DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

FOR US POSTAL SERVICE DELIVERY:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
National Institutes of Health (MSC 7507)
Rockville, Maryland 20892-7507

FOR HAND DELIVERY OR EXPRESS MAIL:
Office for Human Research Protections
6100 Executive Boulevard, Suite 3B01
Rockville, Maryland 20852

Telephone: 301-402-5567
FAX: 301-402-2071
E-mail: mc2a@nih.gov

November 22, 2000

Jack O. Burns, Ph.D.
Vice Provost for Research
Office of Research
University of Missouri-Columbia
205 Jesse Hall
Columbia, MO 65211

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1502

Research Activity: Curtis, JJ, *et al.* Continuous Warm Blood Cardioplegia: A Randomized Prospective Clinical Comparison. *International Journal of Angiology.* 5:212-218; 1996.

Dear Dr. Burns:

The Office for Human Research Protections (OHRP), formerly the Office for Protection from Research Risks (OPRR), has reviewed your August 12, 1999 report regarding the above referenced research. OHRP apologizes for the delay in its response.

In reviewing the documents submitted to OHRP by the University of Missouri-Columbia (UMC), as well as additional documents recently provided to OHRP by Dr. Curtis' attorney, OHRP notes the following:

(1) The abstract entitled "Continuous Warm Blood Cardioplegia: A Randomized Prospective Clinical Comparison" (Curtis, *et al. The Journal of Thoracic and Cardiovascular Surgery*, 1993) that was submitted for presentation at the 19th Annual Meeting of the Western Thoracic Surgical Association in June 1993 included the following statements:

(a) "Seventy-eight consecutive patients undergoing isolated coronary artery bypass grafting by a single surgeon were randomized to receive one of two myocardial preservation techniques."

(b) "Control patients (C), n = 38 had myocardial protection by moderate systemic hypothermia, topical cold saline, myocardial arrest with antegrade dilute blood/cold potassium cardioplegia with subsequent intermittent retrograde administration of the same solution every 10-15 minutes during the aortic cross-clamping."

(c) "The experimental group (WB), n = 40 had myocardial protection at systemic normothermia, myocardial arrest with antegrade high potassium, warm blood cardioplegia with subsequent continuous retrograde administration of low potassium warm blood cardioplegia throughout the period of aortic cross-clamping."

(d) "We conclude that while it is possible to perform coronary artery revascularization with continuous warm blood cardioplegia with low morbidity and mortality, no clear advantage was demonstrated and there is a technical preference for a bloodless field."

(2) The scientific journal article entitled "Continuous Warm Blood Cardioplegia: A Randomized Prospective Clinical Comparison" (Curtis JJ, *et al. International Journal of Angiology*. 5212-218; 1996) included the following statements:

(a) "Prompted by these observations, we report herein a randomized, prospective clinical experience that was performed for the purpose of testing the hypothesis that coronary artery bypass surgery utilizing warm blood cardioplegia will result in decreased morbidity and mortality compared with our usual myocardial preservation technique."

(b) "The specific aims of this prospective study were to compare the influence of continuous warm blood vs intermittent cold, dilute blood crystalloid cardioplegia on myocardial preservation, postoperative bleeding, and the incidence of postoperative dysrhythmia."

(c) "Materials and Methods: Consecutive patients undergoing isolated primary coronary artery revascularization were randomized to receive our usual myocardial preservation technique or continuous warm blood cardioplegia."

(d) "Rarely, the warm blood cardioplegia was interrupted for several moments to accomplish extremely demanding anastomoses."

(e) "Patient demographics, clinical and hemodynamic data of the two groups, were recorded and analyzed by appropriate statistics. Endpoints monitored included requirement for pharmacologic or mechanical assistance to separate from cardiopulmonary bypass, hemodynamics on arrival into the intensive care unit,

> ECG and creatinine kinase (CK) changes, hospital stay, and mortality. The ECG was monitored continuously throughout the hospital course. The incidence of resumption of spontaneous rhythm after aortic declamping was noted and the number of episodes of cardiac defibrillation required in the operating room were recorded."
>
> (f) "Seventy-eight consecutive patients undergoing isolated primary coronary artery bypass grafting by a single surgeon (JJC) were randomized to receive either continuous cardioplegia (n = 40) or cold intermittent cardioplegia as described in Materials and Methods (n = 38)."
>
> (g) "This randomized prospective study was discontinued for data analysis purposes after two patients receiving continuous warm blood cardioplegia sustained new Q-wave myocardial infarctions contrasted with none in the intermittent cold cardioplegia group ($p = 0.25$). There was concern that this might be due to technical error, as precise visualization of the coronary arteriotomy was more difficult in the continuous warm blood group. This is reflected in the increased cross-clamp time requirements per graft in the continuous warm cardioplegia group."

