Children's Hospital of Wisconsin

Subject Label

CHILDREN'S HOSPITAL OF WISCONSIN INSTITUTIONAL REVIEW BOARD
STATEMENT OF VOLUNTEER CONSENT FOR RESEARCH STUDY

TITLE OF STUDY: Caphosol Study: A Randomized Controlled Open-Labeled Trial Investigating Topical Caphosol for Prevention of Oral Mucositis in Children, Adolescents and Young Adults Receiving Chemotherapy

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Name of Subject _____ **Medical Record No.** _____

If you are a parent or legal guardian of a child who may take part in this study, permission from you and the assent (agreement) of your child may be required. When the word "you" appears in this consent form, it refers to you or your son or daughter; "we" means the doctors and other staff.

We invite you to take part in this research study. Taking part in this research study is your decision. You do not have to participate. You may stop or decide to leave the study at any time. If you stop or leave the study, you will not be penalized. You will still receive any treatments, help, or benefits coming to you. The information in this Consent form is supposed to help you understand what the research team thinks is hurting your health, and what they think can be done to treat your condition.

This form explains what will happen in the research study. The researchers may be reviewing this form with you and can answer any questions you may have. This form also tells you about the risks, discomforts, and other information about the study.

Medical language is hard to understand for most people. If there is anything that you do not understand or are unsure about, please ask questions. You should only agree to take part in this research study and sign the Consent form if you understand what will happen to you, what the risks are, and that your questions have been answered.

A. WHAT IS THE PROBLEM?

This study is a clinical trial (a protocol, or research study involving patients) of an experimental new treatment for children and young adults who will be receiving chemotherapy. Clinical trials only include patients who choose to take part.

This study is being carried out by the Pediatric Clinical Trials Office (CTO) for the Medical College of Wisconsin. Treatment will take place at Children's Hospital of Wisconsin.

You are being asked to take part in this research study because you are about to receive chemotherapy. Patients receiving chemotherapy are at risk of getting a painful inflammation (swelling) of the mucous membranes (the skin inside your mouth) called mucositis.

It is common to enroll children and adolescents with cancer in a clinical trial that seeks to improve cancer treatment over time. Clinical trials include only people who choose to take part. You have a choice between other treatments for mucositis and this clinical trial.

Please take your time to make your decision. Discuss it with your friends and family. We encourage you to include your child in the discussion and decision to the extent that she or he is able to understand and take part.

B. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

In this study, researchers want to find out if there is a difference in development of oral mucositis using Biotene mouth rinse compared to Caphosol mouth rinse.

Caphosol , manufactured by EUSA Pharma, is a mouth rinse designed to moisten, lubricate and clean the mouth, including the mucosa of the mouth, tongue and oropharynx. Studies with adults have shown that Caphosol is beneficial in the prevention and treatment of oral mucositis in patients receiving high-dose chemotherapy and/or radiation therapy. This data supported adding caphosol to treatment plans designed to prevent treat oral mucositis.

The use of Caphosol to prevent oral mucositis in children receiving chemotherapy is experimental.

The overall goal of this study is to:

- To determine if topically administered Caphosol at the start of chemotherapy is a viable option to prevent the development of oral mucositis in children, adolescents and young adults.
- To determine the tolerability of four times daily Caphosol therapy.

What is the Current Standard Treatment for This Disease?

There is no standard of treatment to prevent oral mucositis in children, adolescents, and young adults. Treatments that have been used in the past to try to reduce mucositis or make patients more comfortable include ice chips, mouthwashes, and a variety of different drugs. Many different treatments are used and work to some extent, but none have prevented mucositis from occurring in the first place or have been shown to make it heal faster.

How Many People Will Take Part In This Study?

About 96 subjects from infant to 25 years of age will take part in this study. 48 subjects will receive Caphosol and Biotene and 48 subjects will receive Biotene only as a comparison group. All 96 subjects will be from Children's Hospital of Wisconsin.

C. WHAT IS INVOLVED IN THIS STUDY?

What Will Happen on This Study That is Research?

