THE UNIVERSITY OF TEXAS HEALTH SCIENCE CENTER-HOUSTON
INFORMED CONSENT

A PHASE-II THERAPEUTIC TRIAL OF MILD WHOLE BODY HYPERTHERMIA (40°C)
COMBINED WITH 5-FLUOROURACIL, LIPOSOMAL DOXORUBICIN, AND DAILY LOW-DOSE
INTERFERON-α IN PATIENTS WITH ADVANCED MALIGNANCY

AN INVITATION TO PARTICIPATE IN A RESEARCH STUDY:

You are invited to participate in a research study to be conducted by the physicians of The University of Texas Health Science Center Houston and Hermann Hospital. It is important that you read and understand several general principles that apply to all persons who take part in this study. This research study, HSC-MS-96-205 has been reviewed and approved by the Committee for the Protection of Human Subjects for the University of Texas Health Science Center Houston.

I have been told that I will be one of 45 patients asked to participate in this open treatment study of the safety and efficacy of mild whole body hyperthermia (39.5-40°C or 104°F) combined with two standard chemotherapy drugs, 5-Fluorouracil (5-FU) and liposomal doxorubicin (Doxil). I understand that 5-FU and liposomal doxorubicin are chemotherapy drugs approved by the Food and Drug Administration for treatment of many forms of cancer. Whole body hyperthermia using the Heckel-HT 2000 infrared hyperthermia unit combined with chemotherapy is an investigational procedure.

I understand that my participation in this study is voluntary. I may refuse to participate or I may withdraw my consent at any time without prejudice to further medical care. I understand that continued participation in the study is dependent on my response to treatment.

PURPOSE OF STUDY:

The purposes of this study are (1) to determine how well I tolerate the treatment and (2) to evaluate my tumor response and toxicity to treatment with the use of mild whole body hyperthermia combined with liposomal doxorubicin after a prolonged intravenous infusion of 5-FU.

ALTERNATIVE TREATMENT:

Other forms of treatment that were considered in my case and discussed with me include other chemotherapeutic drugs, surgical removal of tumor, x-ray treatments and high heat whole body hyperthermia. The use of mild whole body hyperthermia with chemotherapy has been chosen over these other options because: (1) all other standard drugs available are felt by my doctors to be less likely to produce tumor regression or prolong my life, (2) surgery or x-ray therapy cannot treat all of my tumor and (3) whole body hyperthermia may increase the antitumor effects of both 5-FU and liposomal doxorubicin.

DESCRIPTION OF STUDY:
I will be considered for this study only if entry tests requirements are met (blood, urine, CT exams, heart and breathing tests). According to the results of these initial evaluations, the doctors may decide against enrolling me in the study. However, if my tests qualify me to receive this combined treatment, I will begin the treatment cycle with a continuous intravenous infusion of 5-FU over five (5) days, followed on day six with mild whole body hyperthermia. A 30 minute infusion of liposomal doxorubicin will be administered 1 hour after ending the mild hyperthermia therapy (7). During the whole body hyperthermia treatment I will be lying on a standard hospital bed, enclosed by a thermal protective vapor barrier tent. My body temperature will be raised to 40°C (104°F) and maintained at this temperature for increments of six hours, but no more than four treatments of six hours. I have been told that I will be conscious at all times during the treatment and will be able to communicate with my doctor and/or her associates throughout the procedure. I will receive medication (midazolam and/or fentanyl) for mild sedation during the hyperthermia treatment period to improve my level of comfort while remaining alert and medicine [Kytril (granisterone) or Zofran (odansetrone)] to prevent nausea due to chemotherapy. I will have appropriate monitoring of my heart and breathing.

I have been told that each patient will receive two monthly treatment cycles of thermochemotherapy followed with an evaluation to determine if further cycles will be of benefit. During the first heat treatment cycle and at specified cycles thereafter, I understand that blood and urine will be collected for studies of optimal drug dosing. I understand that before each cycle begins I will have blood (less than one ounce) collected an electrocardiogram and examination by my doctor. At two-month intervals I will have evaluation of my heart function by resting MUGA examination and CT evaluations of my tumor. After each heat treatment, I have been told that I will need weekly blood test (CBC) to evaluate my response to chemotherapy drugs.

TIME COMMITMENT:

I have been told that I will be required to spend up to 24 hours under an observation status for each heat treatment and have weekly clinic visits of approximately 30-60 minutes for the time I am enrolled in this study.

