**Medical College of Wisconsin and Froedtert Hospital**
**CONSENT TO PARTICIPATE IN RESEARCH**

Name of Study Subject: _____

A Pilot Study to Investigate the Hypomethylating Properties of Freeze-dried Black Raspberries (BRB) in Patients with Myelodysplastic Syndrome or Myelodysplastic Syndrome/Myeloproliferative Neoplasm (MDS/MPN)
(The Black Raspberry Study)

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You are invited to take part in this research study. This form tells you why this research study is being done, what will happen in the research study, possible risks and benefits to you, your choices, and other important information. If there is anything that you do not understand, please ask questions. Then you can decide if you want to join this study or not.

## A1. INTRODUCTION – WHY ARE WE ASKING YOU ABOUT THIS STUDY?

You are being invited to participate in this research study because you have been diagnosed with Myelodysplastic Syndrome or Myelodysplastic Syndrome/Myeloproliferative Neoplasm (MDS/MPN). The purpose of this study is to determine whether treatment with freeze-dried black raspberry powder (BRB) has an effect on your disease.

A total of about 18 people are expected to participate in this study, at the Medical College of Wisconsin/Froedtert Hospital.

The Director of the study is Ehab Atallah, MD in the Department of Medicine. A study team works with Dr. Atallah. You can ask who these people are.

Froedtert Hospital Foundation is funding this study.

## A2. DO I HAVE TO BE IN THIS STUDY?

You can decide whether to take part in this study or not. You are free to say yes or no. If you say no, your regular medical care will not change. Even if you join this study, you do not have to stay in it. You may stop at any time.

A research study is different from routine medical care in three ways: 1) there are extra risks that we will tell you about in this form; 2) you may have some extra medical tests and visits; 3) the study procedures, tests and visits follow a set plan that must be kept.

## A3. WHY IS THIS RESEARCH STUDY BEING DONE?

In this study we want to find out more about, BRB, in people with myelodysplastic syndrome or Myelodysplastic Syndrome/Myeloproliferative Neoplasm (MDS/MPN). We want to find out whether the, BRB, acts similarly to other agents currently used to treat MDS, and whether it causes any problems (side effects). Everyone in this study will receive BRB, which is experimental and is not approved by the U.S. Food and Drug Administration. We are testing BRB to see what effect it has on people with MDS or MDS/MPN. We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. We hope the information from this study will help us develop a better treatment for MDS or MDS/MPN in the future.

## B1. WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

### STUDY PROCEDURES

Before any study tests or procedures are done, you will be asked to sign this consent form. The study doctor will discuss the study with you and answer your questions. If you decide to join the study, some screening tests will be done first to see if you are eligible.

Some of these tests and procedures are considered "standard of care" which means that they would be done even if you were not participating in this research study and some are considered "research" which means they are being done only because you have agreed to participate in this research study.

### Screening procedures:

If you decide to join the study, some screening tests will be done first to see if you are eligible.

- **Complete Medical History:** A complete medical history will be taken including transfusion history and medication history.
- **Demographics:** age, gender, ethnicity
- **Physical Exam**
- **Laboratory Tests:**
    - **Blood Tests:** A small sample of your blood will be collected for routine safety tests
    - **Pregnancy Test:** If you are a female of child-bearing potential, you will be required to have a urine or serum pregnancy test done

If the screening information shows that you meet the requirements, you will be able to participate in the study. If the screening information shows that you cannot be in the research study, the study doctors will discuss other options with you.

**Summary of Study Procedures:**
After screening procedures are performed and you are deemed eligible, you will be enrolled on the study. Treatment will consist of 28 day (4 week) cycles. If, after 3 cycles of therapy, you are tolerating the BRB well, you will be allowed to remain on the study for an additional 9 cycles for a maximum of 12 cycles. You may be removed from the study at any time if you are not tolerating the BRB or if your treating physician decides it is in your best interest.

On the first day of every cycle you will come to the study center for a lab draw of blood in the amount of approximately 20mL for an assessment of your overall health and to receive study drug for that cycle. The following assessments will be performed unless otherwise specified:

- **Physical Exam:** A physical exam will be performed only on Cycle 1 day 1
- **Blood Tests:**
  - A small sample of your blood will be collected for routine safety tests
  - Research blood samples to look for evidence of the study drug in your blood will be collected only on day 1 of the first 4 cycles. Samples will be collected within 3 hours prior to taking your dose and 2 hours after taking your dose.
- **Urine Tests:** These research urine tests will be done prior to your first dose of BRB to determine baseline values of various chemicals of interest
  - Urine will be collected within 3 hours prior to your first dose of BRB and 3 hours after your first dose. This is only done on cycle 1 day 1.
- **Bone Marrow Aspirate/Biopsy:** As part of your routine care, you may have a bone marrow aspirate/biopsy procedure to assess your disease if your doctor believes it is necessary.