The study involves the use of Caphosol and/or Biotene* used as an oral rinse. Subjects (people participating in the study) will receive 1 of 2 different arms which are explained below. The study arms use either the Caphosol along with the Biotene as an oral rinse (the experimental arm), or the Biotene only as an oral rinse (the control/ comparison arm) starting on the first day of chemotherapy. You will use the oral rinse 4 times each day. However, if you develop severe mucositis, you have the choice to use the study rinse up to 6 times each day.

Treatment with Caphosol and Biotene), or the Biotene rinse only, will continue for 7 days after completion of chemotherapy AND until the Absolute Neutrophil Count (ANC)** is greater than 500 after white blood cell count recovery or until the symptoms of oral mucositis resolve; whichever occurs last. If you do not have mucositis at all, you will stop treatment on Day 7 but study doctors will continue to examine your mouth until your white blood cell count recovers.

*Biotene is a soothing rinse that gently cleans and helps relieve dry mouth symptoms. This is used as standard of care for oncology patients getting chemotherapy to help prevent mouth infections.
** Absolute Neutrophil Count is a measure of the number of Neutrophils, a type of white blood cell that fights infection

Each participant will use a Study Diary to document any incidence of oral mucositis beginning after the start of chemotherapy. You will also record the severity of oral mucositis. This study will compare the results of the two arms and evaluate the effect and tolerability of using Caphosol as a preventative for oral mucositis.

Caphosol Arm: Subjects in the Caphosol Arm will begin using Caphosol the same day they begin chemotherapy, at least 4 times per day, and will continue to use Caphosol for 7 days after completion of chemotherapy **AND** until the Absolute Neutrophil Count (ANC) is greater than 500 after white blood cell count recovery **OR** until the symptoms of oral mucositis resolve; whichever occurs last. You will also keep a diary to write down your symptoms while using Caphosol. Your study team will explain what kinds of things to write down in this diary.

Subjects in the Caphosol arm will also use Biotene, the standard of care, as a rinse but must wait for 15 minutes after using the Caphosol rinse.

Control Arm: Subjects in the Control Arm will **not** receive Caphosol as a preventative, but will use Biotene only to rinse and spit. Biotene is standard of care for our oncology patients getting chemotherapy to help prevent mouth infections. You will also keep a diary to write down your symptoms while using Biotene. Your study team will explain what kinds of things to write down in this diary.. If you develop oral mucositis and your care team thinks it's in your best interest to add Caphosol as a treatment, you will be removed from study and you will then receive Caphosol as prescribed by your care team.

Random Assignment

Subjects (people participating in the study) will receive 1 of 2 different arms. The arm they receive is decided by a process called randomization. Randomization means that the treatment is assigned based on chance. It is a lot like flipping a coin, except that it is done by computer to make sure that there are about the same number of people on each treatment arm of the study. You will have an equal chance of being placed in either of the arms. The randomization process is described in the COG Family Handbook for Children with Cancer.

Treatment

Caphosol Arm: Subjects randomized to the **Caphosol Arm** will use Caphosol and Biotene 4 times per day as follows:

- Each dose consists of one blue and one clear ampule.
- Mix the contents of 1 blue ampule (Caphasol A) and 1 clear ampule (Caphasol B), in a clean glass.
    - Note: Caphosol must be used within 15 minutes of mixing.
- Using 1/2 of the solution, swish thoroughtly and gargle (if you are able) for one minute and then spit. Repeat using the remaining ½ of the solution.

  - For subjects who are 6 years old or younger and are not able to swish the full 15ml (half of the solution), you may reduce the amount of solution used to 5-10 mL for each rinse.
  - If you are unable to rinse and spit, caregivers may paint your mouth (using medical sponge swabs) with the solution two times.
    - Mix the blue ampule with the clear ampule as above. Soak up ½ the solution and use the swab to coat the inside of the patient's mouth. Repeat using the remaining solution.
- You are to avoid other oral medications, other mouth cares and food or drink for 15 minutes after using Caphosol.
- Use Biotene (5-10 mL) to swish and spit after the 15 minutes has passed. Biotene is part of our standard of care to prevent oral infections in oncology patients.
- You may increase the use of Caphasol from 4 times per day to 6 times per day if you have symptoms of mucositis.

