UNIVERSITY OF ILLINOIS
AT CHICAGO

Office for the Protection of Research Subjects (OPRS)
Office of the Vice Chancellor for Research (MC 672)
203 Administrative Office Building
1737 West Polk Street
Chicago, Illinois 60612-7227

January 25, 2013

Kristina C. Borror, PhD
Director, Division of Compliance Oversight
Office for Human Research Protections
Department of Health and Human Services
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

RE: Acknowledgement of an Unanticipated Problem (Local Serious Unanticipated Adverse Event)
Research Protocol # 2008-0624
"Affective Neuroscience of Pediatric Bipolar Disorder"
Sponsor: National Institutes of Health; Grant #5R01MH081019
Principal Investigator: Mani Pavuluri, MD

Dear Dr. Borror:

In fulfillment of the reporting requirements in accordance with 45 CFR 46.103(b)(5) and on behalf of the University of Illinois at Chicago (UIC) Institutional Review Board #1 (IRB00000115), I am writing to report an unanticipated problem (adverse event) involving risks to subjects or others that occurred in a research study for which Dr. Mani Pavuluri, Director of the Pediatric Mood Disorders Clinic at UIC, is the investigator.

Dr. Pavuluri submitted a report of the unanticipated problem to the IRB on January 18, 2013. The review and acknowledgement of the report by the IRB Chair occurred on January 22, 2013.

As stated in the report, the adverse event involved the following:

> The subject consented and completed an evaluation with the Principal Investigator (PI) on [redacted] During this appointment, the subject endorsed manic symptoms, including a history of irritable and aggressive behaviors. Subject indicated that current medications did not address symptoms. As a result, the PI provided a wash-out regimen and rescue medications to ease the transition before completing study procedures.
>
> On [redacted] the subject completed baseline procedures, including clinical assessments; neurocognitive and neuropsychological testing; fMRI testing; and blood draw for genetic testing. Following this appointment, the subject began medication treatment, in addition to rescue medications, on the morning of [redacted] A follow-up appointment was completed on

[redacted] During this visit, the subject endorsed heightened irritability due to conflicts in the home. There was no indication that the increase in irritability was atypical for this subject.

On [redacted] he subject was admitted to the h for a 10-day, inpatient treatment program due to increased irritability and aggression. The PI was notified on [redacted] at which point the subject was withdrawn from the study to ensure that proper care could be completed by physicians at the hospital.

The review of this event report was conducted by the IRB Chair via UIC policy. It was determined that the event represents a Local Serious Unanticipated Adverse Event. The event was determined to have occurred locally since this was a UIC subject, and to be serious, as it required hospitalization to manage. The event was also determined to be unanticipated, as serious irritability and aggression requiring hospitalization is not a listed risk within the consent and protocol. Lastly, the event was determined to be possibly related to the research, as the study procedures likely contributed to the increased severity of the subject's symptoms. While the subject has a history of irritability and aggression of mild to moderate intensity, this was the first episode serious enough to require hospitalization. The Chair concurred that current measures were appropriate, and no further action is required to prevent immediate harm to the subject.

The convened IRB will review the unanticipated problem report and Chair's determination at their February 6, 2013 meeting.

I believe these actions regarding this adverse event are being appropriately addressed. I will provide a follow-up report if the IRB makes any additional determinations or corrective actions. If you have any questions, please contact me at (312) 413-8731 or jfischer@uic.edu.

Sincerely,

[redacted]

James H. Fischer, PharmD
Director, Office for the Protection of Research Subjects
Human Protections Administrator, Office for the Vice Chancellor for Research
FWA #00000083

cc: Mitra Dutta, PhD, Vice Chancellor for Research
Clyde Wheeler, PhD, Associate Director, Investigator Outreach and Quality Improvement
Patricia West-Thielke, PharmD, Chair, IRB #1
Anand Kumar, MD, Head, Department of Psychiatry
Mani Pavuluri, MD, Principal Investigator
Marjorie A. Garvey, Program Official, National Institute of Mental Health