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Informed Consent Form for Parents of Children Ages 1 Month through 17 Years Who are Receiving Treatment for Solid Tumor Cancers at *INSTITUTION* To Participate in Research Using Lymphoseek

Title:	A Prospective, Open-Label, Multicenter Study of Lymphoseek® as Lymphoid Tissue Targeting Agent in Pediatric Patients With Melanoma, Rhabdomyosarcoma, or Other Solid Tumors Who Are Undergoing Lymph Node Mapping
Protocol:	NAV3-18
Sponsor:	Cardinal Health 414, LLC Dublin, Ohio United States
Investigator:	
Site:	

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Introduction

I am Dr. #######, working for *Name of INSTITUTION*. We are doing research on solid tumors in children. These kinds of cancers in children are very rare.

I am going to give you information and ask you to have your child participate in this research. You do not have to decide today whether or not you agree that your child may participate in the research. Before you decide, you can talk to anyone you feel comfortable with including any member of the study team. This form is called an informed consent document and explains the purpose of the study including the risks associated with participating in the study.

There may be some words that you do not understand. Please ask me to stop as we go through the information and I will take time to explain. If you have questions later, you can ask them of me, the study doctor or the staff.

Why is this study being done?

Children with solid tumors have their tumors removed as part of their treatment whenever possible. Tumors sometimes spread to lymph nodes. Finding out if the tumor has spread to the lymph nodes helps your doctors determine the kind of care your child needs.

The purpose of this research study is to learn if using a drug called Lymphoseek can safely identify lymph nodes in children. Lymphoseek is approved by the U.S. Food and Drug Administration (FDA) for lymphatic mapping in adults with solid tumors. The use of Lymphoseek in this study is investigational because it is being tested in children.

Type of Research Intervention

This study involves two types of services. Some services are related to the research. Other services may be related to your child's usual medical care.

In this study, Lymphoseek will be injected in or around your child's tumor on the day of his or her surgery. Vital blue dye (Lymphazurin) may also be injected according to *Name of INSTITUTION's* standard-of-care. Lymphoseek is a radioactive mapping drug that sticks to lymph nodes and is able to be seen with a special camera or a hand-held detector. Lymphazurin is a blue dye that passes through lymph nodes and can be seen by the human eye. After injection of these drugs, this study will use a procedure called lymphatic mapping. The lymphatic system is made up of the tissues and organs involved in immunity, which aid in the fight against infection and cancer. Lymph nodes are small, bean-shaped organs located within the body throughout the lymphatic system.

Lymphatic mapping will take place during your child's surgery and is used to find the sentinel lymph node, a node where cancer cells are most likely to spread from your child's tumor. Lymphatic mapping is a widely used technique for detecting lymph nodes in adults with solid tumors like melanoma and breast cancer.

Additional language for institution where lymphatic mapping is standard of care:

Name of INSTITUTION uses lymphatic mapping in normal medical care during surgery for children with tumors. Lymphatic mapping in children is performed in the same manner as mapping

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in adults by using either vital blue dye by itself, using a radioactive mapping drug by itself, or by using vital blue dye combined with a radioactive mapping drug. The dye and/or the radioactive mapping drug travel through lymphatic channels to the nearest lymph node. The mapping drugs and dye allow the surgeon to determine if the tumor has spread to your child's lymph nodes. Vital blue dye may or may not be used in this study depending on the institution's standard-of-care. The use of Lymphoseek alone or vital blue dye in combination with Lymphoseek is for research purposes and is not considered routine medical care at our hospital.

Additional language for institutions where lymphatic mapping is NOT the standard of care:

Name of INSTITUTION does not use lymphatic mapping during surgery in children's normal medical care. This mapping would be an additional procedure performed with your child's surgery. Lymphatic mapping in children is performed by either using vital blue dye by itself, using a radioactive mapping drug by itself, or by using vital blue dye combined with a radioactive mapping drug. The dye and/or the radioactive mapping drug travel through a child's lymphatic channels to the nearest lymph node. The mapping drug and dye allow the surgeon to determine if the tumor has spread to your child's lymph nodes. Mapping lymph nodes and the use of Lymphoseek alone or vital blue dye in combination with Lymphoseek are for research purposes and are not considered routine medical care at our hospital.

