VOLUNTEER AGREEMENT AFFIDAVIT

For use of this form, see AR 70-25 or AR 40-38; the proponent agency is OTSG

PRIVACY ACT OF 1974 ARM1.950119.009c

Authority:	10 USC 3013, 44 USC 3101, and 10 USC 1071-1087
Principle Purpose:	To document voluntary participation in the Clinical Investigation and Research Program. SSN and home address will be used for identification and locating purposes.
Routine Uses:	The SSN and home address will be used for identification and locating purposes. Information derived from the study will be used to document the study, implementation of medical programs, adjudication of claims, and for the mandatory reporting of medical conditions as required by law. Information may be furnished to Federal, State and local agencies.
Disclosure:	The furnishing of your SSN and home address is mandatory and necessary to provide identification and to contact you if future information indicates that your health may be adversely affected. Failure to provide the information may preclude your voluntary participation in this investigational study.

PART A(1) - VOLUNTEER AFFIDAVIT

Volunteer Subjects in Approved Department of the Army Research Studies

Volunteers under the provisions of AR 40-38 and AR 70-25 are authorized all necessary medical care for injury or disease which is the proximate result of their participation in such studies.

I, _____, SSN _____,

having full capacity to consent and having attained my _____ birthday, do hereby volunteer/give consent as legal representative for _____ to participate in an investigational study entitled "SWOG 9015:A Randomized Trial of Pre- & Post-Operative Chemotherapy Compared to Surgery Alone for Patients with Operable Non-Small Cell Carcinoma of the Lung, Phase III" *(Research study)*

under the direction of COL Jeffrey Berenberg, MC

conducted at Tripler Army Medical Center

(Name of Institution)

The implications of my voluntary participation/consent as legal representative; duration and purpose of the research study; the methods and means by which it is to be conducted; and the inconveniences and hazards that may reasonably be expected have been explained to me by

_____

I have been given an opportunity to ask questions concerning this investigational study. Any such questions were answered to my full and complete satisfaction. Should any further questions arise concerning my rights/the rights of the person I represent on study-related injury, I may contact

the Center Judge Advocate

at Tripler Army Medical Center, Tripler AMC, HI 96859-5000 (808) 433-5311

(Name, Address and Phone Number of Hospital (Include Area Code))

I understand that I may at any time during the course of this study revoke my consent and withdraw/have the person I represent withdrawn from the study without further penalty or loss of benefits; however, I/the person I represent may be required (military volunteer) or requested *(civilian volunteer)* to undergo certain examination if, in the opinion of the attending physician, such examinations are necessary for my/the person I represent's health and well-being. My/the person I represent's refusal to participate will involve no penalty or loss of benefits to which I am/the person I represent is otherwise entitled.

_____

PART A (2) - ASSENT VOLUNTEER AFFIDAVIT *(MINOR CHILD)*

I, _____, SSN _____ having full capacity to assent and having attained my _____ birthday, do hereby volunteer for _____ to participate in _____

_____

(Research Study)

_____

under the direction of: _____

conducted at: _____

(Name of Institution)

(Continue on Reverse)

If I agree to take part in this study, I will be put on study in a manner similar to the toss of a coin called randomization. Randomization is commonly used in studies such as this and the chance of my receiving either one of the following two treatments is equal.

Treatment Arm I

VP-16 will be injected into a vein over a period of 30-60 minutes for 3 days in a row (Days 1-3).
Carboplatin will be injected into a vein over a period of 30-60 minutes on Day 1.
A second course of chemotherapy will be repeated in 3 weeks.

After each course of chemotherapy, my doctor will check my disease for a response. If at any time my disease gets worse, my doctor will take me off study and offer me other treatment. If my disease has completely disappeared, partially disappeared or remained the same, 3-5 weeks after I complete my chemotherapy, I will undergo surgery to have my tumor removed.

If my tumor is completely removed when I recover from surgery, I will have 3 additional courses of the same chemotherapy (VP-16/carboplatin). The chemotherapy will be given every 21 days for a total of 3 courses.

If my white blood count drops low because of my chemotherapy, my doctor may give me G-CSF to treat the low blood count. My doctor may continue giving me G-CSF for all courses of chemotherapy. I will receive G-CSF starting on Day 4 of each course and continue each day until my white blood count has increased. G-CSF will be injected underneath the skin (subcutaneously). I will have blood tests two times a week while I receive G-CSF.

Treatment ARM II

I will undergo a surgical resection (thoracotomy) of my lung tumor. The surgery will be explained to me by my surgeon.

If my tumor is completely removed after surgery, I will be followed without further treatment. If my surgeon is unable to remove all my tumor, I will be taken off study and offered other treatment.

ALTERNATIVE THERAPY: I understand that other treatments may be available such as treatment with other single or combination chemotherapy. However, my doctor feels that my treatment on this study will give at least as good a chance of controlling my cancer as I might expect from other therapies. I understand that my doctor can provide detailed information about my disease and the various treatments available.