(3) The human subjects described in the abstract and journal article referenced above underwent coronary artery bypass surgery with warm or cold cardioplegia between June 1991 and March 1992.

(4) In his April 3, 1992 letter to Dr. Laura Hillman, former Chair of the Institutional Review Board (IRB) at UMC, Dr. Curtis stated the following:

> "The Division of Cardiothoracic Surgery has in the last year utilized two types of myocardial preservation during cardiopulmonary bypass. One technique involves continuous warm cardioplegic arrest to the heart with normal body temperature. The other technique is cold cardioplegic arrest to the heart and care cooling. Both techniques are reported in the literature. We have retrospectively viewed our data and no major differences in outcome were noted. However, we wish to determine if there is any beneficial effect associated with either the warm or cold cardioplegic arrest. Up to this time, the choice of myocardial preservation technique has been the surgeon's choice of either cold cardioplegic arrest or warm cardioplegic arrest."

(5) The IRB-approved protocol entitled "A Comparison of Warm and Cold Cardioplegic Arrest During Open Heart Surgery" (protocol #4460) and submitted to the IRB under Dr. Curtis' April 3, 1992 letter included the following statements:

> (a) "State Hypothesis: Continuous warm cardioplegia will be associated with less ischemic, hypothermic and reperfusion injury as noted by fewer dysrhythmias, fewer intraoperative and postoperative myocardial infarctions, less inotropic therapy, and less difficulty in weaning from cardiopulmonary bypass when compared with cold cardioplegia."
>
> (b) "For many years cold cardioplegic arrest has been the standard for myocardial protection during open heart surgery. Within the last 2 years normothermic (warm) cardioplegic arrest of the heart has been introduced. Both techniques have been used at this facility. We retrospectively viewed our data and no major differences in outcomes were noted. To determine if warm cardioplegia arrest is beneficial we wish to conduct a prospective, randomized study."

(6) In her April 30, 1992 letter to Dr. Curtis, approving protocol #4460, Dr. Hillman stated the following:

> (a) "[The IRB] found this project to impose significant risk to the research subject."
>
> (b) "[The IRB] requires that you obtain the informed written consent of each research subject."

(7) Your August 12, 1999 report indicates that no subjects were ever enrolled in protocol #4460.

(8) On a REQUEST FOR EXEMPTION form dated July 8, 1993, Dr. Curtis stated the following regarding the research project entitled "Normothermic Cardiac Preservation":

> "Brief Summary of the Project: Some patients received cardiac preservation with normothermic solution and some received hypothermic cardiac preservation. We wish to review the charts for various outcome variables to determine any differences in the two techniques."

(9) In his May 7, 1998 letter to the IRB, Dr. Richard A. Schmaltz, a co-author on the 1996 article in the *International Journal of Angiology*, stated the following:

> "After doing a few cases [of open heart surgery with continuous warm cardioplegia] I felt that for resident teaching purposes that this would be a more difficult modality to use because the continuous flow which is required causes some difficulty in the visualization of the open arteriotomy."

(10) In his May 14, 1998 letter to the IRB, regarding the research described by Curtis *et al* in their 1996 article in the *International Journal of Angiology*, Dr. Curtis stated the following:

> "I trust that after our discussion it was clear that no experimentation or investigation of patients requiring consent was performed. At the time that patients in question were operated, there was no intent to perform a formal investigation. Once the Division decided to perform an investigation, a IRB proposal was submitted. During retrospective review of data, a small subset of patients were found to be randomized by circumstances of preparation for their surgery. It was this small subgroup that was reported as randomized. That clinical comparison was covered by a second IRB proposal."

(11) In his June 4, 1998 letter to Dr. Steve Standiford, former Chair of the IRB at UMC, regarding the research described by Curtis *et al* in their 1996 article in the *International Journal of Angiology*, Dr. Schmaltz stated the following:

> "First of all, no 'experimentation' of patients was performed. I do many variations of surgical technique, based on the needs at the time, and also what may benefit the patient. The warm blood caridoplegia was a variation of giving cardioplegia. Second, in order to have some semblance of order, we very loosely decided to use the warm blood cardioplegia on an odd-even number basis. This is per the best I can recollect."