Regardless of the kind of lymphatic mapping procedure your child will have, during surgery the study will include the use of a hand-held machine to find lymph nodes that may have the radioactive mapping drug inside. Those lymph nodes will be removed and looked at under a microscope.

Participant Selection

We are asking your child to take part in this research because he or she has a solid tumor. About 27 children will take part in this study at up to 10 hospitals in the US.

Lymphoseek has been found to be effective in finding sentinel lymph nodes in adults with melanoma and other solid tumors. It is important to determine whether or not Lymphoseek can safely find sentinel lymph nodes in children because finding these nodes may help doctors figure out if cancer cells have spread. Knowing this is very helpful to doctors who treat adults with cancer.

Voluntary Participation

Your decision to have your child participate in this study is entirely voluntary. It is your choice whether to have your child participate or not. If you choose not to consent, all the services you and your child receive at this clinic will continue and nothing will change. If you do decide to allow your child to participate, you can change your mind later and stop your child's participation in the study, even if you agreed earlier. Your decision to withdraw your child from the study will not affect the services that you and/or your child receive at this clinic.

If you decide to withdraw your child from participation, no additional follow up will be required for this study, but your physician will continue to follow your child after surgery as part of his or her routine care.

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Information on Lymphoseek

Lymphoseek has been tested in 10 clinical trials with adults. Of these clinical trials, Lymphoseek and vital blue dye have been compared in 2 clinical trials - one with adult breast cancer and one with adult melanoma patients. In each of the studies used to compare Lymphoseek and vital blue dye, Lymphoseek worked better than using vital blue dye for finding the lymph nodes. This study has been designed to test the safety of Lymphoseek and to compare how it works relative to vital blue dye (when it is used as standard-of-care) in children.

Lymphoseek is made by Cardinal Health 414, LLC (a subsidiary of Cardinal Health, Inc. [Cardinal]) who is working with your study doctor's local hospital to have it tested in children. Lymphoseek has attached to it a radioactive substance called ^{99m}technetium. Technetium can be detected by a gamma (radiation) camera and by using a radiation-detecting probe that's held by the surgeon during surgery. Lymphoseek, which binds to your child's lymph nodes, can be seen in images (pictures) taken using a camera (SPECT scanner, which is a "tunnel" that surrounds the patient). The camera detects the radiation given off by the decay of Lymphoseek and produces images of where Lymphoseek was located in your child's body. The gamma probe can also detect the radiation given off by the decay of Lymphoseek and can track the drug in your child's body.

If I agree to have my child join this study, what would my child need to do?

If you choose to allow your child to participate in this study, after you sign this informed consent document, your child's participation would include the following procedures and events. You may stay with your child during each of the visits and the procedures, with the exception of *Institution to list procedures in which parents cannot accompany child.*

Screening Visit

- The screening visit will take approximately 1 to 2 hours and may occur over more than one day. The information gathered during this visit will help your doctor confirm that your child is appropriate for the study.
- You and/or your child will give details about your child's medical history and medications your child has taken over the last 28 days. This information will help the study doctor determine your child's performance status (how severe the cancer is and how it affects everyday life).
- Your child will have an ECG. This stands for an electrocardiogram, which records the electrical activity of your child's heart.
- Your child's blood will be taken (about 1 tablespoon) and your child will be asked for a urine sample for routine testing. The blood and urine samples obtained during this research procedure will be used only for this study. (The blood and urine samples may be obtained the day of your child's surgery before drug injection rather than the screening visit).
- A physical examination (routine examination of your child's body including assessing height and weight) will be performed.
- Male children of childbearing age must be willing to use a condom during sexual intercourse or will practice abstinence while in the study.
- Female children of childbearing age must agree to the use of two physician-approved contraceptive methods or practice complete abstinence while in the study.