RISKS AND BENEFITS: It is not possible to know whether or not I will benefit from this treatment program. A possible benefit to me might be better disease control and longer life. In addition to the side effects (harmful effects) described under the drugs, an additional risk may include an allergic reaction to the drugs.

Although the drugs have been tested before with the side effects listed below, there is the possibility of other side effects occurring which have not been seen before.

If I am pregnant or nursing a child, I cannot take part in this study. If I am able to bear or father a child, I must use effective birth control because it is not known what the effects of the drugs used in this study will be on an unborn child.

The drugs used in this study ~~has~~ have the potential to cause abnormalities in the developing fetus.

It has been explained to me that if I am to receive the drugs that I should not be pregnant at the time the drugs are started and should not become pregnant for 12 months after they are stopped. Pregnancy within those 12 months after drug administration may create a potential risk to the unborn baby.

The drugs will not be given to an individual whose pregnancy test is positive (or who is unable to state that she is not pregnant). If your pregnancy test is positive, a confirmatory pregnancy test will be done.

In order to participate in this study, I should have avoided becoming pregnant from the first day of my most recent menses.

To avoid becoming pregnant, I should either abstain from sexual relations or practice a method of birth control. Except for surgical removal of the uterus, birth control methods such as the use of condoms, a diaphragm or cervical cap, birth control pills, IUD, or sperm killing products are not totally effective in preventing pregnancy. The only ways to completely avoid drug associated risk to the unborn baby are (1) do not become pregnant or (2) do not receive these drugs.

Adverse effects of the drugs including fever and allergic or toxic reaction might affect a developing fetus. Further, the drugs might result in unknown risks of deformities or death to the unborn baby. A negative pregnancy test does not absolutely prove that your are not pregnant. Regardless of the results of the pregnancy test which you were administered as part of the screening for this study, you should not participate if you think there is a possibility that you might be pregnant.

The side effects which have been observed in some patients with Carboplatin, VP-16, G-CSF and surgery are:

<u>Carboplatin (CBDCA)</u>

This drug can affect several organs (or parts) of the body, in addition to the cancer cells. Nearly everyone has some type of stomach upset such as loss of appetite, nausea and/or vomiting. Nausea and vomiting usually begin 1 to 6 hours after the drug has been given and usually does not last for more than 24 hours, but loss of appetite may persist for up to a week.

Sometimes the drug can cause high-frequency (above normal speech) hearing loss only detectable by hearing tests (audiograms). Permanent or temporary ringing in the ear can occur.

Carboplatin can decrease the blood cells produced in the bone marrow. This can lead to:

1) decreased (lower) white cells and may make it easier to get infections.
2) lower number of red cells which can make it hard to breathe and cause dizziness, weakness and extreme tiredness.
3) lower platelets (blood clotting cells) which can result in easy bruising or bleeding for a longer time.

The drug's effect on the bone marrow is only temporary and blood transfusions are available if needed until the bone marrow recovers. Blood samples will be taken often to monitor (follow) these side effects of the drug on the bone marrow.

When used in high doses, temporary liver damage and lung scarring have been reported. More recently, anemia due to damage of red blood cells and abnormal clotting of blood have also been noted.

Other complications, although rare, that can occur are loss of taste, allergic reactions and loss of muscle or nerve function which may cause weakness or numbness similar to having one's hand "fall asleep", and may be associated with some clumsiness of movement. Also two cases of visual impairment have been reported, patient improved with medication.

VP-16 (VP-16-213, Etoposide)

This drug can affect several organs (or parts) of the body, in addition to the cancer cells.

There is a 25% chance that the stomach and intestine can be affected causing mild nausea or vomiting. These usually develop shortly after the drug is given and usually last less than 24 hours. Diarrhea is rare.

VP-16 can reduce the blood cells produced in my bone marrow. This can lead to:

1) decreased (lower) white cells and may make it easier to get infections.
2) lower number of red cells which can make it hard to breathe and cause dizziness, weakness and extreme tiredness.
3) lower platelets (blood clotting cells) which can result in easy bruising or bleeding for a longer time.

The drug's effect on the bone marrow is only temporary and blood transfusions are available if needed until the bone marrow recovers. Blood samples will be taken frequently to monitor (follow) these effects of the drug on the bone marrow.

Temporary hair loss (not only from the scalp but possibly underarms, beard, eyelashes and pubic area) can occur. The loss is sometimes total but the hair does grow back when the drug treatment is stopped. When the hair grows back it may or may not be the same color or texture.

Giving the drug too rapidly into the vein may cause burning at the site and also can result in lowering of the blood pressure. To avoid this, the drug will be given over at least 30 minutes. If some of the drug accidentally leaks out of the vein where it is being given, there may be severe irritation and/or damage to the surrounding tissue. Any pain or unusual feeling should be reported so that the vein can be checked.

