PATIENT INFORMATION SHEET AND INFORMED CONSENT FORM AND HIPAA AUTHORIZATION

Name of Research Study: Multi-center, open-label, uncontrolled study to assess contraceptive efficacy and safety of Mirena during extended use beyond 5 years in women 18 to 35 years of age including a subgroup evaluation of a treatment effect on heavy menstrual bleeding

Study #: BAY 86-5028 / 18649

Sponsor: Bayer HealthCare Pharmaceuticals Inc.
100 Bayer Boulevard (P.O. Box 915)
Whippany NJ 07981-0915, USA

Study Doctor Name: **Michael L Twede MD, FACOG**

Research Site Address(es):

Physicians' Research Options LLC/Corner Canyon OB/GYN Clinic
11724 S State St Ste 200/201
Draper UT 84020

Daytime Telephone Number(s): 801-576-2050

24-hour Contact Number(s): 801-576-2050

You should keep a copy of this form. If you have any questions or problems during the study, call the phone number(s) above.

INTRODUCTION

Your doctor would like to invite you to consider taking part in the above research study. Your doctor considers you to be suitable to take part in this research study, as you are currently using Mirena for contraception (i.e., birth control) or for birth control and heavy menstrual bleeding (HMB). You can agree to participate in this study if: you are healthy, between 18 and 35 years old, have had the Mirena in place for at least 4 years and 6 months (or will have met this criteria by the time you sign this consent form) and you are willing to continue Mirena use for birth control or birth control and heavy menstrual bleeding for up to 8 years in total.

This study will evaluate how effective Mirena, a levonorgestrel-releasing intrauterine system (LNG IUS), is at preventing pregnancy when used beyond 5 years up to 8 years. In addition, approximately 10% of the total number of women in the study would have been prescribed Mirena for birth control and HMB; these women will form the HMB subgroup to show that the efficacy of Mirena in terms of reducing heavy menstrual blood loss is maintained during the extended use.

Your decision whether or not to participate in this study is entirely voluntary. This document tells you about the study, why the study is being done, what will happen to you if you take part in the study, and the possible risks and benefits of participating in this study. Please take the time to read this document carefully and please feel free to talk about it with your partner, family members, family doctor or others.

Your study doctor will also talk to you about the information in this document in detail. Please ask your study doctor or the study staff at the clinic to explain anything that may not be clear to you.

If you choose to take part in this study, you will be asked to sign this document. You will get a fully signed and dated copy of this letter and consent form.

Even after choosing to take part in the study and after signing the consent form, you are still free to withdraw from the study, at any time without giving a reason. If you withdraw from the study before you complete the 3-year follow up, we will ask you to return for a post-study assessment to check your health.

PURPOSE OF THIS STUDY

Mirena, the intra-uterine system (or, intrauterine device [IUD]) that you are currently using has been approved for use as a reliable method of birth control for up to 5 years. Mirena can also lessen menstrual blood loss in women who have heavy menstrual flow and who also want to use a birth control method that is placed in the womb to prevent pregnancy. Mirena was initially approved in the United States by the Food and Drug Administration (FDA) in 2000. Mirena is made by a company called Bayer HealthCare Pharmaceuticals Inc.

Mirena works by releasing small amounts of a drug substance (levonorgestrel) every day. Levonorgestrel (LNG) is a sex hormone drug substance (a progestin) that has been used in birth control for more than 30 years. As the hormone reservoir of Mirena still contains LNG after Mirena has been in the womb for more than 5 years, Mirena continues to release LNG also after this time point, and may continue to protect against pregnancy beyond 5 years.

In earlier clinical studies, fewer than 1 in 100 women using Mirena became pregnant during 5 years. Additionally, in the clinical trial performed in women with heavy menstrual bleeding (HMB) and treated with Mirena, almost 9 out of 10 were treated successfully and their blood loss was reduced by more than half.

Beyond 5 years of use, the effectiveness of Mirena as a birth control method was studied in 263 women. Early results (at the point when 108 women have used Mirena for 6 years) showed one confirmed pregnancy or a failure rate of less than 1 per 100 women over a year.

The purpose of this study is to find out whether Mirena continues to be an effective and safe birth control method for up to 8 years of use. This means that during the study, you will continue to use the Mirena that you are currently using for another 3 years, i.e. for up to a total of 8 years. The study also aims to assess menstrual blood loss in the group of women who were prescribed Mirena for both birth control and as a treatment for HMB. Resulting data from the HMB subgroup will confirm whether the effect of Mirena on menstrual blood loss is maintained beyond 5 years, and up to 8 years of use. The sponsor of the study is also interested in learning about your satisfaction with Mirena.

During some visits, blood and urine samples will be collected to evaluate the safety and efficacy of the study drug as well as assess any interaction your body may have with the study drug (pharmacokinetics (PK): how your body handles the study drug). Please note that for safety reasons, the study doctor may decide additional examinations or laboratory tests are necessary.