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Visit 1: Injection of Lymphoseek, SPECT Imaging (if applicable), and Surgery

- Before the study drug is injected
  - If your child is a female who is able to have children, a urine pregnancy test will be taken within 48 hours before injection. If your child is pregnant she will not be able to participate in the study.
  - If not collected at the Screening Visit, your child's blood may be taken (about 1 tablespoon) and your child will be asked for a urine sample for routine testing. The blood and urine samples obtained during this research procedure will be used only for this study.
  - Vital signs, which includes the assessment and recording of your child's blood pressure, heart rate, breathing rate, and temperature.
  - An interview about any changes in your child's health and medications from the screening visit will be conducted.
- Injection of the study drug
  - Your child will be injected with Lymphoseek. The amount of the injection is very small, about 0.1 – 1.0 mL, or less than 1/4 of a teaspoon
- After study drug injection
  - Vital signs, which include assessing and recording your child's blood pressure, heart beat, breathing rate, and temperature. Vital signs will be collected 10 minutes, 30 minutes and 1 hour after injection.
  - Your child will have an ECG at least 10 minutes after injection to record the electrical activity of your child's heart.
  - A SPECT scan may be performed (described in detail below).
- Surgery
  - Vital blue dye may or may not be injected depending on the *Name of INSTITUTION's* standard-of-care.
  - Your child's surgeon will use a hand-held radiation-detecting probe similar to a Geiger counter to track the Lymphoseek drug and help locate the sentinel lymph nodes during surgery.
  - Your child's lymph nodes will be removed if enough Lymphoseek or vital blue dye is found in them.
- After Surgery
  - Your child's blood will be taken (about 1 tablespoon) and your child will be asked for a urine sample for routine testing. The blood and urine samples obtained during this research procedure will be used only for this study.
  - You and/or your child will be asked about any side effects your child may have experienced.

Visit 2: Safety Follow Up (4-14 days after surgery)

- Vital signs, which includes the assessment and recording of your child's blood pressure, heart rate, breathing rate, and temperature.
- A physical examination (routine examination of your child's body) will be performed.
- You and/or your child will be asked about any changes in your child's health and medications.

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SPECT Imaging Procedure (if performed)

- After your child is injected with the Lymphoseek study drug, they will rest lying flat on his or her back on the scanner bed. His or her body will be positioned in the large, donut-shaped SPECT scanner. The SPECT scan will occur for duration of 45 minutes. SPECT scanners detect the radiation in the study drug to create a picture of the lymph nodes in your child's body.

How long will my child be in the study?

The screening period begins after you have signed this consent form. A follow up visit will occur 4-14 days after your child receives the radioactive mapping drug. Total participation may last up to 1.5 months.

What side effects or risks can my child expect from being in the study?

While the possibility of adverse (bad) reactions happening during this study is very low (based on the information available from use of Lymphoseek in adults), it is possible that your child may experience adverse reactions or discomfort. Every child taking part in the study will be watched carefully for any side effects; however, doctors don't know all of the side effects that might happen. It is important that you talk to your study doctor about any changes in health that your child experiences while taking part in this study. All side effects or changes in your child's normal health should be reported, even those changes you might not consider to be important.

In clinical trials of Lymphoseek, no patients experienced serious adverse reactions and the most common adverse reactions were injection site irritation and/or pain (<1%).

The vital blue due, named Lymphazurin, has been shown to produce an allergic reaction in a small number of people. These reactions may include itching, swelling and in rare instances shock. Serious allergic reactions may be life-threatening. Your child will be monitored to see if he or she develops this type of reaction. If your child does develop a reaction, he or she will receive prompt treatment. Lymphazurin can also cause a blue color around the injection site that can be seen for up to 48 hours after injection or temporarily change the color of your child's urine.

