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Northwest Community Clinical Oncology Program (NWCCOP)

315 Martin Luther King Jr. Way

Tacoma, WA 98405

Phone: (253) 403-1461

Fax: (253) 403-1615

Sponsored and Funded by the National Cancer Institute

CONSENT FORM

CIRB C40101: Cyclophosphamide and Doxorubicin (CA x 4 cycles) versus Paclitaxel (4 cycles) as Adjuvant Therapy for Breast Cancer In Women with 0-3 Positive Axillary Lymph Nodes: A Phase III Randomized Study (Randomization to Treatment groups 2 and 4 is no longer available, effective 12/15/07)

INVESTIGATORS:

Lauren K. Colman, MD, Chris Chen, MD, Jay Klarnet, M.D., W. Welby Cox, MD, FACP, Xinda Wang, MD, Daniel Moore, MD, Troy Wadsworth, MD, 1003 South 5th Street-3rd Floor, Tacoma, WA 98405 (253) 403-1677.

Robert McCroskey, MD, Sibel Blau, MD, Andrea Rose, MD, 400-15th Avenue SE, Puyallup, WA 98372 (253) 841-4296.

Frank Senecal, MD, Thomas Baker, MD, Lorrin Yee, MD, Moacyr Oliveira, MD
1624 South I Street, Tacoma, WA 98405 (253) 383-3366.

Paul Robertson, MD, Steven Gorton, MD, James Lechner, MD, Harry Griffith, MD,
Xingwei Sui, MD, 4525 Third Ave. SE, Suite 200, Lacey, WA 98503 (360) 754-3934.

Dustan Osborn, MD, Ronald Goldberg, MD, Nicole Grous, MD, Joseph Ye, MD,
Min Kang, MD, 3920 Capital Mall Drive SW, Suite 100, Olympia, WA 98502
360-753-4700 and 222-2nd Street NE, Suite B, Auburn, WA 98002 (253) 887-9333.

John Rieke, MD, Suraj Singh, MD, Carolyn Rutter, MD, 1003 South 5th Street, 1st Floor,
Tacoma, WA 98405 (253) 403-4994.

Michael Liao, MD, 400 -15th Ave SE, Puyallup, WA 98372 (253) 697-4829

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This is a clinical trial (a type of research study). Clinical trials include only patients who choose to take part. Please take your time to make your decision. Discuss it with your friends and family.

You are being asked to take part in this study because you have had breast cancer that has been removed by surgery, with either no lymph nodes or as many as 3 lymph nodes under your arm involved with cancer.

WHY IS THIS STUDY BEING DONE?

You have recently had surgery to remove your breast cancer. Your doctor has determined that adjuvant chemotherapy (adjuvant means “in addition” to the surgery) is advisable for your stage of breast cancer. Previous clinical trials have shown that use of chemotherapy reduces the likelihood that the cancer will come back in other parts of the body, such as the lungs, liver, bone, or elsewhere. A commonly used chemotherapy treatment, which has been a standard treatment for many patients with your type of cancer, is the combination of cyclophosphamide and doxorubicin (CA), given through a vein every 2 or 3 weeks for 4 treatments.

The purpose of this study is to compare the effectiveness of the standard adjuvant chemotherapy CA with the chemotherapy drug paclitaxel. In addition, we will learn more about the side effects of each treatment, and compare them with each other, in order to measure the effectiveness and tolerability of the treatments.

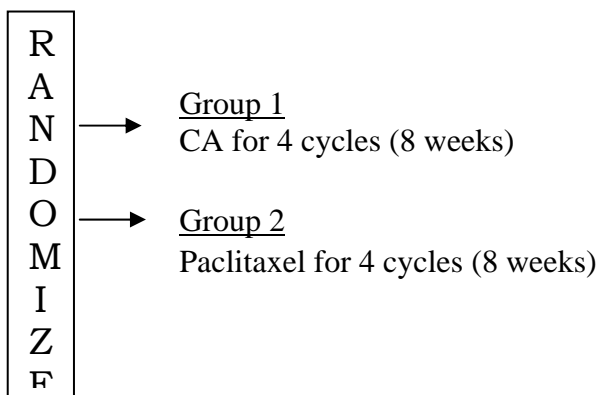
Cyclophosphamide and doxorubicin have been approved by the Food and Drug Administration of the United States (FDA) for the treatment of breast cancer. Paclitaxel given after combination chemotherapy has been approved for the adjuvant treatment of breast cancer that had spread to the lymph nodes. Paclitaxel is also approved for the treatment of breast cancer that has grown or that has spread to other parts of the body after previous chemotherapy. The use of paclitaxel as an adjuvant treatment for breast cancer that has not spread to the lymph nodes, as used in this study, are considered to be investigational or research.