The study aims to enroll a total of 360 eligible women to take part in this study. One of the institutions taking part in this study is listed on the first page of this document. The main study doctor for this institution is the doctor named as the Principal Investigator on the first page. This study will use competitive enrollment. This means that when the targeted total number of women has been achieved (i.e., 360 women have entered the treatment phase of the study), enrollment will be closed. Therefore, it is possible that you may be in the screening phase (i.e., signed this consent form, had some tests performed), and ready to begin the study, but it is possible that you may be discontinued without your consent if the target number of subjects has already begun the study.

STUDY PROCEDURES

The total duration of your participation in the study will be between 3 years and 3 years and 6 months. This study will have 8 scheduled study visits: a screening visit (Visit 1), a baseline visit (Visit 2), 5 visits during the treatment phase (Visit 3 to 7), an end-of-treatment visit (EOT, Visit 8), and an end-of-study follow-up phone call.

While you are a in the study, you are not allowed to participate in another study testing drug(s). If you are planning to do so, you have to inform your study doctor immediately.

Pregnancy Tests:

The study doctor will ask you to have a urine pregnancy test before you start the study and during each office visit to make sure that you are not pregnant. In addition to the urine pregnancy tests performed by the site at each study visit, you will be provided with home urine pregnancy tests to be used whenever you suspect that you might be pregnant. If the results of a home pregnancy test are positive or if you are unsure whether you are pregnant after performing the test, you should immediately contact the study site to schedule a visit and have a confirmatory test performed.

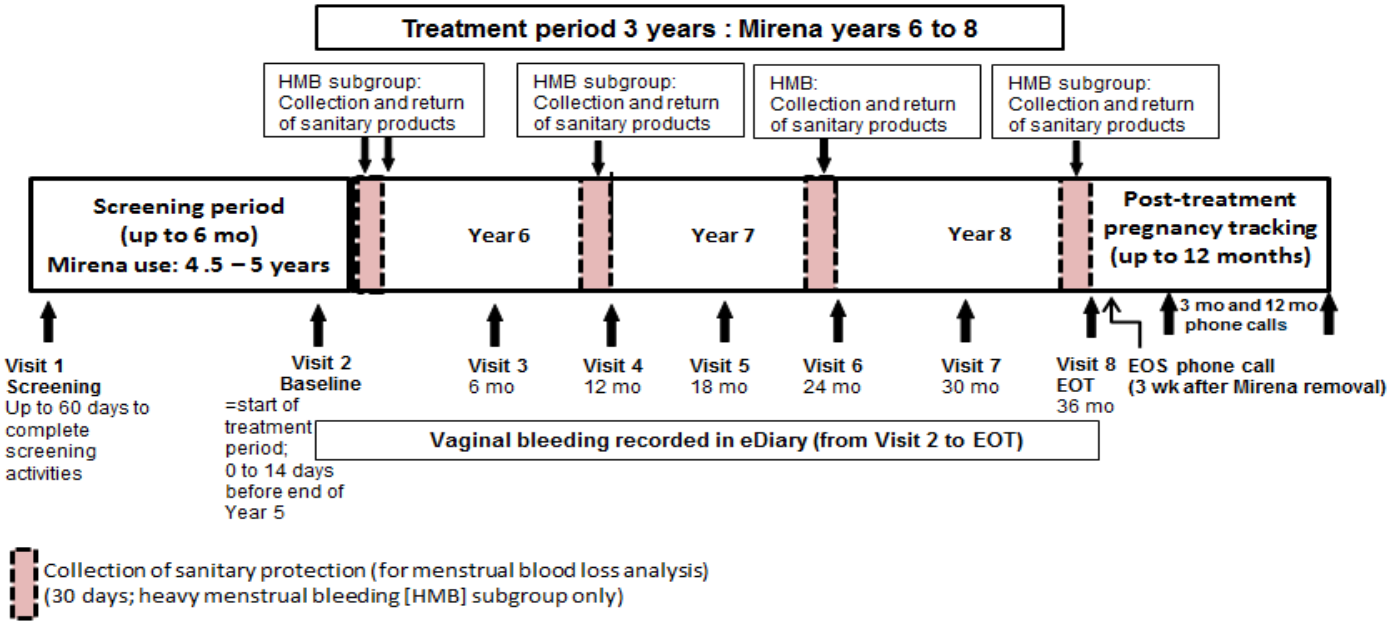
In the event of a positive urine pregnancy result, the pregnancy will have to be confirmed according to the study site's local standard of care (blood pregnancy testing). If you become pregnant anytime during the study, you will have to discontinue your participation in the study. All pregnancies occurring during the study (including those detected during the screening period) will be followed until the final outcome of the pregnancy (i.e. the outcome will be asked and recorded).

You will also be asked to contact the study doctor immediately if you become pregnant less than 3 months after the removal of the Mirena. If there is suspicion that the pregnancy started while you were still using Mirena, further investigations will be conducted, and the outcome of the pregnancy will be recorded.

