



Office for Human Research Protections
The Tower Building
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 301-402-5567

FAX: 301-402-2071

E-mail: mcarome@osophs.dhhs.gov

October 24, 2001

Wyatt R. Hume, D.D.S., Ph.D.
Executive Vice Chancellor
Office of the Chancellor
University of California, Los Angeles
Box 951405
Los Angeles, California 90095-1405

**RE: Human Research Subject Protections Under Multiple Project Assurance
(MPA) M-1127**

**Krishnamoorthy J, King BH. Open-Label Olanzapine Treatment in Five
Preadolescent Children. *Journal of Child and Adolescent Psychopharmacology*. 1998;
9(2):107-13.**

Dear Dr. Hume:

The Office for Human Research Protections (OHRP) has reviewed your September 4, 2001 report responding to allegations of noncompliance with Department of Health and Human Services (HHS) regulations for the protection of human research subjects (45 CFR Part 46) that were presented in OHRP's June 1, 2001 letter regarding the above-referenced publication.

The allegations involved the following:

- (1) Children were enrolled in a clinical trial for which there was a failure to minimize risks to subjects and to ensure that risks were reasonable in relation to anticipated benefits, in contravention of the requirements of HHS regulations at 45 CFR 46.111(a)(1) and (2).
- (2) The clinical trial research failed to comply with the requirements of HHS regulations at 45 CFR Part 46, Subpart D (Additional DHHS Protections for Children Involved as Subjects in Research).

Based upon its review of your report, OHRP finds no evidence to substantiate the above allegations. In particular, OHRP acknowledges your statements that the above-referenced publication represented a retrospective compilation of information from medical records and that the patients described in the publication were not prospectively enrolled in any research clinical trial.

Furthermore, based upon your report, OHRP acknowledges the following:

- (1) The authors of the above-referenced publication failed to submit a request to claim exemption from University of California, Los Angeles (UCLA) Institutional Review Board (IRB) review or for approval to perform a retrospective chart analysis on the clinical course of the five patients described in the publication, in accordance with UCLA institutional policy.
- (2) The authors of the above-referenced publication are no longer faculty members at your institution.
- (3) UCLA has established (a) a procedure requiring certification of exemption from IRB review by an IRB administrator or the Director of UCLA's Office for Protection of Research Subjects; and (b) a substantive human research education program for all UCLA investigators.
- (4) The current version of the UCLA Claim of Exemption form was distributed most recently to UCLA investigators campus wide in February 2000.
- (5) In June 2000, you distributed a memorandum to all UCLA faculty, students, and staff stating that "no UCLA faculty, staff, or students may conduct human subject research without obtaining prospective IRB approval or a certified Claim of Exemption from IRB review."

As a result, there should be no need for further involvement of OHRP in this matter. Of course, OHRP must be notified should new information be identified which might alter this determination.

In your report, you requested OHRP guidance regarding whether individual or grouped case reports constitute human subject research as defined by HHS regulations at 45 CFR 46.102(d).

In response, OHRP provides the following guidance:

- (1) HHS regulations at 45 CFR 46.102(d) define research as a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

An activity involving systematic investigation of medical records for the purpose of developing or contributing to generalizable knowledge would satisfy the definition of research. With respect to the above-referenced publication, it appears that the authors systematically extracted specific clinical data (age; gender; diagnoses; previous drug treatments; and dose, duration, therapeutic effects, and adverse effects of olanzapine) from the medical records of a series of five children with psychiatric disorders for the purpose of contributing to generalizable knowledge about the response to, and side effects of, olanzapine treatment in children. Indeed, based upon the analysis of their collected data, the authors concluded that the clinical value of olanzapine might not be comparable in children to what might be expected based upon findings in adults.

(2) HHS regulations at 45 CFR 46.102(f) define human subject as living individual about whom an investigator conducting research obtains (a) data through intervention or interaction with the individual, or (b) identifiable private information.

Research involving a retrospective review of medical records would involve human subjects when the investigators obtain identifiable private information about living individuals. With respect to the above-referenced publication, it appears that the authors obtained identifiable private information (medical record information) about children with psychiatric disorders. Whether these children were alive at the time the information was obtained is unclear.

(3) Under HHS regulations at 45 CFR 46.101(b)(4), research is exempt from the requirements of HHS regulations for protection of human subjects when the research involves the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subject.

OHRP acknowledges that research activities involving the study or collection of data from existing medical records is exempt if information from the records is recorded in a manner that subjects cannot be identified, directly or through identifiers linked to the subject.

Regarding the above-referenced publication, your report indicated that you were able to identify the patient records for the individuals referenced in the publication. This suggests that the authors recorded information from the medical records in a manner that the patients could be identified. As a result, if the activity described in the publication involved human subject research, it may not have been exempt from the requirements of the HHS regulations for the protection of human subjects.

OHRP appreciates the continued commitment of your institution to the protection of human research subjects. Please do not hesitate to contact me should you have any questions.

Sincerely,

Michael A. Carome, M.D.
Director, Division of Compliance Oversight

cc: Dr. Albert Carnesale, Chancellor, UCLA
Dr. Carmine Clemente, Chair, IRB-01, UCLA
Dr. Robert Figlin, Chair, IRB-02, UCLA
Ms. Judith Brookshire, Director, Office for Protection of Research Subjects, UCLA
Mr. Steve Peckman, Associate Director, Office for Protection of Research Subjects, UCLA
Commissioner, FDA
Dr. David Lepad, FDA
Dr. James McCormack, FDA
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. George Gasparis, OHRP
Dr. Jeffrey Cohen, OHRP
Dr. Kamal Mittal, OHRP
Mr. Barry Bowman, OHRP