Control Arm: Subjects randomized to the **Control Arm** will use Biotene 4 times per day as follows:

- Use 5 to 10 mL of Biotene to swish and spit
  - For patients unable to successfully rinse and spit, caregivers may paint their mouth (using medical sponge swabs) with the solution two times. Prior to swabbing the patient's mouth, pour Biotene into a cup and using the medical sponge, soak up the solution and use the swab to coat the inside of the patient's mouth. Repeat with a second swab.

Research Study Procedures

You will have tests and procedures as defined by the chemotherapy treatment you are receiving. At each clinic visit your care providers will assess your pain level and the need for further oral pain relief based on your responses.

Research Measurements

The only test that will be done because you are part of this study is the careful measurement of mouth sores. There should be no extra visits because of this study. The time to discharge home or the number of visits after discharge home will not be increased due to participating in this study.

Oral Mucositis Measurements: Subjects that participate in this clinical trial will have oral mucositis measured daily throughout treatment starting on Day 1 of scheduled chemotherapy. This will involve recording details such as your ability to eat, and the amount of pain you have. Each mucositis measurement will take about 5 minutes. A healthcare provider will ask you questions about your mucositis.

These are the measurements that will be completed by a trained healthcare professional:

1. Pain Rating Scale

Measurements will be done before treatment starts, and then daily until one of the following occurs:

1. 7 days have passed since the scheduled chemotherapy; and
2. You have adequate white blood cell recovery; and
3. You are discharged from the hospital to go home
4. You no longer agree to participate in daily mucositis measurements

How Long Will You Be in the Study?

Subjects in this clinical trial may participate for each of their scheduled chemotherapy cycles. Depending on your chemotherapy schedule, your participation may last up to 6 or 8 months.

Your doctor or study doctor may decide to take you off this study for the following reasons:

- If he/she believes that it is in your best interest
- If you experience side effects from the treatment that are considered too severe
- If new information becomes available that shows that another treatment would be better for you
- If the study is stopped
- If you do not follow study directions

You can stop participating at any time. However, if you decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first. They will help you stop safely.

D. WHAT ARE THE RISKS TO YOU IN THIS RESEARCH STUDY?

Risks for Subjects Who Receive Caphosol (Study Risk)

The use of a Caphosol rinse may cause complications in children. However, there are no known risks or side effects when Caphosol is used as a mouth rinse in adults. If Caphosol is swallowed accidentally, no side effects are expected. There is a risk of salty or unpleasant taste. ***There are no known interactions with other medicines.***

Risks for Subjects Who Receive Biotene Rinse (Study Risk)

The risk of receiving any side effects from using the Biotene rinse is very small. Biotene products have been found not to cause any significant side effects. Biotene products are made of

natural ingredients, and are free of alcohol, sugar, and gluten, which are common causes of allergies and product sensitivities. However, there is still a risk of allergic reaction or sensitivity to Biotene. The use of natural ingredients and low-foaming formulas that restore moisture to the mouth minimize the risk of encountering any side effects.

In addition to the risks described above, there may be unknown risks, or risks that we did not anticipate, associated with being in this study.

Reproductive Risks

Women should not become pregnant and men should not father a baby while on this study because it is not known if the Caphosol used in this study can be bad for an unborn baby. If you or your partner can get pregnant, it is important for you to use birth control or not have sex while on this study. Check with your study doctor about what kind of birth control methods to use and how long to use them. Some birth control methods might not be approved for use in this study. Women should not breastfeed a baby while on this study. Also check with your doctor about how long you should not breastfeed after you stop the study treatment(s).