To summarize, you have been asked to participate in this study because you:

- are between 18 and 35 years of age
- are currently using Mirena for birth control
- are currently using Mirena to control heavy menstrual bleeding and for birth control
- have had the same Mirena for at least 4 years and 6 months at the start of screening (Visit 1)
- are currently in need of a birth control method, and will likely be needing birth control also in the next 3 years

Below is a list of the visits for this study and description of what will happen at each visit.



Before any study procedures are done, you will be given a full explanation about your participation in the study. You will be given time to ask questions about the study before you make any decision to participate. If you are willing to participate, you will be asked to read this document and sign it.

Screening V1

The following screening examinations will only be performed once you sign this form:

- You will be asked about your demographic data, medical history, smoking habits, and alcohol consumption;
- In addition to your medical history, you will be asked about your reproductive and menstrual history;
- You will be asked about any medications that you are currently taking;
- A urine pregnancy test will be performed. If you are found to be pregnant, you cannot participate in the study;
- The study doctor will conduct a physical exam as well as a gynecological exam that will include breast palpation (examination by touch), and a Pap smear. If you have had a Pap smear within the last six months and the results are normal (with no need for follow up), the Pap smear will not be done;
- The study doctor will also conduct a pelvic exam to be sure Mirena is in the proper place inside the womb, has not moved and the removal threads are still visible;
- Your vital signs will be taken, including measuring your heart rate and blood pressure. Your height and weight will also be recorded during this visit;

- You will be tested for Chlamydia. If your results are positive, you must also be tested for Gonorrhea. There will not be an additional sample taken from you for this test. The same sample used for the Chlamydia test will be used to test Gonorrhea;
- Blood samples will be taken for serum chemistry, hematology, and FSH (follicle-stimulating hormone);
- Urine samples will be collected for urinalysis
- You will be told if you are participating in the **HMB subgroup**. If you are using Mirena to control your heavy menstrual bleeding (HMB) (and as birth control) you will be part of this subgroup.

Baseline V2

If you are found to be eligible to take part in the study, the following procedures will take place:

- A urine pregnancy test will be done. If you are found to be pregnant, you cannot participate in the study;
- The study doctor will also conduct a pelvic exam to be sure Mirena is in the proper place inside the womb, has not moved and the removal threads are still visible;
- You will be asked how satisfied you are with Mirena on a 5-point scale (from very satisfied- to very dissatisfied)
- You will be asked questions about any symptoms, illnesses and medication changes you have had since your last study visit. It is important to tell the study doctor or the nurse about any changes in health that may have happened even if you do not think that they are related to the study;
- A PK blood sample will be taken to determine LNG levels in your blood;
- You will be given home pregnancy kits with instructions. You can perform the pregnancy test whenever you suspect that you are pregnant. In any of the following situations, you should perform the pregnancy test at home:

    - If you do not get your period for 2 consecutive cycles;
    - If you do not have your period and have other symptoms of pregnancy (for example nausea, tiredness, breast tenderness);
    - The results of the test must be negative in order for you to be in the study. If the result is not clearly negative, you must contact your study doctor or study nurse immediately;

- You will also receive a handheld electronic diary (eDiary). At the baseline visit, your study doctor or study staff will explain in detail how to use the eDiary.

    - During the study, you will be asked to complete the eDiary at a minimum every 72 hours. You will use the eDiary to record any bleeding and use of any back-up birth control. As Mirena does not protect against HIV infection (AIDS) and other sexually transmitted infections (STIs), you may need to use condoms for protection; if you do, you must record this in your eDiary. The only back-up contraception allowed in the study is the use of a barrier method (e.g. condoms).

- Your eDiary entries will be reviewed monthly by the study staff and during every study visit for compliance with entry. The entries will be reviewed via the internet, so you will not need to bring your handheld device with you to every visit.

- **For HMB subgroup**: you will be provided with sanitary products (towels and/or tampons) that must be used for any menstrual bleeding throughout the study until the last visit (visit 8). The used sanitary products are needed to quantify your menstrual blood loss. **Therefore these used sanitary products must be kept and will need to be brought to the site at the specified time points (see chart below)** for shipping to the central laboratory for assessment. If you cannot travel to the study site to return your used study provided sanitary products, please talk to your study doctor or study team.

Dispense of kit	**Begin collection of used study provided sanitary products:**	**Return of used study provided sanitary products**
Baseline Visit	After baseline for 30 days.	2 weeks and 30 days after baseline visit
Visit 3	30 days prior to visit 4	2 weeks before and at visit 4
Visit 5	30 days prior to visit 6	2 weeks before and at visit 6
Visit 7	30 days prior to your End of Treatment visit (i.e., Mirena removal)	2 weeks before and at End of Treatment visit

If you record in your eDiary that no bleeding occurred during a specific time frame, you will not be asked to return your kit since there was no sanitary protection used during that time period.