Radiation occurs naturally in the environment and is used in treating and examining patients for medical reasons. Radiation exposure increases other health risks including cancer. Lymphoseek uses a very small amount of radiation. The amount of radiation received from the study drug is similar to the radiation you get flying from New York to Los Angeles 7 times.

SPECT Imaging, which is optional in this study (camera used to take pictures of lymph nodes), also uses a small amount of radiation to increase the quality of the picture. The total amount of radiation your child will receive from the radioactive mapping drug and the scan is about the same as what he or she would receive naturally over the course of two years. The risk of developing health problems or cancer from this radiation exposure is very small, but there may be some risk and the risk may be cumulative (adds up over time). If you have additional questions about the radiation exposure to your child, you should ask to speak to the radiology doctor and your study doctor.

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Are there benefits to my child for taking part in the study?
Your child will not receive any direct medical benefit as a result of being in this study, but the information obtained during this study may benefit other pediatric patients. Your child's doctor may also use the information obtained from this study when looking at your child's overall health and treatment choices.

What are the costs of my child taking part in this study?
Lymphoseek is provided at no cost to you.

Additional cost language dependent on the standard of care at the institution.

Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. This discussion should include the costs of treating possible side effects.

Will my child be paid for taking part in this study?
You and your child will not be paid for participating in this study.

OR

Your child will not be paid for volunteering while being in this study. However, you will receive a stipend for incidental costs you may incur while on the study. You will receive the following amounts for each completed visit:

Screening Visit: _____
Injection, Imaging, and Surgery: _____
Post-Injection Safety Follow Up Visit: _____

If you feel that the payment listed may interfere with your making a good decision about whether or not you should volunteer to be in this study, you should not agree to participate.

You may be required to report the payment received for this study to the Internal Revenue Service as taxable income.

You have to provide your social security number because the IRS may be told how much you were paid to take part in this study.

[OTHER PAYMENT TERMS I.E. IF YOU WITHDRAW FROM THE STUDY, IF DOCTOR DECIDES TO WITHDRAW YOU FROM THE STUDY OR STUDY TERMINATES EARLY.]

Use and disclosure of your child's personal health information
"Patient Information" means the health information contained within your child's medical or other healthcare records, which also includes personal identifying information such as your child's name, address, or birthdate. The information that we collect from this study will be kept confidential. *«SiteName»* will take appropriate steps to keep your child's personal health

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information private. However, there is no guarantee of absolute privacy. Any information about your child will have a number on it instead of his or her name. Only the research team at *«SiteName»* will be able to link the assigned number to your child's name. In some instances, in order to ensure the scientific value of the study, the parties named below will be able to view your child's study information.

The following parties may view your child's identifying information:

Cardinal Health, Inc.
Representatives of Cardinal Health, Inc.
The Food and Drug Administration (FDA)
The Office for Human Research Protections (OHRP) - a regulatory agency that oversees research in humans
Other governmental agencies, including those governmental agencies in other countries
«IRBName» An Independent Review Board (IRB) is a group of people that reviews research studies. The main goal of this review is to protect the rights and well-being of the human subjects participating in research studies.
Officials of «SiteName»

Will the results of this study be shared?
Yes, when the study is finished, the results of this study will be shared with professionals in the research community. Your child will not be identified with any of the results of the study.

Right to Refuse or Withdraw
You do not have to agree to allow your child to participate in this study if you do not wish to do so. Refusing to allow your child to participate will not affect your child's treatment at «SiteName». If you want to stop your child's participation in this study, you may do so at any time. Withdrawing your child from the study will not affect your child's regular care at «SiteName».

What other choices does my child have if he or she does not participate in this study?
The alternative is not to allow your child to participate. Your child will continue to receive his or her routine medical care if he or she does not participate in the study.

Alternative drugs for Lymphoseek is another mapping drug named sulfur colloid. It has radioactive technetium attached, like Lymphoseek. These drugs may be available for use by your doctor if you decide not to allow your child to participate in the study.