(12) In his June 12, 1998 letter to Dr. Curtis, regarding the research described by Curtis *et al* in their 1996 article in the *International Journal of Angiology*, Dr. Standiford stated the following:

> (a) "By a majority vote of 11 yes, 2 no and 1 abstention, the Board determined that research was conducted."
>
> (b) "The Board adopted the statement by a majority vote of 12 yes, 1 no and 1 abstention that: based on the evidence, we believe many patients were prospectively randomized to cardioplegia technique and entered into the normothermic heart surgery registry and that data was retrospectively analyzed for publication . . . ."
>
> (c) "By a vote of 12 yes and 2 no, the Board found Dr. Curtis conducted the research described in the article."
>
> (d) "By a vote of 13 yes and 1 no, the Board believed IRB approval was required. By a vote of 11 yes and 1 no and 2 abstentions, the Board believed full IRB review and approval was required before randomization of any subject to cardioplegia technique. By a vote of 11 yes, 0 no and 3 abstentions, the Board believed application for exemption from IRB review was required prior to analysis of the normothermic heart surgery registry data in preparation for submission to Western Thoracic Surgical Association."

(e) "By a vote of 12 yes to 2 no, the Board believed written informed consent was required for all patients prospectively randomized."

(13) In his July 28, 1998 letter to OPRR, Dr. Jack Burns, Vice Provost for Research at UMC, reported the findings of the IRB summarized in the preceding paragraph.

(14) The minutes of the December 16, 1998 IRB meeting included the following statement regarding the research described by Curtis *et al* in their 1996 article in the *International Journal of Angiology*:

> "Dr. [C.] made a motion that the Board direct the Principal Investigator to notify the subjects or the families of deceased subjects by letter. The Board will monitor and approve the letter and process before it is sent. The motion passed with 12 positive votes, no negative votes, and one abstention."

(15) The minutes of the January 27, 1999 IRB meeting included the following statement:

> "Dr. [B.] made a motion to reconsider the motion which passed at the December 16, 1998 IRB meeting. The motion passed with 10 positive votes and 3 negative votes. Dr. [B.] then made the following motion: 'Based on our investigation of Dr. Curtis' research described in the article entitled "Continuous Warm Blood Cardioplegia: A Randomized Prospective Clinical Comparison", we have found that Dr. Curtis used his patients in a research trial without their consent. We believe that it is the responsibility of the University to inform these patients, or the families of the deceased patients, of this violation of their right to informed consent. We recommend that the University do so immediately.'"

(16) In their February 2, 1999 letter to Dr. Brady Deaton, the UMC Provost, regarding the research described by Curtis *et al* in their 1996 article in the *International Journal of Angiology*, Dr. Bernard Ewigman, Dr. Gomez-Sanchez, and Dr. Huxley, members of the Research Dishonesty Inquiry (Ad Hoc) Committee, stated the following:

> "We learned that [Dr. Curtis] took all of the registry data to the statistician for analysis. This included all patients who had been operated on since the surgeons at this center began using this standard technique. He wanted to find out if his question could be answered based on the registry data. The statistician indicated that it could not be answered unless he excluded two groups of patients; the cases of other surgeons besides himself, and his own cases prior to the time he advised the operating technicians to prepare cardioplegia solution based on even or odd hospital number. The statistician advised him that if he excluded those two groups of cases he could do an analysis that would, in effect, be a 'randomized trial.'"

(17) In his April 27, 1999 letter to the *International Journal of Angiology*, Dr. Curtis stated the following:

> "The article 'Continuous Warm Blood Cardioplegia: A Randomized Prospective Clinical Comparison,' which appeared in the *International Journal of Angiology* 5:212-218 (1996) authored by Jack Curtis, MD, . . . has come under critical scrutiny by the University of Missouri Health Sciences Center. I write to explain the use of terms 'randomized' and 'prospective' which were used to describe this clinical comparison of a concurrent cohort of patients.
>
> "The term 'prospective' was used because standardized data were collected on each patient and entered into a computerized registry in close proximity to the delivery of patient care.
>
> "The term 'randomized' was used because the subgroup of patients reported were found on review of the registry to be randomized by the process of the perfusionists preparation for the operative procedure. Our cardiopulmonary perfusionists were prepared to use warm blood cardioplegia if the last digit of the patient's hospital number was an odd number. Surgeons had the option to use warm or cold cardioplegia. The patients reported consistently received treatment cardioplegia set by the perfusionist."