Treatment V3-V7

The procedures below will be performed at every visit unless otherwise specified.

- A urine pregnancy test will be done. If you are found to be pregnant, you will have to discontinue your participation in the study.
- You will be given home pregnancy kits. You can perform the pregnancy test whenever you suspect that you are pregnant.
- You will be asked questions about any symptoms, illnesses and medication changes you have had since your last study visit. It is important to tell the study doctor or the nurse about any changes in health that may have happened even if you do not think that they are related to the study;
- Your eDiary entries will be reviewed monthly by the study staff and during every study visit to ensure that you are completing your entries correctly. The entries will be reviewed via the internet, so you will not need to bring your handheld device with you to every visit. You will use the eDiary to record your any bleeding and use of any back-up birth control method;
- You will be asked how satisfied you are with Mirena on a 5-point scale (from very satisfied- to very dissatisfied) **(Visit 6);**

- The study doctor will conduct a pelvic exam to be sure Mirena is in the proper place inside the womb, has not moved and the removal threads are still visible;
- The study doctor will conduct a physical exam as well as a gynecological exam that will include breast palpation (examination by touch) (**Visit 6);**
- Your vital signs will be taken, including measuring your heart rate and blood pressure. Your weight will also be recorded during this visit (**Visit 6);**
- A PK blood sample will be taken to determine LNG levels in your blood **(this will not occur at every visit; two randomized samples will be taken at two of the visits 3-6);**
- Blood samples will be taken for serum chemistry, hematology **(Visits 4 and 6);**
- Urine samples will be collected for urinalysis **(Visits 4 and 6);**
- **For HMB subgroup**: you will return your used sanitary products in the kit provided by the study site. You will receive another kit with instructions for collection. **(Visits 3,5, and 7)**

End of Treatment (End of Year 8 of Mirena Use)

If you discontinue the study for any reason, an end-of-treatment evaluation will be performed and all study procedures listed below will be performed. You must have Mirena removed by your study doctor before you withdraw from the study.

- A urine pregnancy test will be done.
- You will be asked questions about any symptoms, illnesses and medication changes you have had since your last study visit. It is important to tell the study doctor or the nurse about any changes in health that may have happened even if you do not think that they are related to the study;
- Your eDiary entries will be reviewed monthly by the study staff and during every study visit to ensure that you are completing your entries correctly. You will need to bring your handheld device to this visit and return it to the study staff or study doctor.
- The study doctor will conduct a pelvic exam to be sure Mirena is in the proper place inside the womb, has not moved and the removal threads are still visible;
- The study doctor will conduct a physical exam as well as a gynecological exam that will include breast palpation (examination by touch), and a Pap smear. If you received a Pap smear within six months of the screening visit and the results are normal (with no need for follow up), the Pap smear will not be done;
- Your vital signs will be taken, including measuring your heart rate and blood pressure. Your weight will also be recorded during this visit
- A PK blood sample will be taken to determine LNG levels in your blood
- Blood samples will be taken for serum chemistry, hematology;
- Urine samples will be collected for urinalysis;
- The study doctor will perform the procedure to remove Mirena. You will be asked about your level of pain during the removal of Mirena;
- You will be asked how satisfied you are with Mirena on a 5-point scale (from very satisfied to very dissatisfied
- You will be given a home pregnancy kit. You must perform the pregnancy test on the day of your three-week follow-up phone call.

- **Handling of used Mirena:** to evaluate the performance of Mirena during extended use, your used Mirena device will be returned to the sponsor's representative. They will measure the amount of drug substance left in Mirena once it is removed. Further instructions will be provided by the study site.
- **For HMB subgroup**: you will return your used sanitary products in the kit provided by the study site. You will not be given any additional sanitary products to use.

Pregnancy Follow-up (up to 12 months after EOT)
The study team may contact you three (3) times within the year following Mirena removal to collect important information if you happen to become pregnant. Please refer to the 3-week, 3-month and 12-month follow up call below.

If you wish to become pregnant while you are in the study, please tell your study doctor immediately. Your participation in the study will be discontinued but the clinic will call you at 3 and 12 months after removal of Mirena to ask if you have become pregnant. If you are discontinued, you will still be asked to complete the End-of-Treatment visit as described above.

If you think you may have gotten pregnant while you were in the study, or if you prematurely discontinue the study because you want to get pregnant, you may be asked if your study doctor can collect information about your pregnancy, your delivery and the health of your baby. The study doctor will ask you and your partner to sign an Informed Consent for permission to collect encoded data on the pregnancy and the birth of your child. Your and your partner's decision to allow the collection of information about the pregnancy is entirely voluntary and will not affect your participation in the study.

3-week Follow-up Call
The study team will contact you by phone approximately 3 weeks after Mirena is removed. They will ask if you are pregnant after Mirena was removed.