HOW MANY PEOPLE WILL TAKE PART IN THE STUDY?

About 4646 women will take part in this study.

WHAT IS INVOLVED IN THE STUDY?

If you agree to participate, you will be “randomized” into one of the study treatment groups described below. Randomization means that you are assigned to a group by chance. The treatment group you are assigned to is chosen by a computer. Neither you nor your study doctor will choose which group you will be in. You will have an equal chance of being assigned to either of the 2 groups.



Group 1

If you are assigned to this treatment group, you will receive standard CA combination chemotherapy as an outpatient in the clinic. You will be given cyclophosphamide through a vein, followed by doxorubicin through a vein on day 1, every 14 days. This 14 day period is called a treatment cycle. You will receive 4 cycles of this treatment.

Group 2

If you are assigned to this treatment group, you will be given medications before the paclitaxel that have been shown to prevent allergic reactions, which can be severe. You will then be given the drug paclitaxel as an outpatient in the clinic. You will be given the paclitaxel through a vein, over 3 hours on day 1, every 14 days. This 14 day period is called a treatment cycle. You will continue to receive this treatment every 14 days for 4 cycles.

All Treatment Groups

Filgrastim or sargramostim, medications that are stimulators of white blood cell growth, is recommended to be given as an injection under the skin, for about a week after each treatment, beginning 2 days after the treatment and continuing until about 10 days after the treatment. You, a family or a friend may be taught to give these injections at home. Pegfilgrastim is another medication that stimulates white blood cell growth. It is given as an injection under the skin, as a single dose, 24-36 hours following each cycle of treatment.

After you have completed the study treatment, if your breast cancer is the type that is responsive to hormones your doctor may recommend hormonal therapy. Tamoxifen may be recommended for women who have not yet experienced menopause. Tamoxifen, anastrozole, exemestane or letrozole may be recommended for women who have experienced menopause.

If your breast cancer is the type that is responsive to trastuzumab (also known as Herceptin®) your doctor may recommend treatment with this drug.

If the type of surgery you had to remove your breast cancer was a “lumpectomy” you will receive radiation therapy to the breast. If the type of surgery you had was a “mastectomy” your doctor may also recommend that you receive radiation therapy to the breast. If you are going to receive radiation therapy it may be given before the study chemotherapy has been started or after it has been completed.

Testing and Follow-up

If you take part in this study, you will have the following routine tests and procedures before the study treatment begins: you will be asked to give your medical history and have a physical examination, blood tests, an electrocardiogram (EKG) and a chest x-ray.

During the time that you are receiving the study treatment, a physical examination and blood tests will be done on day 1 of each treatment cycle. EKGs will be done as your study doctor feels necessary.

After the study treatment has been completed, the physical examinations will be done every 6 months for 2 years, then annually thereafter. The blood tests and chest x-rays will be done as your doctor feels necessary.

HOW LONG WILL I BE IN THE STUDY?

We think you will receive study treatment for about 2 months. After the treatment has been completed your doctor will follow your medical condition for up to 15 years to learn about the long-term effects of the study treatment.

Your study doctor will discontinue the study treatment if: the breast cancer returns in the breast or an area outside the breast; you experience intolerable side effects; you and your study doctor decide that it is in your best interest to stop; or if new information becomes available which suggests that the study treatment is unsafe or not effective for you.

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to your study doctor first.

WHAT ARE THE RISKS OF THE STUDY?