Other complications, although rare, are mouth ulcers, fever, chills and headache. Very rarely, patients have had allergic reactions to the drug causing a red skin rash and difficulty breathing. There may also be some numbness, tingling of the hands or feet, and weakness due to nerve tissue damage.

Because it is not known what the effects of this drug will be on an unborn child, effective birth control must be used.

Very rarely, acute leukemia has also been known to be a reaction to this drug after long term use.

G-CSF

G-CSF may cause mild to moderate bone pain, muscle cramps and/or back and leg pain. In addition, flu-like symptoms, which include fever, chills, fatigue and headaches may occur. Occasionally, nausea and skin rashes have been reported.

An allergic reaction can cause shortness of breath and low blood pressure, but close monitoring will be done if this happens.

There may be hair thinning and an increase in the size of the spleen, an increase in the alkaline phosphatase blood test and lowered platelet count with prolonged administration of G-CSF. This drug is not given over a prolonged period in this study.

Surgery

The complications of surgery (thoracotomy) to remove lung cancer are well-known. They include: bleeding, infection in the chest (empyema) or in the incision, shortness of breath and pneumonia. Less frequently, patients may experience abnormal heart rhythms or poor healing of the end of the windpipe requiring re-operation for treatment. The overall risk of serious or life-threatening complications is less than 10%. Rarely, there are side effects from the anesthesia.

Your surgeon will discuss with you these potential complications and any other problems that might take place in your particular case.

NEW INFORMATION: I understand that if no benefit occurs from my treatment, I will be informed of this, the treatment will be stopped, and further treatment will be discussed at that time. If new information about any of these treatments develops or any other new treatment for my condition is discovered, my doctor will tell me.

COSTS AND PAYMENTS: Laboratory tests (including blood and urine), x-rays and scans will be done as required to check the effects of my treatment. There is no cost to me for participation in this study other than the usual cost of care.

SAFEGUARDS: Every reasonable effort will be made to minimize the side effects or reactions to the therapy. If symptoms should occur, they will be treated appropriately and promptly. If the side effects are severe, the drugs may have to be discontinued.

CONFIDENTIALITY: I understand that any information obtained from this research will be kept strictly confidential. Individual data will be submerged in results, so there will be no unauthorized use of data. All data and consent forms will be kept in a secure place. Information regarding my medical records will be given only to other doctors and researchers within the Southwest Oncology Group, the National Cancer Institute, the Food and Drug Administration, and Tripler local authorities to evaluate the results of this study. I will also release pathologic specimens, laboratory samples, x-rays, and copies of my medical records which will be made available for review.

INVESTIGATIONAL DRUGS: none

NUMBER OF PATIENTS TO BE ENROLLED: 400; approximately 8 from Tripler Army Medical Center

EXPECTED DURATION OF YOUR PARTICIPATION IN THE STUDY: 1 year

UNFORESEEN RISKS FROM PARTICIPATION: There may be unforeseen risks in the treatment given in this study.

CIRCUMSTANCES UNDER WHICH YOUR PARTICIPATION MAY BE TERMINATED WITHOUT YOUR CONSENT: (a) Health conditions under which your participation possibly would be dangerous. (b) Other conditions that might occur that would make your participation detrimental to your health.

DOMICILIARY CARE STATEMENT: The extent of medical care provided, should it become necessary, is limited and will be within the scope authorized for Department of Defense (DOD) health care beneficiaries. Necessary medical care does not include domiciliary care.

FOR FURTHER INFORMATION: Please contact the principal investigator,
Dr. Jeffrey L. Berenberg, COL, MC
Department of Medicine, Hematology-Oncology Section
Tripler AMC, Hawaii 96859-5000 Phone Number: (808) 433-4089

FREE WITHDRAWAL: I understand that I am free to refuse to take part in this study or stop at any time and that my decision will not affect my care in any way or cause a loss of benefits to which I might otherwise be entitled.

NO COMPENSATION FOR ILLNESS OR INJURY: I understand that in the event of an injury or illness resulting from this research procedure, no monetary compensation will be made, but any immediate emergency medical treatment which may be necessary will be made available to me.

VOLUNTARY CONSENT: I certify that I have read the above information, or it has been read to me, that I understand the risks and benefits involved and that any questions I have about this study have been or will be answered by the doctor and that permission is freely given. I understand that my consent does not take away any of my legal rights in case of negligence as to anyone who is working on this project.

IF THERE IS ANY PORTION OF THIS EXPLANATION THAT YOU DO NOT UNDERSTAND, ASK THE INVESTIGATOR BEFORE SIGNING.
You will be provided a copy of this consent form.

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I have read the above explanation and agree to participate in the investigational study described.

Typed Name & Signature of Volunteer	Date
Typed Name & Signature of Legal Guardian	Date
Typed Name & Signature of Witness	Date