At your last visit to the study site (End-of-treatment visit) your study staff will give you a urine pregnancy test to take at home. You must take this test the day of your 3-week follow-up phone call.

If you discontinue the study for any reason, the study team will still contact you for this information.

3-month Follow-up Call
If you prematurely discontinue from the study, the study team may contact you by phone approximately 3 months after Mirena is removed. They will ask if you are pregnant.

12-month Follow-up Call
If you prematurely discontinued from the study because you wished to become pregnant, the study team will contact you by phone 1 year after Mirena is removed. They will ask if you are pregnant.

YOUR RESPONSIBILITIES FOR THIS STUDY

If you decide to take part in this study, it is important that you agree to:

- Continue to use Mirena according to the instructions given by your study doctor or the study staff;
- Go to your study visits and complete all telephone follow up calls. As soon as you know that you will not be able to go to a study visit, please contact your study doctor or the study staff to schedule a new visit;
- Complete all required entries in your handheld eDiary at a minimum every 72 hours. The study doctor and study staff will teach you how to use the device and what information you are required to enter.
- Truthfully answer any questions from your study doctor or the study staff when asked about any changes in your health, visits to other doctors or hospital admissions, or changes in your medication, including prescribed medications, over the counter medications, herbal remedies, and vitamins.;
- Perform home pregnancy test if you believe you may be pregnant and contact the study site immediately if results of a home pregnancy test are positive or if you are unsure whether you are pregnant after performing the test;
- Provide needed information for the study, including outcome of any pregnancy if you become pregnant during the study;
- Tell your study doctor or research study staff if ever you change your mind about taking part in the study.
- Use and collect sanitary products for women in the HMB subgroup.

POSSIBLE RISKS

We ask you to carefully consider the possible risks or discomforts involved in participating in the study before you agree to take part.

Loss of Contraceptive Efficacy

Mirena used past 5 years may be less effective at birth control and you may have an unplanned pregnancy.

Side Effects of Mirena

Published data on the safety of Mirena use beyond five (5) years are limited but so far have not given evidence to any new safety concerns arising from the use of Mirena for up to eight (8) years. Listed below are the side effects known to occur in Mirena users in general. All side effects can be different from person to person. You may or may not have experienced them while you were using Mirena in the past.

The common side effects of Mirena include:

- **Expulsion.** Mirena may come out by itself. This is called expulsion. You may become pregnant if Mirena comes out. If you think that Mirena has come out, use a backup birth control method like condoms and spermicide and call your study site.

- **Missed menstrual periods.** About 2 out of 10 women stop having periods after 1 year of Mirena use. Limited data on use of Mirena beyond 5 years indicates that in some women, menstrual periods may re-appear under continued use. When Mirena is removed, your menstrual periods will come back.
- **Changes in bleeding.** The majority of Mirena users notice a change in their menstrual bleeding pattern (bleeding and spotting between menstrual periods, especially during the first 3 to 6 months, sometimes irregular or heavier bleeding, but usually the bleeding becomes lighter and shorter over time. One of the purposes of this study is to assess the menstrual bleeding pattern in women using Mirena for longer than 5 years.
- **Cysts on the ovary.** About 12 out of 100 women using Mirena develop a cyst on the ovary. These cysts usually disappear on their own in a month or two. However, cysts can cause pain and sometimes cysts will need surgery.

Other side effects include:

- **Observed in 10 percent of Mirena users or more**: Abdominal/pelvic pain, headache/migraine, genital discharge, and vulvovaginitis,
- **Observed in less than 10 percent of Mirena users**: Breast pain, painful menstruation, typically involving abdominal cramps (dysmenorrhea), back pain, acne, depression/depressive mood, loss of hair (alopecia), unwanted male-pattern hair growth on a woman's face, chest, and back (hirsutism), and nausea;
- **Rarely, Mirena can cause serious side effects including:**

    - **Pelvic inflammatory disease** (PID, a serious pelvic infection which is usually transmitted via sexual intercourse). There is a slightly higher risk for PID when an IUD is inserted. After that, the risk is similar to women not using an IUD. An IUD does not protect from sexually transmitted disease or PID. You have a higher chance of getting PID if you or your partner has sex with other partners. PID can cause serious problems such as infertility, ectopic pregnancy or pelvic pain that does not go away. PID is usually treated with antibiotics but may in single cases require surgery. If pelvic inflammatory disease is not successfully treated, Mirena must be removed and you will have to discontinue your participation in the study.
    - **Perforation**. Mirena may become attached to (embedded) or go through the wall of the womb. This is called perforation. This occurs most often during insertion but it may not be discovered until some time later. If this occurs, Mirena may no longer prevent pregnancy. If perforation occurs, Mirena may move outside the womb and can cause internal scarring, infection, or damage to other organs and you may need surgery to have Mirena removed. The risk of perforation is increased in women who were breastfeeding at time of IUS insertion. As you have been using Mirena for more than 4 years since placement, this may not be an important serious side effect to consider in this study.