(18) Your August 12, 1999 report indicated that Provost Deaton decided not to notify subjects of their involvement in the research described by Curtis *et al* in their 1996 article in the *International Journal of Angiology*.

(19) An April 27, 2000 document entitled "In re The Matter of Dr. Jack J. Curtis, the University of Missouri - Columbia, the University of Missouri Hospitals and Clinics, the Internal Review Board (IRB), and Various Individuals Involved in the Matter" that was provided to OHRP by Dr. Curtis' attorney included the following statements:

(a) Page 26, "**Analysis of the Patient Data Registry (i.e., 'The Registry')**":

> "Primarily, [such registries] are kept for the following purposes: . . . . 4. Research - Physicians pull data from the Registry for use in research. This research may be prospective or retrospective. *The data is collected regardless of whether it will be used for research.* . . ." [italics in original]

(b) Page 28, "**Registry Use in the Curtis Matter**":

> **"1. Initial Purpose for Setting the Registry Up for Specific Evaluation of the Warm Blood Cardioplegia Technique:**

> **"-Internal Decision Making Purposes**
> **-Warm-blood cardioplegia was gaining popularity throughout the industry. As a Department, the surgeons wanted to focus on using this technique for a period of time in order to consider whether they wanted to utilize the technique more frequently in the Department on a regular basis. They then planned to look at their performance, comfort level, and satisfaction with the warm blood technique by reviewing data from the Registry. Therefore, the initial purpose was for Internal Decision-Making Purposes within the Department."** [emphasis in original]

(c) Page 29, **"Use of Patient Numbers for Warm or Cold Technique"**:

> "As will be discussed, *infra*, the surgeons within the Department had decided to affirmatively try the warm blood cardioplegia technique for a period of time in order to gain experience with and compare it with cold technique for internal analysis only. Thereafter, they planned to make departmental and individual decisions about its continued use as a viable option for cardioplegia at the University."

OHRP Findings Regarding the Research Described in the Above Referenced 1993 Abstract and 1996 *International Journal of Angiology* Article

Based upon its review of the above referenced materials, OHRP makes the following determinations regarding the research described in the above referenced abstract and *International Journal of Angiology* article:

(1) Department of Health and Human Services (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. Activities which meet this definition constitute research for the purposes of the Federal Regulations at 45 CFR Part 46 whether or not they are conducted or supported under a program which is considered research for other purposes. HHS regulations at 45 CFR 46.102(f) defines human subject as a living individual about whom an investigator conducting research obtains (i) data through intervention or interaction with the individual; or (ii) identifiable private information.

OHRP finds the activities involving comparison of warm versus cold cardioplegia during coronary artery bypass grafting surgery under the direction of Dr. Curtis falls within the HHS definitions of research involving human subjects. In specific, OHRP finds that Dr. Curtis in a prospective and systematic manner alternated between warm and cold

cardioplegia in a consecutive series of patients undergoing coronary artery bypass grafting surgery between June 1991 and March 1992 and prospectively collected postoperative clinical data, including data on morbidity and mortality. Furthermore, the UMC IRB made the same determination in 1998.

(2) HHS regulations at 45 CFR 46.109(a) and the UMC MPA (see Part 1, section II.B) require that all research involving human subjects that is not exempt be reviewed and approved by the IRB.

OHRP finds that this research was conducted without IRB review and approval. Furthermore, the UMC IRB made the same determination in 1998.

(3) HHS regulations at 45 CFR 46.116 stipulate that, except as provided by the regulations, no investigator may involve a human subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative. This regulatory requirement is based upon the principle of respect for persons, one of the three basic ethical principles embraced by UMC in its MPA and presented in the Belmont Report, upon which the HHS regulations are premised. In its discussion of this ethical principle, the Belmont Report states that "individuals should be treated as autonomous agents. . . . In most cases of research involving human subjects, respect for persons demands that subjects enter into the research voluntarily and with adequate information."

OHRP finds that this research was conducted without the investigators obtaining the legally effective informed consent of the subjects or the subjects' legally authorized representatives. Furthermore, the UMC IRB made the same determination in 1998.

