DEPARTMENT OF HEALTH & HUMAN SERVICES

Office of the Secretary
Office of Public Health and Science

Office for HumanResearch Protections
The Tower Building
1100 Wootton Parkway, Suite 200
Rockville, Maryland 20852

Telephone: 301-402-3006
FAX: 301-402-2071
E-mail: rmeyer@osophs.dhhs.gov

March 26, 2003

Robert M. Glickman, M.D.
Dean
New York University School of Medicine
550 First Avenue
New York, NY 10016-8304

RE: Human Research Subject Protections Under Multiple Project Assurance (MPA) M-1177

Research Project: A Phase I Study of 9-Amino-20-(S)-Camptothecin (9-AC) Using Prolonged Continuous Infusion [NCI # T92-0163]
Principal Investigator: Howard Hochster, M.D.
Protocol Number: NYU 92-37

Dear Dr. Glickman:

The Office for Human Research Protections (OHRP) has reviewed New York University School of Medicine's (NYUSM's) November 12, 2001 report that was submitted in response to OHRP's September 4, 2001 letter to NYUSM regarding allegations of possible noncompliance with the Department of Health and Human Services (HHS) regulations for the protection of human subjects (45 CFR part 46) involving the above-referenced research.

Based upon review of your November 12, 2001 report, as well as additional documentation submitted by NYUSM on February 19, 2003, OHRP makes the following determinations regarding the allegations presented in OHRP's September 4, 2001 letter:

(1) The complainant alleged that a subject should not have been enrolled in the above-referenced research because the subject had responded favorably to paclitaxel (Taxol®) therapy.

NYUSM's November 12, 2001 report stated the following in response:

> (a) "The patient referred to in the complaint letter had been initially treated with a combination of taxol and another drug. The patient did initially respond well to taxol therapy, but, in February 1996, her disease became resistant to taxol."
>
> (b) "In March 1996, there was no chemotherapeutic agent registered for second line therapy. Consequently, at that time it was logical to suggest to the patient that she consider enrolling in a study to test an experimental drug (i.e. 9-AC)."

Based on the statements in (a) and (b) above and its review of other information presented in your report, including the eligibility criteria for the above-referenced research, OHRP finds that the above allegation was not substantiated.

(2) The complainant alleged that the informed consent document for the above-referenced research failed to adequately describe the benefits to the subject which may reasonably be expected from the research, as required by HHS regulations at 45 CFR 46.116(a)(3). In particular, the informed consent document for the above-referenced research indicated that the efficacy and side effects of the experimental drug (9-AC) would be similar to other alternative drugs or drug combinations used in therapy for advanced cancers. However, the complainant alleged that such comparisons to other drugs and drug combinations are incorrect because the efficacy and side effects had not yet been determined for 9-AC.

NYUSM's November 12, 2001 report stated the following in response:

> "The comparison to other agents quoted in the letter of complaint is taken from the 'Alternative Treatments' section of the consent form, in which we try to give the potential protocol subject some perspective of the benefits and risks of the experimental therapy relative to those of other available therapies. In the preceding sections, all known toxicities of this agent, as summarized in the Investigator's Brochure, were outlined, as well as a warning about unknown risks. A separate section outlined the extent and limitations of the therapeutic objectives of the study. In the context of the

alternative therapies section, therefore, the quoted statement is correct; there remains no evidence that any second-line therapy for ovarian cancer is any better than another, and the toxicities, both as
predicted in the consent form and as experienced by this patient are comparable to those of other second-line agents for this disease."

Based on the above statement and its review of other information presented in your report, including clinical data from three prior clinical trials with 9-AC, OHRP finds that the above allegation was not substantiated.

As a result of the above determinations, 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 these determinations.

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

Sincerely,

Robert J. Meyer
Compliance Oversight Coordinator
Division of Compliance Oversight

cc: Ms. Annette Johnson, NYUSM
Ms. Rise Schwab, NYUSM
Dr. Keith Krasinski, Chair, NYUSM IRB
Ms. Elan Czeisler, Director, NYUSM IRB
Ms. Soo Bang, NYUSM
Dr. Howard Hochster, NYUSM
Mr. Mark S. Brody, NYUSM

Commissioner, FDA
Dr. David A. Lepay, FDA
Dr. John Mather, ORCA, ORD,VA
Dr. Bernard A. Schwetz, OHRP
Dr. Melody H. Lin, OHRP
Dr. Michael A. Carome, OHRP
Dr. Kristina Borror, OHRP
Ms. Shirley Hicks, OHRP
Mr. George Gasparis, OHRP
Ms. Yvonne Higgins, OHRP
Ms. Melinda Hill, OHRP