- There are reported events where it is not always possible to determine whether they were caused by Mirena, and include the following: increased blood pressure, Mirena breakage, blood clot in the legs, lungs or in the brain.

Pregnancy Risks

If you get pregnant with Mirena: It is very rare for a woman to become pregnant with Mirena in place for up to 5 years. If you do become pregnant with Mirena in place, the risk that the pregnancy could develop outside the womb (ectopic pregnancy) is increased. About 1 in a 1000 women correctly using Mirena have an extrauterine pregnancy per year. An ectopic pregnancy is a serious condition that needs immediate medical attention. The following symptoms could mean that you may have an extrauterine pregnancy, and you should see your healthcare professional immediately:

- Your menstrual periods have ceased, and then you start having persistent bleeding or pain.
- You have pain in your lower abdomen.
- You have normal signs of pregnancy, but you also have bleeding and feel dizzy.

If the pregnancy develops in the correct place, i.e. the womb, your Mirena will be removed as soon as possible and you will need to discontinue from the study. There is an increased risk for miscarriage, infection, or preterm labor for a pregnancy with an intrauterine system in place. The removal of Mirena during an ongoing pregnancy is however also associated with a risk of miscarriage. Talk with your study doctor and your personal healthcare provider about these risks.

For more information on side effects with Mirena, ask your healthcare provider. It is important that you tell the study doctor or research staff immediately if you have any side effects or any other problems with your health, even if you do not think they are related to the study.

Possible Risks or Discomfort from Study Procedures

There are also possible risks and discomforts from the procedures you may experience during the study. These include:

- Blood draws: The risk of blood drawing includes discomfort at the site of the blood draw with bruising, bleeding, infection, and rarely, fainting or nerve damage. Other possible discomforts may occur during the following situations:
    - Pap smear (cervical smear): You may feel some pressure or mild discomfort when the speculum is inserted into your vagina.
    - Pelvic exam to visualize Mirena threads: You may feel some pressure or mild discomfort
    - Mirena Removal: You may experience, discomfort, mild bleeding, and pain during the removal procedure
    - For HMB subgroup only: You may feel some discomfort using the study provided sanitary products as these may be different from the products you normally use. Please let your study doctor know if you are experiencing discomfort with the study provided sanitary products.

- For HMB subgroup only: You may feel embarrassed or uncomfortable bringing used sanitary products with you the study site. Please discuss this with your study doctor.

POSSIBLE BENEFITS
Possible benefits from taking part in this study may include:

- Extended duration of use of Mirena up to 8 years may offer you a benefit to continue the use of Mirena beyond 5 years for birth control and/or to control your menstrual blood loss if you have heavy menstrual bleeding.
- By extending the duration of use, you can avoid the need to remove the current Mirena and replace it with a new Mirena for another 3 years (thus avoiding the small, but existing aforementioned risks which are associated with a new insertion procedure).
- Taking part in this study will help doctors to learn more about Mirena. This may help other women looking for long-acting reversible birth control methods in the future.

We cannot promise that you will get any benefits from this study.

ALTERNATIVE OPTIONS
You do not have to take part in this study to receive the birth control method of your choice, or - if applicable for you - get continued treatment for your heavy menstrual periods.

If you decide not to take part in this study or decide to have Mirena removed, you may want to think about other options for continued birth control and/or to control your menstrual blood loss. One option is to have a new Mirena inserted or to explore other methods of birth control. Your study doctor can talk with you about these other options and their risks and benefits.

COSTS
You will not be paid for your participation in this study. If you have to travel more often for appointments related to the study, the sponsor will reimburse your travel expenses up to $60.00 per on-site visit. For more information please talk to your study doctor.

On completion of the study, if you decide to replace the Mirena with a new one at the time of removal, the sponsor will provide a new Mirena free of charge. And, if you are in the HMB subgroup and have to stop the study early due to any bleeding issues, the sponsor will provide a new Mirena free of charge. In either case, the free Mirena product will only be sent to the study site following up with you as part of this Study. Please note that the insertion of the new Mirena is not a study procedure. You, or your insurance provider, may be billed by your provider for the cost of the insertion procedure,

You will be compensated for compliance of eDiary data entry if your compliance rate is assessed to be equal to or greater than 85% as reviewed by clinical site staff each month during your participation the study. You will receive payments in the following amount at the end of each month: $30.00.

Greenphire will act as an agent of Bayer HealthCare Pharmaceuticals Inc. to manage the reimbursement process. You will be issued a Greenphire ClinCard, which is a debit card that your funds are loaded onto at the completion of a study visit. When a visit is completed, funds will be approved and loaded onto your card. The funds will be available within 1 business day and can be used at your discretion. You will be issued one card for the duration of your participation. You will be given instructions which will explain how to use your card. If your card is lost or stolen, you can contact the study team for a replacement card.