While on the study, you are at risk for these side effects. You should discuss these with your study doctor. There also may be other side effects that we cannot predict. Other drugs will be given to make side effects less serious and uncomfortable. Many side effects go away shortly after the study drugs are stopped, but in some cases side effects can be serious or long-lasting or permanent.

CYCLOPHOSPHAMIDE + DOXORUBICIN (CA)

Likely

- Temporary lowering of the number of white blood cells (cells that help your body fight infection)
- Temporary lowering of the number of red blood cells (may cause a feeling of tiredness, and shortness of breath)
- Temporary lowering of the number of blood platelet cells (cells that help your blood clot)
- Nausea, vomiting or diarrhea
- Loss of appetite
- Temporary loss of scalp and body hair
- Skin and nail discoloration
- Sores in the mouth and/or throat
- Urine may turn red for 1-2 days (due to the color of the doxorubicin)
- Irritation of the bladder (where urine is stored)
- Sensitivity to sunlight
- Premenopausal women may experience irregular periods or stop menstruating altogether for a time. The ability to have children may be permanently impaired.

Less Likely, But Serious

- Blood in the urine
- Heart damage
- Irregular heart beat (may occur right after the drugs are given)
- Congestive heart failure (a decrease in the heart's ability to pump effectively, which may lead to shortness of breath)
- Skin tissue damage if some of the drug leaks from the vein while it is being given
- Acute leukemia
- Serious, potentially life threatening allergic reaction

PACLITAXEL

Likely

- Temporary lowering of the number of white blood cells (cells that help your body fight infection)
- Temporary lowering of the number of red blood cells (may cause a feeling of tiredness, and shortness of breath)
- Temporary lowering of the number of blood platelet cells (cells that help your blood clot)
- Diarrhea
- Loss of scalp and body hair
- Temporary or mild numbness or tingling in the fingers or the toes
- Temporary pain in the muscles and joints

Less Likely

- Nausea, vomiting
- Mouth sores (like canker sores)
- Problems with liver function (as seen on a blood test)

Less Likely, But Serious

- Allergic reactions, which may include rash and shortness of breath (may happen while the drug is being given)
- Slow or irregular heart beat
- Low blood pressure
- High blood pressure
- Numbness or tingling in the fingers or toes that may cause difficulty in walking or buttoning clothes on a long term basis

Reproductive risks: Because the drugs in this study can affect an unborn baby, you should not become pregnant while on this study. If you are a woman of childbearing potential you must practice an effective, non-hormonal method of birth control while receiving study treatment and for at least 2 months after completing or discontinuing study treatment. Ask about birth control counseling and more information about preventing pregnancy. You should not nurse your baby while on this study.

Medications which must not be taken while receiving study treatment:

Hormone therapy including oral contraceptives “the pill”, postmenopausal hormone replacement therapy and raloxifene. If you are taking any of these medications you must discontinue their use before study entry. Your study doctor will discuss this with you.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

If you agree to take part in this study, there may or may not be direct medical benefit to you. We hope the information learned from this study will benefit other patients with breast cancer in the future.

WHAT OTHER OPTIONS ARE THERE?

Other treatment options include: adjuvant chemotherapy with CA, or different drugs, and possibly radiation therapy or hormonal therapy.

Your doctor will discuss the treatment options with you.

WHAT ABOUT CONFIDENTIALITY?

Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be published, but individual patients will not be identified in these publications.

Your medical record, including identifying information may be inspected and/or photocopied by: The Cancer and Leukemia Group B (CALGB), the National Cancer Institute (NCI), the Food and Drug Administration of the United States, or other Federal or state government agencies in the ordinary course of carrying out their governmental functions. If you are participating in this study through the Cancer Trials Support Unit (CTSU is a clinical trials mechanism sponsored by the NCI to provide greater access to phase III trials), a record of your progress will also be kept by the CTSU. If your record is used or disseminated for such purposes, it will be done under conditions that will protect your privacy to the fullest extent possible consistent with laws relating to public disclosure of information and the law-enforcement responsibilities of the agency.

WHAT ARE THE COSTS?

Taking part in this study may lead to added costs to you or your insurance company. Please ask about any expected added costs or insurance problems.