E. WHAT IF PROBLEMS OCCUR DURING THE STUDY OR WITH TREATMENT?

Your health is more important than following the research plan. If any changes are needed to protect your health, we will talk with you about them before they are made. We will also tell you if a better treatment is discovered somewhere else. If you want, this treatment will be given to you in place of or in addition to the current plan. A Data Safety and Monitoring Committee, an independent group of experts, will be reviewing the data from this research throughout the study. We will tell you about the new information from this or other studies that may affect your health, welfare, or willingness to stay in this study.

If you think you have been injured as a result of the experimental parts of this research study, you should immediately contact Michael Burke, MD at 414-955-4170. You may also call the Chairperson of the Children's Hospital of Wisconsin Institutional Review Board that reviewed this research study at 414-266-2986.

In the event that this research activity results in an injury, care for such injuries will be billed in the ordinary manner to you or your insurance company. Insurance companies may refuse to pay for injuries sustained while participating in a research study or while receiving a treatment that is considered experimental. If you think that you have suffered a research-related injury, let the study physician(s) know right away.

By signing this form, you do not waive your legal right to seek other compensation for study related injuries.

F. WHAT ARE THE POSSIBLE BENEFITS TO YOU IN THIS RESEARCH STUDY?

We hope that you will get personal medical benefit from participation in this clinical trial, but we cannot be certain.

Taking part in this study may or may not make your health better. While doctors hope Caphosol will be useful to prevent oral mucositis, there is no proof of this yet. We expect that the information learned from this study will benefit other patients in the future.

G. WHAT ARE THE FINANCIAL RISKS TO YOU IN THIS RESEARCH STUDY?

If you take part in this study, the Caphosol will be billed to your insurance company, so there will be added costs to you or your insurance company. Caphosol is more expensive than Biotene. Some third party payers (insurance companies, HMOs, etc.) may not pay for hospitalization, treatments or procedures which are determined to be experimental or research related. The study has no plans to pay for medical treatment. All costs not paid by your insurance will be your financial responsibility. Please ask about any expected added costs or insurance problems. Financial Counselors are available to discuss insurance, costs and other issues.

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.

For more information on clinical trials and insurance coverage, you can visit the National Cancer Institute's Web site at *http://www.cancer.gov/clinicaltrials/learningabout*. You can print a copy of the Clinical Trials and Insurance Coverage information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy of Clinical Trials and Insurance Coverage.

H. WILL YOU BE PAID FOR TAKING PART IN THIS RESEARCH STUDY?

There are no plans to pay you for taking part in this study.

I. DO YOU HAVE TO TAKE PART IN THIS RESEARCH STUDY?

You do not have to participate in this study. You may choose not to be in this study. If you decide not to be in this study, you will not be penalized and you will not lose any benefits to which you are entitled. You will still receive the best medical care this hospital can provide.

If you choose to participate, you are free to withdraw at any time. Your decision to withdraw will not change the quality of care that you receive from the Medical Staff. However, if you

decide to stop participating in the study, we encourage you to talk to the researcher and your regular doctor first so any risks from the treatment can be evaluated by your doctor and he or she will tell you how to stop safely. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

You also have the right to know about new information that may affect your health, welfare, or your willingness to participate in the study. You will be provided with this information as soon as it becomes available. A committee closely monitors study reports and notifies the Principal Investigator if changes must be made to the study. Members of the Data Safety Monitoring Committee meet twice a year to discuss results of treatment.

What Other Options Are There?

Instead of being in this study, you have these options:

- Current standard therapy even if you do not take part in the study. Standard therapy is to receive Caphosol after mucositis is diagnosed
- Taking part in another study

Please talk to your doctor about these and other options.

J. WHAT IF YOU HAVE MORE QUESTIONS?

For questions about the study or a research-related injury, contact the researcher, Michael Burke, MD at 414-955-4170. Dr. Burke or a member of the Investigation team will be available 24-hours a day, 7 days a week at 414-266-3050. If additional questions arise, you can ask your doctor. Also, the research study has been reviewed and approved by the Children's Hospital of Wisconsin Institutional Review Board, whose purpose is to see that the rights and welfare of research participants are adequately protected, and that risks are balanced by potential benefits. A member of this committee is available to speak to you if you have any questions or complaints at 414-266-2986.