You will be asked to mix 25g of BRB powder with 8 ounces of water twice daily. You will drink the 25g BRB/water mixture in the morning and then again at night, separated by at least 6 hours. If you cannot tolerate the taste of the BRB with water mixture, you can combine the BRB with milk, ice cream, or in a smoothie.

During the 28-day cycles, you will be asked to keep track of when you take each BRB dose (morning and evening) in a drug diary. You will bring your completed drug diary with you when you come for your next clinic visit. If you miss a dose, you will be asked to bring any missed doses back with you to your next clinic visit. Study drug must not be thrown away. If you do not follow the treatment schedule, or miss too many doses, you may be taken off the study.

**Follow-up:**
Approximately thirty days after your last dose, you will return to the study center to assess your overall health and disease. The following assessments will be performed unless otherwise specified:

- **Physical Exam:** A physical exam will be performed
- **Blood Tests:**

  - A small sample of your blood will be collected for routine safety tests
  - Research samples to look for evidence of the study drug in your blood.
- **Bone Marrow Aspirate**- This procedure may occur if your doctor believes that it is necessary.

You will come to the study center approximately 15 times during the study (including this visit). The study staff will tell you when to come in for your study visits.

## B2. HOW LONG WILL I BE IN THE STUDY?

You will be in this research study for about one year (approximately 52 weeks).

## B3. CAN I STOP BEING IN THE STUDY?

You are free to withdraw from the study at any time. If you leave, your regular medical care will not change. If you are thinking about leaving, please tell the study doctor.

- The doctor can tell you about the effects of stopping, and you and the doctor can talk about what follow-up care would help you the most.
- You might be asked to come back for one more visit to check your health.
- You might be asked to return your research drug containers.

The study doctor may take you out of this study at any time. This would happen if:

- They think it is in your best interest.
- You do not follow the study rules.
- The whole study is stopped.

If this happens, the study doctor will tell you.

## B4. ARE THERE ANY SPECIAL INSTRUCTIONS WHILE I AM IN THE STUDY?

You will complete a drug diary for each cycle to document when you took each dose of study drug and bring it with you for each clinic visit.

You will be asked to keep a food diary of when you eat foods that contain compounds that are similar to the study drug. You will need to bring this diary with you for each clinic visit. The diary contains a list of foods that will need to be tracked on a daily basis during each cycle. You will also meet with a nutritionist on day 1 of every cycle to discuss your diet habits as they relate to the study drug.

## C1. WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE STUDY?

There are risks to taking part in any research study. There is a risk that the study drug, BRB, will not help your condition or may make it worse. There also may be problems (side effects) we do not know about yet, from BRB itself, or how it combines with other drugs you are taking. If we learn about new important side effects, we will tell you.

We watch everyone in the study for problems (side effects). **You need to tell the study doctor or a member of the study team immediately if you experience any**

**problems, side effects, or changes in your health.** If you have severe side effects, call Dr. Atallah immediately at 414-805-6700. In an emergency, call 911.

## C2. RISKS OF FREEZE-DRIED BLACK RASPBERRY POWDER (BRB)

The BRB itself may cause problems (side effects). Side effects may be mild or very serious. Some can last a long time or never go away.

Drugs can affect individuals in different ways. In a previous study, subjects consumed 45g of BRB for 14 days and it was well tolerated with no reported side effects. However, side effects are always a possibility and you should report any changes to your health while taking the BRB drug to your study doctor.

## C3. OTHER RISKS OF THIS RESEARCH STUDY

Other procedures that are part of the study also involve some risks.

**Blood Samples**: Blood draws may cause pain, bleeding, and/or bruising. You may faint and/or get an infection with redness and irritation at the place where the needle enters your vein.

**Bone Marrow Aspirate/Biopsy Collection –** Bone marrow is collected using a needle under local anesthesia to aspirate (draw out) marrow tissue from the inside of your bone (usually pelvic or hipbone). The risks on bone marrow biopsy and aspirate include pain, bleeding, bruising, and/or discomfort at the biopsy site. Infection is also possible but rare.

## C4. REPRODUCTIVE RISKS

### Risks to women who could become pregnant

The drug in this study might affect a baby, before or after the baby is born. We do not know if the drug causes harm to a baby, so we do not want anyone who might be pregnant to enter the study. You should not become pregnant or nurse a baby while in this study. You must tell the study doctor right away if you think you are pregnant. You will be asked to have a pregnancy test to be sure you are not pregnant at the start of the study.