In the case of injury or illness resulting from this study, emergency medical treatment is available but will be provided at the usual charge. No funds have been set aside to compensate you in the event of injury.

You or your insurance company will be charged for continuing medical care and/or hospitalization.

You will receive no payment for taking part in this study.

WHAT ARE MY RIGHTS AS A PARTICIPANT?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or willingness to continue in this study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

A Data and Safety Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study.

WHOM DO I CALL IF I HAVE QUESTIONS OR PROBLEMS?

For questions about the study or a research-related injury, contact the researcher at the number listed on the cover sheet.

For questions about your rights as a research participant, contact the MultiCare Institutional Review Board (which is a group of people who review the research to protect your rights) at 253-403-3844.

It may be necessary to contact you at a future date regarding new information about the treatment you have received. For this reason, we ask that you notify the institution where you received treatment on this study of any changes in address.

If you move, please provide your new address to the following person:

Karyn Hart
Research Coordinator
Northwest CCOP
315 Martin Luther King Jr, Way
Tacoma, WA 98405
(253) 403-2394

WHERE CAN I GET MORE INFORMATION?

You may call the NCI's **Cancer Information Service** at
1-800-4-CANCER (1-800-422-6237) or **TTY: 1-800-332-8615**

Visit the NCI's Web sites...

cancerTrials: comprehensive clinical trials information

http://www.cancer.gov.clinical_trials/

CancerNet™: accurate cancer information including PDQ

http://www.cancer.gov/cancer_information/

You will get a copy of this form. You may also request a copy of the protocol (full study plan).

SIGNATURE

You are deciding whether or not to take part in this study. If you sign, it means that you have decided to volunteer to take part in this study, and that you have read and understood all the information on this form.

Patient's name (printed or typed)

Patient's Signature Date

Physician name (printed or typed)

Physician Signature Date

Signature of person conducting the
Informed consent discussion

Date

RELATED TISSUE STUDIES

In addition to the treatment study, the researchers are also interested in studying some of the tissue that was taken from you in the normal course of treatment and care. If you agree, a sample of your breast cancer tissue, which was taken at the time of diagnosis for routine testing, will be sent to a CALGB research laboratory for future research studies.

Where does tissue come from?

After a person has had a biopsy (or surgery) and all tests have been done, there may be some left over tissue. Sometimes, this tissue is thrown away because it is not needed for the patient's care. Instead, a patient can choose to have the tissue kept for future research. People who are trained to handle tissue and protect donors' rights make sure that the highest standards of quality control are followed by the CALGB. If you agree, only left over tissue will be saved for research. Your doctor will not take more tissue during surgery than needed for your care.

Why do people do research with tissue?

Research with tissue can help to find out more about what causes cancer, how to prevent it, how to treat it, and how to cure it. Research using tissue can also answer other health questions. Some of these include finding the causes of diabetes and heart disease, or finding genetic links to Alzheimer's.

The research that may be done with your breast cancer tissue samples probably will not help you. However, it might help people in the future who have breast cancer or other diseases.

What type of research will be done with my tissue?

Many different kinds of studies use tissue. Some researchers may develop new tests to find diseases. Others may develop new ways to treat or even cure diseases. In addition, some of this tissue may be used to establish products that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

Will I find out the results of the research using my tissue?

You will receive the results of your biopsy, but you will not receive the results of research done with your tissue. This is because research can take a long time and must use tissue samples from many people before results are known. Results from research using your tissue may not be ready for many years and will not affect your care right now, but they may be helpful to people like you in the future.

How am I protected?

Tissue samples will be stored at a CALGB Pathology Coordinating Office. The CALGB Statistical Center will perform all analyses of data and store all study results. Your tissue sample will not be stored with your name on it. Instead, it will be labeled with a special CALGB identification number. The only location where your name and special identification number will be stored together is at the CALGB Statistical Center. The greatest effort will be made to see that all personal information that can identify you is kept under conditions that protect your privacy.

Information about your participation in future studies and results of any tests performed on your sample will be kept only at the CALGB Statistical Center. This information will not be made available to your doctors or to individual researchers at CALGB. Test results from this study will not be put in your medical records. All study information, including test results, is stored under conditions that limit access in order to protect the privacy of the women participating in this study.

