesota Board of Medical Practice, and the University itself. It has also claimed earlier that the University of Minnesota Institutional Review Board and the Minnesota Attorney General's Office reviewed the case and concluded that there was no problem. The University fails to mention in its correspondence the 2012 investigation by the Minnesota Board of Social Work, which found that the study coordinator for the CAFÉ study and the one responsible for overseeing Markingson's care, had committed numerous professional violations in the context of the clinical trial. This social worker worked under the supervision of senior faculty members of the University of Minnesota. The University also fails to mention the initiative by the Minnesota Legislature, which reacted by enacting a statute prohibiting the clinical trial recruitment of people under a stay of commitment.

Below is a table indicating the various alleged reviews, what they found, and why the authors and signatories of the October 21, 2013 letter call for an independent inquiry. We identify also two initiatives that we characterize as recognizing serious problems.

(Compiled by Trudo Lemmens & Shannnon Gibson in the context of the request for an Independent Inquiry, formulated in the October 21, 2013 letter Lemmens-De Vries-Dreger-Shepherd-Reverby-Kassirer *et al*)

DATE AND TYPE OF INQUIRY	FINDINGS/CONCLUSION	REASONS FOR INSUFFICIENCY
July 22, 2005: Issuance of Establishment Inspection Report from inspection conducted by Food and Drug Administration Investigator Sharon L. Matson. Actual inspection conducted on January 2-6, 11, 19, 21 and 26, 2005.	The FDA investigator concluded that there was "no evidence of misconduct or significant violation of the protocol or regulations." Report also noted that "[q]uestions regarding psychiatric diagnosis would have to be addressed through medical review at CDER."	The FDA investigation focused on compliance with regulations and with the protocol. It was arguably conducted superficially. It failed to interview Mary Weiss, Dan Markingson's mother, a key witness who had been calling the research team to withdraw Dan from the study for many months. An attempt was made to interview Markingson's case worker (David Pettit), was contacted, but no interview was conducted (FDA investigator was told that informed consent from living relative was required for such interview, but this was not pursued). The FDA investigation did not identify as a key problem the use of civil commitment orders to induce someone to participate in a clinical trial, a practice the Minnesota

	Full report available at: http://www.scribd.com/doc/49641428/fda-inspection-markingson-suicide	legislature has since prohibited by statute. The report simply accepts the claim by the research coordinator and researchers that standard treatment was provided. The FDA report does not identify or discuss potential COIs of investigators or of the IRB (see further). Concerns have been raised about the COI of investigators and the pressure on the research unit to recruit a sufficient number of patients, yet the FDA investigator did not look into this. It also appears to have missed some alleged serious problems with consent-related documents that were revealed subsequent to its investigation (and noted by the Minnesota Board of Social Work). We looked at the available evidence, which in our view raises serious questions. *Carl Elliott wrote a detailed critical analysis of the FDA report, which we have also reviewed. He noted the following additional issues: "The FDA inspector failed to note that during the period leading up to his enrollment, Markingson had been repeatedly judged incapable of consenting to neuroleptic drugs. On November 14, 2003 Dr. Olson signed a commitment document stating that Markingson 'lacks the ability to make decisions regarding such treatment.' On November 17, a pre-petition screening team recommended commitment, noting Markingson's bizarre beliefs and his refusal to acknowledge his mental illness. On November 19, a court-appointed clinical psychologist confirmed those assessments, writing that Markingson 'is believed not to have the capacity to make decisions regarding neuroleptic medication.' Yet on November 21, when Markingson was asked to consent to the CAFÉ study, this assessment of his mental state was reversed and he was judged competent.* In summary, the FDA investigation failed to address key questions about whether Markingson provided meaningful consent or even had the ability to consent (or refuse to consent) to enter into the CAFÉ study. **In addition to considering these questions, a further investigation could also help identify why so many important problems were not identified by a key regulatory body.**