Where Can You Get More Information?

Resources for additional information on clinical trials and cancer care include:

The COG Family Handbook for Children with Cancer has information about specific cancers, tests, treatment side effects and their management, adjusting to cancer, and resources. Your doctor can get you this Handbook, or you can get it at http://www.childrensoncologygroup.org/familyhandbook

If you are in the United States, you may call the NCI's Cancer Information Service at: 1–800–4–CANCER (1–800–422–6237)

You may also visit the NCI Web site at http://www.cancer.gov/

- For NCI's clinical trials information, go to: http://www.cancer.gov/clinicaltrials/

Visit the COG Web site at http://www.childrensoncologygroup.org
Information about long term follow-up after cancer treatment can be found at:
http://www.survivorshipguidelines.org/

You will get a copy of this form. You may also ask for a copy of the protocol (full study plan). A copy of the signed consent, assent (if applicable), and HIPAA Authorization will be kept in your medical record.

K. WILL INFORMATION BE CONFIDENTIAL?

Children's Hospital of Wisconsin/Children's Health System, its researchers and their designees will maintain the privacy and confidentiality of your personal and health information to the extent permitted by law. 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. Also, scientific data from this study, without identifiable information, may be presented at meetings and published so that it may be useful to others, as long as it is not identifiable with you. You may read your medical record.

Organizations that may look at and/or copy your research or medical records for quality assurance and data analysis include:

- Representatives of the National Cancer Institute (NCI) and other US and International governmental regulatory agencies involved in overseeing research
- Children's Hospital of Wisconsin Institutional Review Board (CHW IRB)
- The Food and Drug Administration (FDA) may inspect study records

L. PERMISSION TO PROCEED

The signing of this consent does not release your doctors from their responsibility for your proper medical care at all times.

The proposed research study and consent has been explained to you by:

_____	_____	_____
Name of Principal Investigator or Designee	Signature of Principal or Designee	Date

When you sign this form, you agree that you have read the above description of this research. You also agree that you have had a chance to discuss the research study with a member of the research team; that your questions have been answered, and that you want to take part in this research.

_____	_____
Signature of Subject or Authorized Representative	Date

Children's Hospital of Wisconsin

_____ _____
Signature of Subject or Authorized Representative Date

AGE OF MAJORITY SIGNATURE: (To be signed when the subject reaches age of majority (18 years of age)

Now that you have reached the age of majority (18 years old), we are asking for your consent for continued participation in this research study. The age of majority means you are considered an adult and are able to sign legal contracts and consents for yourself.

When you sign this form, you confirm that the purpose of the research, the study procedures, and the possible risks and discomforts as well as potential benefits that you may experience with your continued participation have been explained to you. Alternatives to your continued participation in the study also have been discussed. You have read the informed consent and/or it has been explained to you. You were given the opportunity to ask questions about the information, all of your questions have been answered, and you want to take part in this research. A copy of this signed informed consent form will be given to you.

By signing below, you agree to continue your participation in this research study.

Participant _____ Date _____

PI or Designee _____ Date _____

CONSENT OF NON-ENGLISH SPEAKING SUBJECTS:

A witness signature is required for all consent conferences involving an interpreter. Witness cannot be the Interpreter.

An oral translation of this document was administered to the subject in _____ (state language) by an individual proficient in English and _____ (state language). See the attached short form (as applicable) for documentation.

_____
Name of Interpreter

_____ _____ _____
Name of Witness Signature of Witness Date

ASSENT OF MINOR:

"The above has been explained to me and I agree to participate."

_____ _____

Signature of Minor Date

WAIVER OF MINOR'S ASSENT:

In my opinion, this child is not capable of assent because _____

_____

_____ _____

Signature of Principal Investigator or Research Team Designee Date