(4) HHS regulations at 45 CFR 46.111(a)(1) and (2) require that in order to approve research covered by the regulations the IRB shall determine, among other things, that risks to subjects are minimized and reasonable in relation to anticipated benefits, if any, to the subjects and the importance of the knowledge that may reasonably be expected to result.

OHRP finds that because Dr. Curtis failed to obtain IRB review and approval for this research these regulatory requirements, among others, were not satisfied.

Action 1 - Required: The UMC IRB-02, in conjunction with the investigators and appropriate UMC officials, must develop a satisfactory plan, including both the means and the content, for contacting all surviving subjects (or the surviving relatives of subjects who were are now deceased) who participated in the human subject research referenced in the 1996 *International Journal of Angiology* article referenced above, and informing them of their previous unwitting participation in the research, the risks associated with the research, and the nature of the noncompliance by the investigator with the requirements of

HHS regulations at 45 CFR Part 46. By January 12, 2001, please submit to OHRP a written report regarding the IRB's determinations and plan for this matter and the documentation underlying these determinations, including relevant IRB minutes and the proposed text for debriefing the surviving subjects (or the surviving relatives of subjects who are now deceased).

Action 2 - Required: UMC, in conjunction with all of its investigators and clinical practioners, as well as relevant administrators, must audit and identify all ongoing research projects involving human subjects that are not exempt under HHS regulations at 45 CFR 46.101(b) and confirm that all such research has been reviewed and approved by one of the UMC IRBs. UMC must suspend immediately any nonexempt research involving human subjects that has not been reviewed and approved by one of the UMC IRBs. By January 12, 2001, please provide OHRP with a report on the results of this audit and a list of any research activities that have been suspended as a result of this audit.

Action 3 - Required: By January 12, 2001, UMC must submit to OHRP a detailed plan for ensuring that all research investigators, all IRB members, and all IRB staff are appropriately educated, on an ongoing basis, about ethical principles and regulatory requirements for the protection of human subjects.

Action 4 - Required: By January 12, 2001 UMC must provide an updated report on the status of Dr. Curtis' compliance with the UMC IRB's requirement to provide the IRB with assurances that he and his staff are knowledgeable about IRB requirements. Furthermore, UMC must provide OHRP with an update on the status of any projects for which Dr. Curtis is listed as principal investigator or co-investigator. This update should include any projects that Dr. Curtis has submitted to the IRB for review along with the action the IRB has taken on such projects.

Additional Finding, Concerns, and Guidance Regarding UMC's Systemic Protections for Human Subjects

(5) OHRP finds that the written IRB policies and procedures submitted with your August 12, 1999 report fail to adequately describe the following activities, as required by HHS regulations at 45 CFR 46.103(b)(4) and (5):

(a) The procedures which the IRBs follow for conducting its initial and continuing review of research.

(b) The procedures which the IRBs follow for reporting its findings and actions regarding initial and continuing review to the institution.

(c) The procedures which the IRBs follow for determining which projects require review more often than annually.

(d) The procedures which the IRBs follow for determining which projects need verification from sources other than the investigators that no material changes have occurred since the previous IRB review.

(e) The procedure for ensuring prompt reporting to the IRBs of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject.

(f) The procedures for ensuring prompt reporting to the IRBs, appropriate institutional officials, the head of any supporting Federal Department or Agency, and OHRP of each of the following events:

(i) Any unanticipated problems involving risks to subjects or others.

(ii) Any serious or continuing noncompliance with the requirements of 45 CFR Part 46, or the requirements or determinations of the IRB.

(iii) Any suspension or termination of IRB approval of research.

Action 5 - Required: By January 12, 2001, UMC must submit to OHRP revised written IRB policies and procedures that adequately describe the operational details for each of the above referenced procedures. In order to assist UMC in revising its IRB policies and procedures, please see the enclosed Guidance for Formulating Written IRB Policies and Procedures.

(6) HHS regulations at 45 CFR 46.115(a)(2) require that minutes of IRB meetings be in sufficient detail to show the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution. OHRP finds that IRB minutes provided with your August 12, 1999 report routinely failed to meet these requirements for protocols undergoing initial and continuing review.

Action 6 - Required: By January 12, 2001, UMC must submit a satisfactory corrective action plan to ensure that minutes of IRB meetings document all information required by HHS regulations at 45 CFR 46.115(a)(2).