What happens if my child is injured because he/she took part in this study?
It is important that you tell your study doctor if you feel that your child has been injured because he or she took part in the study.

In the event your child is injured as a direct result of study conduct, the study sponsor will reimburse you for the reasonable medical costs of your child's medical treatment. In order for the sponsor to reimburse you, the study drug must have been administered in accordance with applicable laws, regulations, and the study plan (protocol) and the costs must not be covered by insurance or any third party coverage.

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Who is paying for the study?
Cardinal Health is paying your study doctor and the hospital to do this study.

What if new information becomes available?
If there is new information or any important new findings that could relate to your willingness to continue your child's participation in this study, we will tell you.

You can then decide if you still want your child to be in the study. If the FDA or Cardinal Health makes changes to the study before the study starts, the study staff will try to notify you before you check-in. If changes are made after the study has started, the study staff will tell you about them as soon as they have been approved. You can use this information to decide if you want your child to stay in the study.

Are there reasons we might take your child out of the study?
Even if you want your child to stay in the study, there may be reasons we need to take your child out of it. Your child may be taken out of this study if:

- We find out it is not safe for your child to stay in the study. For example, your child's health may worsen or we may find out that the study drug might harm your child.
- Your child's healthcare is not being managed properly or is not coming for study visits as scheduled
- The study doctor feels it is not in your child's best interest to continue
- If the sponsor or study doctor decides that the study or your participation should be stopped for any reason

Who do I contact if I have questions or concerns about the study?
If you or your child has any questions, concerns, or complaints about this study or your child's participation in this study, contact your study doctor:

«PI Name and Contact Information»

If you have questions about your child's rights as a research subject or have other concerns about the research, you can contact «IRB Name» at «IRB Phone Number». A description of this clinical trial is available at https://clinicaltrials.gov/ct2/show/NCT02509598, as required by U.S. Law. This website does not include information that can identify your child. At most, the web site will include a summary of the results. You and/or your child can search this website at any time.

In the event of an emergency, dial 911 immediately. If your child requires emergency care, be sure to tell the emergency care provider about your participation in this study. Contact the study doctor as soon as possible.

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PARENTAL CONSENT:

I have been given a chance to ask questions about this research study. These questions have been answered to my satisfaction. I may contact Dr. «LastName» if I have any more questions about my child taking part in this study. I understand that Dr. «LastName» or the company he/she is employed by is being paid by the sponsor for my participation in this study.

I understand that my child's participation in this research project is voluntary. I know that my child may quit the study at any time without harming his or her future medical care or losing any benefits to which he or she might be entitled. I also understand that the investigator in charge of this study may decide at any time that my child should no longer participate in this study.

If I have any questions about my child's rights as a research subject in this study I may contact:

«IRB Name»

«IRB Telephone»

By signing this informed consent document, I have not waived any of my legal rights.

By signing this informed consent document, I acknowledge that I can read, understand, and speak English and that I understand the information in this informed consent document. I understand that my child's study-related medical records may be reviewed by the company sponsoring the study and by government authorities. I have read and understand the above information. I agree to allow my child to participate in this study. I understand that I will be given a copy of this signed and dated form for my own records.

IF YOU DO NOT AGREE WITH THE STATEMENT ABOVE, YOU SHOULD NOT SIGN THIS INFORMED CONSENT DOCUMENT.

_____ _____

Parent/Guardian (signature) Date

_____

Parent/Guardian (print name)

_____ _____

Person who explained this study (signature) Date

_____

Person who explained this study (print name)

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Assent to Participate in Research for Children Ages 12-17

Title: A Prospective, Open-Label, Multicenter Study of Lymphoseek® as Lymphoid Tissue Targeting Agent in Pediatric Patients With Melanoma, Rhabdomyosarcoma, or Other Solid Tumors Who Are Undergoing Lymph Node Mapping

Why is this study being done?
Research studies help doctors and researchers find better ways to take care of and treat children who are sick. This is the way we find out if medicines are safe and if they work.