Greenphire will collect information about you, including name, address, and date of birth. All information is stored in a secure fashion and is deleted from the system once the study has been completed and the funds on the card have been exhausted. Your information will not be shared with any third parties and will be kept completely confidential.

By registering with the ClinCard system and using the ClinCard, you consent to participate in the ClinCard program.

COMPENSATION FOR INJURY

In the event of a research-related illness or injury, you should contact the study doctor who will treat you or refer you for treatment. The study doctor's contact information can be found on page 1 of this form.

If you are injured while participating in this study, you can seek treatment for the usual charge. If your illness or injury is the result of any procedure required by the study that you would not have undergone were it not for your participation in the study, the sponsor will pay usual and customary medical fees for reasonable and necessary treatment, provided you have not already otherwise been properly reimbursed by your insurance, a government program, or other third party coverage for such medical expenses. The sponsor does not maintain responsibility for expenses that are due to pre-existing medical conditions, underlying disease, pregnancy, procedures which would have been performed even if you were not participating in the study, your negligence or willful misconduct, or the negligence or willful misconduct of institution, principal investigators or third parties. No funds have been set aside by the sponsor to compensate you for lost wages, disability or discomfort due to your participation in this study. You do not give up any legal rights as a research participant by signing this consent form.

HOW WILL MY DATA AND BIOLOGICAL MATERIAL BE HANDLED AND USED?

Data

During your participation in the study, personal data, such as your medical history will be reviewed by the sponsor`s representatives involved in monitoring and oversight activities to confirm that you are eligible for the study. The data will be collected on paper or electronically and they will be stored in medical records at your study doctor's office. This personal data will be secured against unauthorized access and kept confidential.

Your Right to Access the Data

Your data that are forwarded to the study sponsor or other parties will contain a code instead of your name. In this way, your identity is kept confidential. We call this encoded data. The list linking the code with your name is kept at the study doctor's site. After participation in the study, your encoded data in addition might be used by authorities for further analyses, not directly related to the study or the study drug.

Your data will be stored at the study doctor's site for at least the duration specified in local regulations (usually up to 15 years).

Detailed information on the handling and use of your data is given in the Informed Consent Form Part – A.

Samples

During your participation in the study samples will be collected from you and evaluated. The samples will be encoded in the same way as your data.

As used throughout this document, term "sample" means any material taken from your body. Common examples are: blood and urine, cells/tissue. Samples specifically planned for this study are as follows: blood, urine (sampling at several visits), pap smear (cervical smear) (sampling at several visits), vaginal swab for chlamydia testing.

Your samples will be used for the following purposes:

- to assess safety and tolerability
- to measure the concentration of the drug substance in Mirena (to find out what your body does with the drug substance in Mirena)
- to measure the menstrual blood loss for women who are part of the HMB subgroup.

CONFIDENTIALITY

During your participation in the study, data (including samples) will be collected. All data collected will be encoded (identified with a number) in order to ensure that your identity will be kept confidential.

The encoded data will be analyzed and prepared for submission to Competent Authorities. The data will be transferred to the pharmaceutical company and/or to

companies within the group of companies of the pharmaceutical company and/or to third parties who perform services for the pharmaceutical company. These companies will use the data in accordance with the purposes of the study as well as for submission to competent authorities.

Representatives of the pharmaceutical company, Competent Authorities or ethics committee staff may require access to your medical records with your personal data (un-coded) to ensure the study is properly conducted and that the data collected is correct. These individuals are obligated to ensure your confidentiality is maintained.

The results of the study (including the information collected from you) will be processed, analyzed, and reported to Bayer HealthCare Pharmaceuticals Inc. or their representative, who are responsible for processing and keeping the data. The written study result may be submitted to Competent Authorities to help them decide if Mirena as an effective intrauterine birth control and / or an effective treatment of heavy menstrual bleeding for women who choose to use intrauterine birth control as their method of contraception can be approved for extended use up to 8 years (currently approved for use up to 5 years). The results will be published in scientific articles. All information in reports/publications and/or presented at meetings will be coded and you will not be identified in person. If your personal data is disclosed to a third party, all appropriate measures will be taken to protect such data.

The study doctor, the sponsor or persons working on behalf of the sponsor, and under certain circumstances, the United States Food and Drug Administration (FDA) and Copernicus Group Independent Review Board (CGIRB) will be able to inspect and copy confidential study-related records which identify you by name.

Additional information and consent regarding data protection must also be read and signed before you can take part in the study.

WHAT WILL HAPPEN TO THE OVERALL RESULTS OF THE STUDY?
Information, that does not include personally identifiable information, concerning this clinical trial has been or will be submitted, at the appropriate and required time, to the government-operated clinical trial registry data bank, which contains registration, results, and other information about registered clinical trials.

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.

The results are intended to be reported in scientific presentations or publications but will not include any information that will personally identify you as a study participant.