(7) Continuing IRB review of research must be substantive and meaningful. In conducting continuing review of research not eligible for expedited review, all IRB members should at least receive and review a protocol summary and a status report on the progress of the research, including (a) the number of subjects accrued; (b) a description of

any adverse events or unanticipated problems involving risks to subjects or others and of any withdrawal of subjects from the research or complaints about the research; (c) a summary of any recent literature, findings obtained thus far, amendments or modifications to the research since the last review, reports on multi-center trials and any other relevant information, especially information about risks associated with the research; and (d) a copy of the current informed consent document. Primary reviewer systems may be employed, so long as the full IRB receives the above information. Primary reviewers should also receive a copy of the complete protocol including any modifications previously approved by the IRB (see OPRR Reports 95-01). Furthermore, the minutes of IRB meetings should document separate deliberations, actions, and votes for each protocol undergoing continuing review by the convened IRB.

When conducting research under an expedited review procedure, the IRB Chair (or designated IRB member(s)) should receive and review all of the above referenced documentation.

OHRP is concerned that continuing review of research by the UMC IRBs fails to satisfy these requirements. Please respond.

(8) OHRP notes that the responsibilities of the Compliance Officer delineated in the written IRB policies and procedures include the following:

> (a) "Reviews all requests for amendments, requests for emergency use of a test article/compassionate use protocols and adverse reactions reports for signature by the Chair. In the absence of the Chair, the Compliance Officer has the authority sign these documents."
>
> (b) "Reviews and approves changes in previously approved consents."

Please note that changes to IRB approved protocols or informed consent documents must be reviewed and approved either by the convened IRB when changes exceed the limit of "minor" changes, or by the IRB Chair (or another voting member designated by the Chair) when the changes are minor [see 45 CFR 46.110(b)]. These responsibilities may not be delegated to the Compliance Officer who is not a voting member of the IRB. Please revise the UMC IRB policies and procedures accordingly.

(9) OHRP strongly recommends that the recording of votes during IRB meetings indicate the continued existence of a quorum by noting the total number of voting members present at the time of the vote for each action and including the number of votes for, opposed, and abstained. Example: Total = 15; Vote: For-14, Opposed-0, Abstained-1 (NAME). Please note that recording votes as "unanimous" is not sufficient.

(10) Please provide a copy of the complete IRB file for the cardiovascular surgery Patient Data Registry, including the following:

(a) The IRB-approved research protocol and any applicable grant applications.
(b) The IRB-approved informed consent documents.
(c) The relevant IRB minutes, including initial review, continuing review, review of changes to the research or the informed consent document, and review of any adverse or unanticipated events.
(d) The IRB's correspondence with the investigators.
(e) All continuing review reports.
(f) A chronological summary of the dates of the IRB's actions.
(g) A copy of all publications, abstracts, and presentations which were derived from this research project for the past 10 years.
(h) Any other pertinent information.

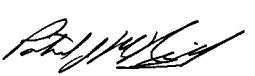
If this registry has not been subject to IRB review and approval, please provide a detailed explanation for why it has not.

(11) HHS regulations at 45 CFR 46.304(b) require that for the review of research involving prisoners as subjects at least one member of the IRB shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity. OHRP notes that the most recent IRB membership rosters submitted to OHRP designate a prisoner consultant as a nonvoting member. Please note that when the IRB reviews research involving prisoners as subjects, the prisoner, or prisoner representative, must be a voting member of the IRB. Please provide the curriculum vitae of the current prisoner representative on the UMC IRBs and a written justification for having him or her serve as an advocate for prisoners.

Please respond to the above concerns and questions no later than January 12, 2001.

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 questions.

Sincerely,



Patrick J. McNeilly, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

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

Enclosure: Guidance for Formulating Written IRB Policies and Procedures

cc: Dr. Charles M. Borduin, Chair, IRB-01XM., UMC
Dr. L. Wayne Hess, Chair, IRB-02, UMC
Dr. Jack Curtis, UMC
Commissioner, FDA
Dr. David Lepay, FDA
Dr. James F. McCormack, FDA
Dr. John Mather, ORCA, Department of Veterans Affairs
Dr. Greg Koski, OHRP
Dr. Melody H. Lin, OHRP
Dr. J. Thomas Puglisi, OHRP
Dr. Clifford C. Scharke, OHRP
Dr. Katherine Duncan, OHRP
Mr. George Gasparis, OHRP
Dr. Jeffrey M. Cohen, OHRP
Mr. Barry Bowman, OHRP