We are asking you to be in this research study because we want to learn more about diseases like melanoma, rhabdomyosarcoma, and other solid tumors in children. This study is voluntary, which means that you can participate in this study if you want to, but you do not have to.

Do I have to do this?
You get to decide if you want to be in this study or not. You can say 'no' or you can say 'yes'. If you decide you don't want to be in this study, it is okay and nothing will change. We will ask your parents for permission to let you participate. If your parent says 'yes', you can still say 'no'. No one will be upset with you for not wanting to be in this study. Your doctors will still take care of you even if you decide not to be in this study. Even if you say 'yes' now, you can change your mind later.

What happens in the study and how long will I be in the study?
The study will be very similar to the routine care for your kind of tumor. What is different is that your doctor will use a drug that has not been previously studied in children rather than the regular drug. Your parents can come with you to every visit and can stay with you during all of your procedures except for *Institution to list procedures in which parents cannot accompany child*.

Before your injection and surgery, we will ask you and your parents about your health. Your doctors will give you a physical exam and check your breathing and your heart. We will take a little bit of your blood and urine for routine tests. When we take your blood, you will feel a prick from the needle, but the hurt will go away quickly.

At your next visit, you will be injected with the study drug (and a blue dye if your doctor chooses) that will help the study doctor find your lymph nodes with a special camera on the day of your surgery. Everybody has many lymph nodes that are part of our immune system and defend our bodies from infections and sickness; they look like small balls that are hard to see because they are normally smaller than the size of this letter "o". The study drug has been created to stay longer inside the lymph nodes that contain the type of tissue found in your tumor. This is why collecting some of your lymph nodes will help doctors know if your tumor has spread. You might also get a scan to help find the lymph nodes if your doctor chooses. The scan is done by a machine that is like an x-ray machine and can find the study drug that is inside the lymph nodes.

About 1-2 weeks after your surgery, you will come back to the clinic to be checked and make sure you are okay with the same kinds of checks you had before. After you are done with this visit, you will be finished with this research study.

Could the research help me?
Nothing really good will happen to you for being in this study. Maybe we will find disease in your lymph nodes and your doctor can use this information for your treatment, but we don't know yet if this will help you in any way or make any difference for you. We hope that we can learn something from doing this study and help answer that question. We hope that someday this research will help other kids who have tumors like you do.

Do I get anything for being in this study?
We will give your parents enough money to bring you to your study visits. *Institution to insert other payments*

Could bad things happen to me if I decide to be in this study?
There is a chance that you might feel uncomfortable or hurt during this study. If that happens, your doctor will help you with these feelings or discomforts. You can tell your doctor to stop any procedure at any time. You will take medication to make you sleep so that you won't remember your injection of the study drug or your surgery, but if you feel bad at any time, it is important to tell your doctor.

The mapping drug and camera for looking at your lymph nodes use radiation. Radiation is invisible, but too much could make you sick. The amount of radiation that you will receive is similar to what you get naturally from the sun and the environment over two years.

Is everybody going to know that I was in this study?
The study doctor and study staff will not tell anyone that you are in this study. Your parents will receive all the information about your treatment in the study.

What happens if I get hurt?
If you get sick during the research, we will take care of you. Your parents have information on what to do if you are hurt or get sick during the research.

Who can I talk to or ask questions to?
You can ask any questions now and later if you want to. Your parents have been given our phone number and address so that you can talk to us or ask us questions whenever you want to. You or your parent can call us or stop by and ask any questions at any time. If you want to talk about this research to someone else you know, like your teachers, your family, or your other doctors, that is okay too.

Assent to Participate

If you want to be in this study, please write your name below. We will write our name too. Our signatures show that we talked about the research and that you would like to be in this study.

[redacted] [redacted]

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Subject's Signature for Assent	Date
Person Obtaining Subject Assent	Date

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