ORDERLY WITHDRAWAL FROM THE STUDY:

I have been told that if I should decide to withdraw my consent and participation from the study, I should do so under a doctor's guidance. I understand that failure to follow my physician's instructions in this regard may result in worsening of my overall condition and increase the likelihood of side effects.

TERMINATION OF PARTICIPATION:

I have been told that I may be removed from this study without my consent, if in my physician's judgment, it would be for my benefit or if I fail to follow the study outline for care as explained to me by my doctor.

BENEFITS:

While we are using a treatment (WBH with chemotherapy) thought to be of benefit to you, actual personal benefit may not result from taking part in the study. However, knowledge may be gained that will be of benefit to others.

RISKS AND SIDE EFFECTS:

I have been told that the risks involved in participation in this study are relatively low as long as I follow my physician's instructions.
Mild whole body hyperthermia has been associated with raised anxiety level due to longer duration of treatment. Patients may also experience fever blisters if they have a history of such disorder, tingling and numbness of fingers or toes, sinus congestion, short term changes in sleep patterns, sinus congestion, fatigue and loss of appetite.

Mild whole body hyperthermia will be performed using the Heckel HT2000 Infrared WBH unit under a Food and Drug Administration approved Non-Significant Risk Investigational Device Exemption (IDE) for establishing the safety and efficacy of simultaneous delivery of mild whole body hyperthermia and chemotherapy.
5-Fluorouracil:

This chemotherapy drug is usually well tolerated. More commonly patients may experience diarrhea and rarely nausea. The drug can cause redness and small ulcers in the mouth and other mucous membranes in some patients. Less common are red painful palms of hands and soles of feet and rarely low white blood cell count and low platelet count which can increase susceptibility to infection, and bleeding.

Liposomal Doxorubicin:

This chemotherapy drug may cause nausea, vomiting, loss of hair; small ulcers in the mouth, low white blood cell count and low platelet count. If extravasation (leaking out of the vein) of doxorubicin should occur from the site of intravenous administration, it can cause significant ulceration of the surrounding tissue. Cardiotoxicity is the major dose limiting toxicity of cumulative doses of the original drug, doxorubicin and can lead to irreversible heart damage. Giving doxorubicin as a liposomal formulation can reduce the likelihood of this event occurring, as we are administering it in this treatment.

Interferon-α:

This cytokine can cause fever, chills and malaise, much like the flu. These symptoms are very minor to non-existent at the low dose you will receive. Any symptoms from interferon can be largely diminished by administering the drug in the evening prior to sleep and taking tylenol (acetaminaphide).

COMPENSATION FOR INJURY:

I have been informed that if I should suffer a physical injury as a result of participation in this study, all necessary medical facilities are available for treatment. However, I understand that I cannot expect personal financial compensation for such injuries from the administrators or participants of this study. I have been told that if I should sustain any injury, I should report it to Dr. Joan M.C. Bull at (713) 500-6821 or Mrs. Nagle 704-1843 (Hyperthermia Dept), and to the Committee for the Protection of Human Subjects (713) 500-5827.

FINANCIAL COMPENSATION:

Because this is an investigational procedure, I will not be charged a professional fee for the hyperthermia treatment by Dr. Bull. However, all costs for hospital observation, tests, anesthesia, medications, and routine clinical evaluations by my physician will be borne by my insurance or me. These costs have been discussed with me in pretreatment counseling, and I have been advised to consult my insurance company as to whether the cost of whole body hyperthermia is covered.

CONFIDENTIALITY AND ANONYMITY:

I understand that representatives of the Food and Drug Administration may review my research and/or medical record for the purposes of verifying data. However, I have been assured that my confidentiality will be preserved within legal limits and the names of patients will not be revealed in any reports or publications resulting from this study.

FOR FURTHER INFORMATION ABOUT THIS RESEARCH STUDY:

I have been told that any questions I have or that may arise during the course of this study will be answered to by satisfaction by Dr. Joan M.C. Bull and her Co-investigators. I may contact her or her associate at (713) 500-6821 or (713) 704-1843.
BEFORE YOU SIGN THIS DOCUMENT:

By signing this consent, you are voluntarily agreeing to participate in this research study. Make sure that questions have been answered to your satisfaction and that you have a clear understanding of the treatment plan. If you have questions regarding your rights as a research subject, call the Committee for the Protection of Human Subjects at (713) 500-5827.

___________________________________________  Date

Signature of Patient

___________________________________________  Date

Name of Patient (Please PRINT)

___________________________________________  Date

Signature of Investigator

___________________________________________  Date

Signature of Investigator/Witness