February 11, 2008: Summary judgment issued in lawsuit commenced by Mary Weiss, the mother of Dan Markingson, against the University of Minnesota and Dr. Charles Schulz.	The court order (Court File No. 27-CV-07-1679) states: 3. "The motion for summary judgment by the Board of Regents for the University of Minnesota and the Institutional Review Board for the University of Minnesota is granted on the basis that they are statutorily immune from liability. All claims against both parties are dismissed with prejudice." 4. "The motion to dismiss and for summary judgment by Dr. Stephen Olson is granted with respect to Count 2." 5. "The motion to dismiss and for summary judgment by Dr. Charles Schulz is granted. All claims against Dr. Schulz are dismissed with prejudice."	An interim ruling of statutory immunity by a court is a decision strictly based on legal rules rather than any exculpatory findings of fact. The court simply ruled that the University was shielded from legal liability in this context, and it is absolutely not, as the University keeps suggesting, a finding by the court that the University did nothing wrong. Statutory immunity for 'discretionary decisions' in the context of research has been granted with reliance on the existence of a good university IRB and governance system, which allows for reliable and independent discretionary judgments, which is precisely at issue here. Note that the Court did allow the case to go forward against one of the doctors involved (thus acknowledging that there was *a prima facie* case to be made about the doctor's negligence), resulting in a subsequent settlement. This *interim* judgment was not appealed, one likely reason being that the University filed a 'assessment of cost' against Mary Weiss, which made it very clear that she could suffer serious financial hardship if she continued to pursue the court case against the university. This disturbing legal tactic of a public university against a mother who just lost her son in the context of University research is in and of itself worth questioning. [Since the court case, questions have also been asked about some of the documents produced in the court case, including 'evaluations to sign informed consent' forms and Dan Markingson's authorization to allow the hospital to share health information with researchers. While we think these concerns merit further investigation, we have not looked into these issues in any detail.]
Complaints filed by Ms. Weiss and her associates with the Minnesota Board of Medical Practice against Dr. Stephen Olson and Dr. Charles S. Schulz.	Complaints against both doctors were dismissed by the Board of Medical Practice because the "facts of the case did not provide a sufficient basis … to take disciplinary or corrective action" [letter 15	- The Board indeed decided that there was insufficient basis to pursue action against Drs. Olson and Schulz. No detailed reasons are given. This does not amount to an 'exoneration' of the doctors involved. The decision contrasts indirectly with the Minnesota Board of Social Work, which found and detailed very serious problems with the conduct of the research coordinator. It is reasonable to question: 1) why the Board of Medical Practice did not find that the problems

	July 2010 Helen Patrikus to Mary Weiss re Dr. Olson]; or "Based on our review, the Board is unable to take any action which would withstand the required tests" [letter 12 February 2009 Helen Patrikus to Mary Weiss re Dr. Schulz] The University has claimed that the Board of Medical Practice investigated the university and found that it "in no way contributed to the unfortunate death of Mr. Markingson."	identified by the Board of Social Work implicated those supervising the social worker, and 2) why it did not identify the problems which others believe merit further inquiry and/or action. - The Board's decision has no bearing on the responsibility of the University. For the limits of what these findings mean, see e-mail June 19, 2013,of Robert Leach, Executive Director, Minnesota Board of Medical Practice, to Mike Howard" *"The Board has no jurisdiction over any institution, clinic, facility, hospital, university or medical school. We do not look at anything other than the professional practice of the individual licensee. When the Board closes a case without action, it does not necessarily "exonerate" that individual practitioner and that is a term the Board would not use. When a case file is closed without action it may mean that the Board did not find a violation of the Medical Practice Act but it also may mean that the Board could not find sufficient evidence of a violation to proceed with disciplinary action."* [http://www.scribd.com/doc/148824761/Minnesota-Board-of-Medical-Practice-email-to-Mike-Howard-About-Scope-of-Board-Actions-June-19-2013] A decision not to pursue professional sanction does NOT mean there has been an investigation into systemic problems with the organization's clinical research and recruitment practices. Moreover, subsequent revelations about questionable consent files were likely not investigated by the Board of Medical Practice.
Date May 26, 2004: Alleged **'r**eview' by the University of Minnesota Institutional Review Board	The University claims that the Institutional Review Board reviewed the case and found no fault.	- See a deposition (sworn testimony) in the Hennepin Court of Richard Bianco, Institutional Official, responsible for overall conduct of human subject protection [http://www.scribd.com/doc/124516926/Bianco-Deposition-excerpts]: Question: "did anyone at the University of Minnesota, or