### Risks of fathering a child

You should not father a baby while taking part in this study because it is unknown if the drug in this study could affect a baby. If your partner is able to become pregnant, one or both of you must use some form of effective birth control. You must tell the study doctor right away if you think your partner is pregnant.

### Birth control methods for all subjects

Check with the study doctor about the birth control methods needed for this study and how long to use them. Some methods might not be good enough for this study. If you are having sex that could lead to pregnancy, you should use birth control while you are in this study.

This may include:

- Not having vaginal sex (abstinence)
- Taking birth control pills orally
- Having birth control shots or patches such as Depo-Provera
- Surgical sterilization (hysterectomy or tubal ligation)
- Use of an intrauterine device (IUD)
- Use of diaphragm with contraceptive jelly
- Use of condoms with contraceptive foam
- Use of diaphragm with condoms ("double barrier")
- Limiting sexual activity to a male partner who has had a vasectomy

You should continue using birth control for 30 days after stopping the study drug.

## C5. ARE THERE ANY BENEFITS TO TAKING PART IN THE STUDY?

We don't know if this study will help you. Your condition may get better but it could stay the same or even get worse. We hope the information from this study will help us develop better treatments for MDS.

## D1. ARE THERE ANY COSTS TO BEING IN THE STUDY?

Most of the medical care that you will receive in this study is considered routine care for your condition and would be recommended whether you join the study or not. Costs for routine care will be billed to you or your insurance carrier.

Activities / costs that are part of the study will not be billed to you or your insurance company. These are the study drug, BRB, and the processing and shipping of research samples. Some insurers will not pay for drugs, tests or hospitalization that are part of research studies, so check with your insurer before you join this study. If you have questions regarding study costs, please contact Dr. Atallah.

If you participate in this research study, the costs of any necessary emergency medical treatment in the event of a research-related injury will be billed to you or your health insurance.

## D2. WILL I BE PAID FOR PARTICIPATING IN THE STUDY?

There is no payment for being in this study

## D3. WHAT OTHER HEALTHCARE CHOICES DO I HAVE?

You do not have to join this study. You are free to say yes or no. If you do not join this study, your doctor can discuss other healthcare choices with you.

Your other choices may include:

- Getting treatment or care for your cancer without being in a research study.
- Taking part in another research study.

- Getting no treatment.

The study doctor can explain both the possible benefits and the risks of other options that are available to you.

## D4. WILL I BE GIVEN NEW INFORMATION ABOUT THE STUDY?

If we learn any important new information about the study drug, that might change your mind about being in the study, we will tell you about it right away. You can then decide if you want to stay in the study.

## D5. WHAT HAPPENS IF I AM INJURED BECAUSE I TOOK PART IN THE STUDY?

Emergency medical treatment for injuries directly related to your participation in this research study will be provided to you. You or your health insurance will be billed for the costs of this emergency treatment. MCW will decide on a case by case basis if they will reimburse you or your insurer for emergency treatment costs. If your research-related injury requires medical care beyond this emergency treatment, you or your insurer will be responsible for the costs of this follow-up care.

At this time, there is no plan for any additional financial payments.

If you believe that you have been injured because of your participation in this study, contact the study doctors right away. Contact information: Dr. Atallah, 414-805-6700.

**Nothing in this consent form affects any legal rights you may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence.**

## D6. WHO CAN ANSWER MY QUESTIONS ABOUT THE STUDY?

- If you have more questions about this study at any time, you can call Dr. Atallah at 414-805-6700.
- If you have questions about your rights as a study participant, want to report any problems or complaints, obtain information about the study, or offer input, you can call the MCW/Froedtert Hospital Research Subject Advocate at 414-955-8844.

## E. PERMISSION TO COLLECT, USE AND SHARE HEALTH INFORMATION

### E1. What health information will be collected and used for this study?

To be in this research study, the study team needs your permission to access, collect and use some of your health information. If you say no, you cannot be in the study. This information may come from questions we ask, forms we ask you to fill out, or your medical record, as described below. We will only collect and use information needed for the study.

The protected health information (PHI) originates from services you will or have received at one or more of the following locations: the Medical College of Wisconsin

(MCW); BloodCenter of Wisconsin (BCW); Children's Hospital of Wisconsin (CHW); any Froedtert Health Affiliate- Froedtert Memorial Lutheran Hospital (FMLH), Inc.; Community Memorial Hospital (CMH) Menomonee Falls, Inc.; St. Joseph's Community Hospital (SJH) West Bend, Inc.; Froedtert & The Medical College of Wisconsin Community Physicians Clinics, Inc. (FMCWCP); the West Bend Surgery Center, LLC; and the Froedtert Surgery Center, LLC.

