QUESTIONS FROM THE COMMITTEE

1. What was the background of the project? What was the original finding? How was the project funded before it was supported by the U.S. Army?

The background for the project originated in some experiences which I had as Chief of the Radioisotope Laboratory at Brooke General Hospital, Fort Sam Houston, Texas, in 1954-1955. I was doing some research with the Surgical Research Unit whose major responsibility is the field of thermal injury. The very severely burned patient who no longer dies in an acute stage but survives in a state unable to regenerate his body tissues struck me as having a striking resemblance to irradiated cancer patients. Also some questions had been posed to me concerning nutritional requirements of cancer patients receiving radiation therapy to which I could find no answer. It seemed that the approach to the total management of the cancer patient receiving radiation therapy was not as well studied as was that of the same patient who would be treated surgically. In addition, the effect on the cancer patient of large doses of radiation given through large fields in relation to systemic effects was not being adequately considered, even though much work was being done on the radiation effects on the tumor and its immediate substrate.

Because of my knowledge of the interest of the Department of Defense in radiation effects on humans, it seemed to me

that this branch of government offered a logical source of funds for the laboratory phases of interest to our group. The General Hospital has never required payment for patient days for patients undergoing diagnosis, therapy or other studies and we were able to hospitalize and treat these patients as necessary without charge to grants or contracts.

The inappropriateness of having any Department of Defense control of patient care was recognized from the inception of the studies and none was exercised.

The formal research protocol was initiated only after funds were received from the Department of Defense, although I had treated occasional private patients with leukemia and lymphoma in my office using whole body radiation and had been impressed with its potentiality. It also had seemed desirable to compare this method of therapy to the many chemotherapeutic agents being developed.

2. During the past 10 years what other research funds were available? What other funds were sought?

As noted above, since there were no charges made to the study for cost of hospitalization and patient services, no other funds were sought. Patient followup was provided by the Tumor Clinic and the Neoplastic Disease Registry, and is also available in the Radioisotope Laboratory from one nurse assigned to followup.

Training funds from NIGMS have been used to support trainees whose research has been in certain aspects of dosimetry.

We are currently about to receive a contribution from an anonymous local donor which will be used to develope a high pressure chromatography system for more refined analysis of UV absorbing compounds in plasma and urine.

Some of the principal investigators are supported in part by endowment funds of the College of Medicine, e.g., Schoepf and Wunker, and there has been support from the General Research fund [5-SO1-FRo5408 (NIH)] and from grants to the Medical Computing Center.

3. Why wasn't support sought from other agencies?

We did not always spend all of the funds allotted under our contracts. Within the limits of our capabilities, we regarded our funding as being adequate.

In regard to seeking support from the National Cancer Institute, the portion of the work devoted to the care and followup of cancer patients had been adequately supported locally.

4. How were the consent forms developed? What was the source of the wording in the current form?

There have been three consent forms used. Copies are attached along with the time periods of their use.

The current form was developed with and of the Research Committee and utilizes a standard form obtained from NIH, apparently developed for normal volunteers. The central sections discussing the radiation therapy and bone marrow procedure were developed specifically for this project using language understandable to the patient.

6. Is there a plan to study palliative effects?

Within the small staff following these patients, it had earlier been determined that for long term analysis of radiation effects on cancer that length of survival could be the only objective end point.

Some data are available on degree of palliation and will be reported elsewhere as discussed at the meeting of November 19.

8. Would this be regarded as more than a Phase I study? When would a Phase III study be considered?

The current status can be regarded as an incomplete Phase II study. In the relatively incomplete categories, we have shown survival which is approximately the same as has been found with other methods even though the controls are not rigorous nor are the methods of measurement entirely satisfactory. Applying better methods of assessing morbidity, the larger categories should be increased by at least 50%. In addition, it would be desirable to include more lymphomas. Additional statistical consultation will be needed before concluding Phase II and preparing for a Phase III study.

9. Why weren't animals used?

The concept of using whole body radiation as a primary method of therapy or followed by localized therapy had already been investigated as cited in the material supplied on November 19. In addition there is an extensive literature on whole and partial body radiation and on irradiation followed by marrow transplantation has been thoroughly reviewed. The animal work has therefore been done but not personally by us.