DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for Human Research Protections
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July 24, 2002

Dr. Lihua Wang
Professor, Deputy Director
Center for Ecogenetics and Reproductive Health
Beijing Medical University
38 Xueyuan Road, Haidian District
Beijing 100083 China

RE: Human Research Subject Protections Under Single Project Assurance (SPA) S-5682-04, S-5682-06, S-5682-07, and S-5682-08

Research Project: Petrochemical Exposure and Reproductive Outcomes
Principal Investigator: Dr. David C. Christiani
HHS Project Number: R01 OH 03027

Research Project: Rotating Shift Work and Reproductive Outcomes
Principal Investigator: Dr. Dr. Xiping Xu
HHS Project Number: R01 HD32505

Research Project: The Genetics of Nicotine Addiction Vulnerability
Principal Investigator: Dr. Xiping Xu
HHS Grant Number: 1R01 DA 12905-01

Research Project: Genetics of Hypertension and its Intermediate Phenotypes
Principal Investigator: Dr. Xiping Xu
HSS Grant Number: R01 HL64109

Dear Dr. Lihua Wang:

The Office for Human Research Protections (OHRP) has reviewed your April 25, 2002 report regarding the above referenced research conducted at the Beijing Medical University (BMU) that was submitted in response to OHRP's March 28, 2002 letter.

Based on its review, OHRP makes the following determinations:

(1) Department of Health and Human Services (HHS) regulations at 45 CFR 46.116 require that informed consent information be in language understandable to the subject or the subject's legally authorized representative. OHRP finds that the informed consent document approved by the BMU Institutional Review Board (IRB) for these studies (particularly "The Genetics of Nicotine Addiction Vulnerability" and "Genetics of Hypertension and its Intermediate Phenotypes") included complex language that would not be understandable to all subjects.

Corrective Action: OHRP acknowledges that the procedures for obtaining informed consent from subjects included an explanation of the research by the investigator in their own words using the local dialect. In addition, the investigator asked the subjects some questions to determine comprehension by the subject. OHRP notes that, while these procedures are good practice, the IRB must approve the language that is presented to the subjects. HHS regulations at 45 CFR 46.117(b)(1) state that the consent form should be a written consent document that embodies the elements of informed consent required by 45 CFR 46.116, which includes the requirement that the information be in a language understandable to the subject.

Required Action: By August, 2002, please provide OHRP with additional corrective actions to address this finding.

(2) In its March 28, 2002 letter to BMU, OHRP expressed concern that several subjects in the project "Genetics of Hypertension and its Intermediate Phenotypes" may have been enrolled and undergone study interventions prior to signing informed consent documents and that subjects did not date the informed consent documents themselves, or that the documents may have been back-dated.

OHRP acknowledges BMU's statements that the date listed was actually the subject's arrival date, not the enrollment date, and that no subjects underwent study interventions prior to signing the informed consent document. OHRP also acknowledges HSPH's statement that for these studies the researchers dated the informed consent documents at the time of obtaining consent to ensure that the dates were all written by the Western calendar rather than the Chinese lunar year.

(3) The informed consent document for project # R01HD32505 in the approved SPA is not the same document that the Harvard School of Public Health IRB reviewed and approved.
Corrective Action: OHRP acknowledges that the BMU accidently submitted with the SPA a

previous draft of the informed consent document. Please clarify whether or not the IRB-approved informed consent document was used in the conduct of the research.

(4) Drs. Lihua Wang and Yingming Huang are listed as both Investigators for for project # R01HD32505 and as IRB members. Harvard School of Public Health has informed OHRP that both IRB members left the room for the vote on this project due to conflict of interest, but this left the IRB without a majority of members at the convened meeting. HHS regulations at 45 CFR 46.108(b) require that, except when an expedited review procedure is used, research must be reviewed at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in a nonscientific area. OHRP finds that a quorum indeed was not present and the actions taken at this meeting on this protocol must be considered invalid.

Corrective Action: OHRP acknowledges that the BMU IRB will re-review this protocol by the convened IRB to decide if the original vote was appropriate. Please provide OHRP with this determination when it is available.

Please submit to OHRP your responses to the above determinations no later than August 30, 2002. If upon further review of the concerns and questions, BMU identifies instances of non-compliance with the HHS regulations for protection of human subjects, please include detailed corrective action plans to address the noncompliance.

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,

Kristina C. Borror, Ph.D.
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Mr. John H. Lichten, HSPH
Ms. Sarah Putney, HSPH
Dr. Troyen A. Brennan, Chair, IRB, HSPH
Dr. David Christiani, HSPH
Dr. Xiping Xu, HSPH
Dr. Ruicong Peng, IRB Chair, BMU
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Dr. Melody H. Lin, OHRP
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Mr. George Gasparis, OHRP
Ms. Yvonne Higgins, OHRP
Mr. Barry Bowman, OHRP