		anyone under your office investigate this case, actually look at the records…" Response Bianco: "Not to my knowledge" Question: "Nobody did that?" Response Bianco: "No" (p. 41) - Minutes of IRB meeting May 26, 2004: "the IRB reviewed and noted the unanticipated problem and adverse event reported for the referenced study received on May 12, 2004, involving subject 00100013". This cannot be seen as a substantial review of the case. It is merely an acknowledgment of reporting of an adverse event by the investigator. - It has also been revealed that the IRB chair (Dr. Adson) had conflicts of interests due to financial relations with the study sponsor and with other pharmaceutical sponsors, and close professional and reporting relations with one of the lead investigators, raising serious concerns about the independence of the IRB and the overall organization of IRB oversight at the University. [for the recent conflict of interest analysis of the IRB, we relied on the following report by Carl Elliott in the Hastings Center blog: http://www.thehastingscenter.org/Bioethicsforum/Post.aspx?id=6582&blogid=140#ixzz2kYfSpw5a]
Review by Minnesota Attorney General's Office	Office of the Attorney General of Minnesota allegedly investigated the death of Dan Markingson	The Office of the Attorney General may have provided investigative services to the Medical Board of Practice. It did not itself come to any determination and what it submitted to the Board is not publicly accessible. See letter June 11, 2013 by Karen Olsen, Deputy Attorney General, to Mary Weis and Mike Howard: "This Office has not made any independent investigation or determination regarding the care rendered to your son." [http://www.scribd.com/doc/147683397/Attorney-General-Office-Letter-Refuting-Claim-That-It-Investigated-Markingson-Death]

Review by Office of the General Counsel of the University (date unknown)	Office of the General Counsel of the University of Minnesota is said to have "reviewed the facts and circumstances surrounding the CAFÉ Research Study and the suicide of Don Markings"	We do not dispute that some review has taken place, but this does not qualify as an independent review. If no concerns were raised about COIs, about how Dan Markingson was recruited, about the governance of research ethics, and if the University would not have shielded itself behind statutory immunity and would have seriously assessed its ethical responsibility and provided reasoned arguments and evidence about how the concerns raised were addressed, this review could have had some credibility. The concerns have not been addressed and there has been no serious review of what went wrong and what the University has learned from it.

Other Initiatives that appear to confirm significant concerns

Minnesota Board of Social Work (26/10/2012)	Minnesota Board of Social Work alleges serious professional violations and concludes an agreement with Jean M. Kenney for corrective action. Issues identified include: performing tasks beyond her professional competence and scope of practice; initialing clinical documents for physicians; dispensing of prescription drugs; failing to address family concerns in a timely fashion; failing to document according to a minimum professional standards, including "critical omissions in the documentation that were relevant to suicide prevention";	The Board clearly identified serious problems in the context of the clinical trial in which Markingson committed suicide. Yet, it focuses only on the responsibility of the research coordinator, who was supervised by senior psychiatrists. The remedial action included some continuing education. The Board's agreement for corrective action does not deal with the accountability of the institution and the supervisors. The problems identified by the Board of Social Work raise further questions about the appropriateness of Markingson's inclusion in the clinical trial and his treatment.

	[http://www.socialwork.state.mn.us/Portals/0/SO-ACA/ACA_Kenney-13622-11082012.pdf] Kenney completed corrective actions, including continuing education and writing of a report.	
Minnesota Legislature 2009: New Legislation on civil commitment "Dan's Law" New rules related to "Release Before Commitment"	New legislation that was adopted in direct response to Dan Markingson's suicide and that severely limits the possibility to include a patient who has a stay of a civil commitment order as research subject in a clinical trial. The general rule is that "the patient is prohibited from giving consent to participate in a clinical drug trial." (253B.095 Subdivision 1(d)(4)) while under a civil commitment order. An exception is provided under strict conditions and court review. If all other treatment options have failed, a treating physician can submit an affidavit indicating that the patient may benefit from participating in the trial. This cannot be the physician running the clinical trial. The court has to be informed and ensure there is no coercion [https://www.revisor.mn.gov/statutes/?id=253B.095]	An initiative that acknowledges indirectly the problematic way in which Dan Markingson was included in a clinical trial. It should help protect psychiatric patients in the future, but it is not an inquiry, of course, and does not explain why and how Dan was included and whether there are other problematic aspects to the clinical trial he was enrolled in and to the way the University and others acted. The provisions in new statute clearly target some of the practices that seem to have been particularly problematic in the recruitment of Dan Markingson: Exceptional inclusion in a trial: only "if the treating psychiatrist testifies or submits an affidavit that the patient may benefit from participating in the trial", **only "after providing other treatment options for a reasonable period of time**", only **after "those options have been ineffective**." "The **treating psychiatrist must not be the psychiatrist conducting the psychiatric clinical drug trial."** The **court must determine** that, "**under the circumstances of the case, the patient is competent to choose to participate in the trial**, that the patient is freely choosing to participate in the trial, that the **compulsion of the stayed commitment is not being used to coerce the person to participate** in the clinical trial,…"