**The health information to be collected and used for this study is:**

- Hospital/Medical Records
- Physician/Clinical Records
- Lab and/or Pathology Reports
- Radiology Reports
- Biological Samples

**E2. Who will see the health information collected for this study?**

The only MCW/Froedtert Hospital employees allowed to handle your health information are those on the study team, those on the Institutional Review Board (IRB) and those who check on the research activities to make sure the hospital's rules are followed.

If the costs of any necessary emergency medical treatment in the event of a research-related injury are billed to your health insurance, your health information may need to be disclosed to the insurer for billing purposes.

The study team may share your information with people who don't work at MCW/Froedtert Hospital because they planned, pay for, or work with us on this study. The federal Privacy Rule may no longer protect your health information once it leaves MCW/Froedtert Hospital. For this study, we plan to share information with those doctors, researchers or government representatives working with us on this study at the institutions or companies listed here:

- Any federal, state, or local governmental agency that regulates the study (such as the U.S. Food and Drug Administration (FDA)
- The U.S. Department of Health & Human Services (DHHS)
- The Office for Human Research Protections (OHRP)
- Other government agencies in this or other countries
- The designated Data Safety Monitoring board and Institutional Review Board which is a committee that has reviewed this research study to help ensure that your rights and welfare as a research participant are protected and that the research study is carried out in an ethical manner, and Privacy Boards and their related staff that have oversight responsibilities for this study.
- Personnel from the study site that provide study related treatment or procedures
- Those required by law

Because this study involves the use of drugs and/or devices, the FDA also has the right to inspect all study records.

We may record your research information, including results of tests and procedures done for research, in your Froedtert Hospital and/or Medical College of Wisconsin medical record. As a result, this research information may be seen by people allowed to see your medical records for healthcare operations or treatment, by those you allow to see your medical records by giving written permission, and by others when required by law.

We will not use your personal health information for a different study without your permission or the permission of a hospital research review board (IRB). Once all personal identification is removed, the information might be used or released for other purposes without asking you. Results of the study may be presented in public talks or written articles, but no information will be presented that identifies you.

**E3. What are the risks of sharing this health information?**
One risk of taking part in a research study is that more people will handle your personal health information collected for this study. The study team will make every effort to protect the information and keep it confidential, but it is possible that an unauthorized person might see it. Depending on the kind of information being collected, it might be used in a way that could embarrass you or affect your ability to get insurance. If you have questions, you can talk to the study doctor about whether this could apply to you.

**E4. How long will you keep the health information for this study?**
If you sign this form, we plan to keep your information without any end-date in case we need to check it again for this study.

**E5. Can I cancel my permission to share this health information?**
If you change your mind later and do not want us to collect or share your health information, you need to send a letter to:

Ehab Atallah, MD
Froedtert Hospital & the Medical College of Wisconsin
Division of Hematology and Oncology,
9200 W Wisconsin Avenue
Milwaukee, WI 53226.

The letter must say that you have changed your mind and do not want the researcher to collect and share your health information. At that time, we may decide that you cannot continue to be part of the study. We may still use the information we have already collected.

**F1. FOR MORE INFORMATION ABOUT THE STUDY**
A description of this clinical trial will be available on http://www.ClinicalTrials.gov as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

You can look up this study by referring to the ClinicalTrials.gov number NCT03140280 or by asking the study team for a printed copy.

## CONSENT TO PARTICIPATE IN THE STUDY

**By signing my name below, I confirm the following:**

- I have read (or had read to me) this entire consent document. All of my questions have been answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits have been explained to me.
- I agree to let the study team use and share the health information and other information gathered for this study.
- I voluntarily agree to participate in this research study. I agree to follow the study procedures as directed. I have been told that I can stop at any time.

**IMPORTANT:** You will receive a signed and dated copy of this consent form. Please keep it where you can find it easily. It will help you remember what we discussed today.

| | | |
|---|---|---|
| **Subject's Name** *please print* | **Subject's Signature** | **Date** |
| | | |
| **Name of Witness (**if applicable**)** *please print* (for short form consent process, or consent of blind or illiterate subject) | **Signature of Witness** | **Date** |
| | | |
| *** Name of person discussing/ obtaining consent** *please print* | **Signature of person discussing/obtaining consent** | **Date** |

** A member of the study team trained and authorized by the Principal Investigator to act on her/his behalf in obtaining informed consent according to the protocol. In all research study protocols the Principal Investigator is responsible and accountable for the study.*