If you decide now to allow your tissue sample to be used in these and future studies and then change your mind at any time about participating in the studies, just contact your institution and let them know that you do not want the researchers to use your sample. Then it will no longer be used for research.

The CALGB will protect your records so that your name, address and phone number will be kept private. Efforts will be made to keep your personal information confidential. We cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results from these studies may be published, but individual patients will not be identified in these publications.
There will be no charge to you for participating in these research studies.

Your participation in these research studies is entirely voluntary. You do not have to participate in this portion of the study to receive the study treatment.

My tissue may be kept for use in research to learn about, prevent, treat or cure cancer.

____ Yes ____ No ____ Initials ____ Date _____

My tissue may be kept for research about other health problems (for example: causes of diabetes, Alzheimer's disease and heart disease).

____ Yes ____ No ____ Initials ____ Date _____

Someone from the CALGB may contact me in the future to ask me to take part in more research.

____ Yes ____ No ____ Initials ____ Date _____

RELATED BLOOD STUDIES

Many factors contribute to the success of chemotherapy, including the way the human body processes the chemotherapy drugs. The researchers conducting the treatment study would also like to collect an additional sample of your blood for the purpose of learning about how certain genes influence the effectiveness and side effects of adjuvant breast cancer treatment with the chemotherapy drug combination of cyclophosphamide plus doxorubicin or paclitaxel given alone. In order to study the genes the DNA must be removed from your blood sample. DNA is the substance that makes up your genes. Genes are the units of inheritance that are passed down from generation to generation. They are responsible for eye color, hair color, blood type and hundreds of other traits.

These tests will not involve the study of cancer genes that can be inherited (passed from parents to children).

About 1 to 2 teaspoons of blood will be drawn before you begin the study treatment.

The results of these research studies will not be given to your doctor or to you, nor will the results have any effect on your treatment.

There will be no charge to you for participating in these studies.

Safeguards of Confidentiality in Studies Involving Genes

- Blood samples will be stored at a CALGB laboratory. Your blood sample will not be stored with your name on it. Instead, it will be labeled with a special CALGB identification number. The CALGB Statistical Center will perform all analyses of data and store all study results. The only location where your initials, special identification number and the results of the laboratory tests will be stored together is at the CALGB Statistical Center. The results from these studies may be published, but individual patients will not be identified in the publications.
- Your blood will be used only for the study of genes involved in cancer.
- If you decide now to give a sample of blood and then later change your mind at any time about participating in the study, you should contact your institution and let them know that you do not want the researchers to use your sample. Then it will no longer be used for research.
- Because it is not possible for the CALGB to know what studies of breast cancer may be appropriate in the future we would like to store your DNA for future studies. Your DNA samples for future studies would be protected as described above. Future investigators must apply to the CALGB and have their research project reviewed and approved by the CALGB. There will be no charge to you for participating in the future research studies.

Your participation in the studies described above and/or in this DNA specimen bank for future studies is entirely voluntary. You do not have to participate in this portion of the study to receive the study treatment.

In addition, your blood may be used to develop products that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.

My blood may be used for the purpose of learning about how certain genes influence the effectiveness and side effect of adjuvant breast cancer, as described above.

____ Yes ____ No Initials ____ Date _____

I agree that my DNA obtained from my whole blood may be kept for use in future DNA research studies to learn more about cancer.

____ Yes ____ No Initials ____ Date _____

Authorization to Use or Disclose (Release) Identifiable Health Information For Research

Participant's Name: _____

Birthdate: _____

1. What is the purpose of this form?

The Cancer Trials Support Unit (CTSU) is an organization that does research to learn about the causes of cancer, and how to prevent and treat cancer. Researchers would like to use your health information for research. This information may include data that identifies you. Please carefully review the information below. If you agree that researchers can use your identifiable health information, you must sign and date this form to give them your permission.

