

Researchers chafe at halt of psychiatric trials

After external reports blast ethics practices, University of Minnesota stops drug-study enrolment.

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30 March 2015 | Updated: 30 March 2015



Michael Dwyer/NYT/Redux/eyevine

A trial that uses a nasal spray version of oxytocin to treat autism is one of 17 that are on hold at the University of Minnesota pending an ethics review.

University of Minnesota psychiatrist Kathryn Cullen had just started recruiting volunteers for the first clinical trial of the anaesthetic ketamine against treatment-resistant depression in adolescents when the university's administration stopped the study in its tracks. On 18 March she received a surprising letter from the university president announcing that he was "suspending enrollment in all Department of Psychiatry interventional drug studies currently active or awaiting approval."

"I was shocked," Cullen says. Hers was one of 17 ongoing or pending studies in the university's psychiatry department in Minneapolis affected by the order. The suspension comes in the wake of a March report from Minnesota's state Office of the Legislative Auditor, which faulted the university for not doing enough to protect human participants. In response, administrators have suspended enrolment in psychiatric clinical trials until they have been reviewed by an external board and the university has revamped its ethical review process. The university presented the state auditor's report on 27 March to its Board of Regents, which approved the administration's plan and appointed William Tremaine, head of the Office of Human Research Protection at the Mayo Foundation in Rochester, Minnesota, to direct its implementation.

Cause for concern

The suspension is part of the fallout from a 2004 incident in which a 27-year-old man named Dan Markingson killed himself while enrolled in a University of Minnesota trial of the antipsychotic drug Seroquel (quetiapine). Critics charged that Markingson was unable to give consent to participate in the trial in his mentally impaired state, and alleged a number of other ethical violations by the researchers that included financial conflicts of interest. Although reviews at the time cleared the university of fault, suspicions lingered about whether its officials had been honest with the investigators.

In 2014, the state auditor took up the matter. Last week's report determined that while it was impossible to link Markingson's death to the study, the case involved "serious ethical issues and numerous conflicts of interest," and that university officials had misled and stonewalled investigators.

It is the second ethical strike against the university this year, following a scathing February report by an external board of experts appointed by the Association for the Accreditation of Human Research Protection Programs. The association's review was sparked by University of Minnesota bioethicists Carl Elliott and Leigh Turner, who rallied more than 170 experts to call for an investigation into whether the university had improved its practices over the past decade.

Brian Herman, vice-president for research at the university, says that the university needed to act after the two reports in order to ensure that its ethics practices were "beyond reproach". In addition to the enrolment suspension, he says the university is taking measures such as adding more people to the review boards that evaluate new research programmes and retaining external oversight groups. He says that he has charged a committee with developing an implementation plan by May 15, although there is no set date for lifting the enrolment moratorium.

Herman says that the university understands that the move is disruptive, but feels the measure is necessary to protect research participants. "At the end of the day, the patient and volunteer comes first," he says.

In limbo

This unpredictability leaves researchers in limbo; they fear that some research could be ruined if the suspension is not lifted soon. Four of the halted studies are led by psychiatrist Suma Jacob, a researcher into autism who joined the university in 2012. One of those studies, a trial of an intranasal spray containing the hormone oxytocin, has enrolled far too few participants to draw meaningful conclusions. If the moratorium stretches into the summer, Jacob says, her supply of the expensive drug will expire — and eventually, so will her funding. "We'll have to just let it go," she says. That will be disappointing to a number of families who were hoping to enrol their autistic children in the study, she says. Both she and Cullen say that they were aware of the controversy surrounding the Markingson case, but had never expected it to affect their own work.

Psychiatrist Stephen Olson, who ran the 2004 Seroquel study, says that he disagrees with the auditors' conclusions about his studies, but understands why the university needed to act. "I think it's probably a necessary thing given the atmosphere that's been stirred up by these recent outside reviews," he says. But he doubts that it is necessary to suspend trials performed by researchers who were not involved in the controversial studies.

Others feel that the moratorium does not go far enough. "I think it's a face-saving measure because they had to do something," says Elliott. "The university is not serious at all about instituting any real reform." He thinks the administration should have the auditor look into ethical review practices and patient consent methods across the university, and determine how many deaths and injuries might have occurred in trials over the past decades. He and Turner want the university to examine several other cases, such as allegations last year by a schizophrenic man that he was forced to join a University of Minnesota study of an antipsychotic drug, and an incident where an imprisoned sex offender participating in a study of Seroquel spiked the oatmeal of his fellow inmates with doses of the drug that he had stolen from the trial.

Several other investigations have yet to reveal their findings. Olson says that the US Food and Drug Administration is comparing his lab's current practices with those in 2004, when he had a different staff.

In the meantime, the psychiatrists are trying to find a bright side. "I believe that our department and psychiatry research has been under such scrutiny for so long," Cullen says. "If we could rebuild trust around our research community, then that would be invaluable."

Nature | doi:10.1038/nature.2015.17203

Updates

Updated: This article has been updated with the Board of Regents decision to adopt the administration's plan.