2. What health information do the researchers want to use?

The researchers want to abstract and use the portions of your medical record that they will need for their research. If you enter a CTSU research study, information that will be used and/or released may include your complete medical record, and in particular, the following:

- the history and diagnosis of your disease
- specific information about treatments you received
- information about other medical conditions that may affect your treatment
- medical data, including laboratory test results, tumor measurements, CT scans, MRIs, X-rays, photographs of radiation therapy target areas, and pathology results
- information on side effects (adverse events) you may experience, and how these were treated
- long-term information about your general health status and the status of your disease
- tissue and/or blood samples, associated data related to the analysis of the samples

You may request a blank copy of the CTSU data forms from the Northwest CCOP to learn what information will be shared.

3. Why do the researchers want my health information?

The Northwest CCOP will collect your health information and share it with the CTSU if you enter a Cooperative Group research study, or to evaluate your eligibility for a study. The CTSU researchers will use your information for the following cancer research study(ies). You are being asked to take part in a study known as CTSU 40101: Cyclophosphamide and doxorubicin (CA) (4 vs 6 cycles) versus paclitaxel (4 vs 6 cycles) as adjuvant therapy for breast cancer women with 0-3 positive axillary lymph nodes: A 2x2 factorial phase III randomized study.

4. Who will be able to use my health information?

The Northwest CCOP will use your health information for research. As part of this research, they may give your information to the following Groups taking part in the research. The Northwest CCOP may also permit staff from these Groups to review your original records as required by law for audit purposes.

the Cancer Trials Support Unit (CTSU), a research group sponsored by the National Cancer Institute (NCI) to provide greater access to cancer trials
National Cancer Institute of Canada Clinical Trials Group (NCIC CTG), the research group coordinating this study.

The company that makes the study drugs and are supporting the study.

NCI US (National Cancer Institute in the United States)

Therapeutic Products Program of Health Canada (because it oversees the use of drugs in Canada)

The Northwest CCOP

public health agencies and other government agencies (including non-U.S.) as authorized or required by law

other people or organizations assisting with CTSU research efforts and the Food and Drug Administration

central laboratories, central review centers, and central reviewers. The central laboratories and review agencies may also give your health information to those groups listed above.

5. *How will information about me be kept private?*

The CTSU will keep all identifiable health information confidential to the extent possible, even though they and other federal research groups are not subject to the same federal privacy laws governing clinical centers. The CTSU will not release identifiable health information about you to others except as authorized by this form, or required by law. If your identifiable health information must be shared with other organizations, the privacy laws that govern those organizations would apply.

6. *What happens if I do not sign this authorization form?*

If you do not sign this authorization form, you will not be able to take part in a research study for which you are being considered.

7. *If I sign this form, will I automatically be entered into the research study?*

No, you cannot be entered into any research study without further discussion and separate consent. After discussion, you may decide to take part in the research study. At that time, you will be asked to sign a separate research consent form.

8. *What happens if I want to withdraw my authorization?*

You can change your mind at any time and withdraw this authorization. This request for withdrawal must be made in writing. Beginning on the date you withdraw your authorization, no new identifiable health information will be used for research. However, researchers may continue to use the health information that was provided before you withdrew your permission.

If you sign this form and enter the research study, but later change your mind and withdraw your authorization, you will be removed from the research study at that time.

To withdraw your authorization, please contact the person below. She will make sure your written request to withdraw your authorization is processed correctly.

Karyn Hart, RHIT, CCRP
Program Coordinator
Northwest CCOP
315 Martin Luther King, Jr. Way
Tacoma, WA 98405
(253) 403-1461

9. How long will this authorization last?

If you agree by signing this form that researchers can use your identifiable health information, this authorization has no expiration date. However, as stated above, you can change your mind and withdraw your permission at any time.

10. What are my rights regarding my identifiable health information?

You have the right to refuse to sign this authorization form. You have the right to review and/or copy records of your health information kept by the Northwest CCOP. You do not have the right to review and/or copy records kept by the CTSU or other researchers associated with the research study.

Signatures

I agree that my identifiable health information may be used and disclosed for research purposes described in this form.

Signature of Patient or Patient's Legal Representative: _____ Date: _____

Printed Name of Legal Representative (if any): _____

Representative's Authority to Act for Patient: _____

Signature of Person Obtaining Authorization: _____

Printed Name of Person Obtaining Authorization: _____