USE OF STUDY DATA

The study sponsor believes that transparency of clinical trial data advances science and medical knowledge, in the best interest of patients and public health, provided that patient privacy is protected. Therefore, a factually anonymized set of your study data will be available for other researchers. Factual anonymization means that several steps are performed to prevent the identification of your person. Such steps include the removal of location identifiers as well as of personally identifiable information and the replacement of original dates by random dates. Moreover, the original subject identification numbers used in the study will be replaced by new numbers and the code key that was used to generate the new identification numbers will be destroyed, to prevent any re-identification. Only this factually anonymized study data set may be provided to academic institutions, pharmaceutical companies, other research entities or individual researchers on request for the purposes of specified and approved medical research and development.

Prior to giving access to the factually anonymized data set, any such third party research request has to be approved by an Independent Scientific Review Board. In addition, the requesting party needs to confirm that the data will only be used for the agreed research purpose, that the protection of data privacy will be strictly adhered to, that approval by an Ethics Committee will be obtained for the research proposal and that the anonymized data will not be transferred to other third parties for future use.

The results of the above-mentioned medical research and development activities may be used commercially, such as for development of pharmaceutical products, but will not generate income or property rights for you.

NEW INFORMATION

During the study, new information about the risks and benefits of the project may become known. Your study doctor will talk with you about any important new information that is learned during the course of the study that may affect your willingness to continue to take part in the study. This new information may also mean that you can no longer take part in this study. In all cases, you will be offered all available care to suit your needs and/or medical condition.

VOLUNTARY PARTICIPATION/WITHDRAWAL

Taking part in this study is entirely voluntary. You do not have to take part in this study.

If you choose to take part and you change your mind later, you are free to take back your consent and to stop being in the study at any time without giving a reason. In that case, we ask you to tell your study doctor or study staff. You may be asked to take part in a final visit or follow-up. If you leave the study early, then you will be asked to agree to be contacted for post treatment pregnancy tracking information. You will be contacted by phone at 3 months after the removal of Mirena. At this time, you will be asked if you have been pregnant after the study.

12-month follow-up contact: You will be contacted by phone if you prematurely discontinue the study because you wish to become pregnant. This call will not be done if you were pregnant at the time of the 3 month call. This call will not be done if you told the study site that you no longer wish to become pregnant during your 3 month call. You will be asked about pregnancies that occur within 1 year after end of treatment (EOT).

Your choice to take part or to stop taking part in this study, will not affect your routine/regular treatment, your relationship with those treating you or your relationship with the place where you are getting treatment. You will still receive care for your condition, there will be no penalty to you and you will not lose any benefits to which you are otherwise entitled.

The data that have been collected until the time of your withdrawal will be kept and used. In addition, it is of high importance to collect as much information as possible on the health of all subjects who take part in the study, including those who withdraw before completing the entire study period, according to legal and regulatory requirements. If health status information is not obtained for withdrawn subjects, it may be difficult to interpret the study results correctly. If you withdraw from the study, it would be very helpful if we could keep in touch with you or any health care professionals involved in your treatment to find out how you are.

PREMATURE END OF THE STUDY OR STUDY TREATMENT
This study or the study treatment may be stopped without your consent.

Reasons why the sponsor can stop the study or put the study on hold include:

- Decisions made in the business or commercial interests of the sponsor.
- Decisions made by the Regulatory Authorities or Ethics Committees.
- If the risks of extending Mirena up to 8 years, become greater than the benefits, due to:

    - Safety findings from this study
    - Results of parallel clinical studies

Reasons why the study doctor can stop your study treatment (remove your Mirena) include:

- Taking part in the study is not beneficial to you.
- Complete or partial expulsion of Mirena.
- You become pregnant.
- You are having bad side effects.
- You are not coming to study visits
- You need to get other treatments for a medical condition that the study does not allow.
- You decide to take part in any other clinical study

WHO TO CONTACT FOR MORE INFORMATION?

Contacts in Case of Emergency and for Questions about the Study
Please contact the study staff if you have any questions about this study, its procedures, risks and benefits, or alternative courses of treatment or in case of emergency. The contact information for the study doctor can be found on page 1 of this form.

If you have questions about your rights as a research subject or if you have questions, concerns, or complaints about the research, you may contact:

Copernicus Group Independent Review Board (CGIRB)
One Triangle Drive, Suite 100
Research Triangle Park, NC 27709
Telephone: 888-303-2224
Email: irb@cgirb.com

CGIRB is a group of people who perform independent review of research.

CGIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact CGIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Please visit the Copernicus Group IRB website www.cgirb.com for more information about research studies and the role of a research subject.

INFORMED CONSENT FORM – PART A
(PARTICIPATION IN THE CLINICAL STUDY)

Multi-center, open-label, uncontrolled study to assess contraceptive efficacy and safety of Mirena during extended use beyond 5 years in women 18 to 35 years of age including a subgroup evaluation of a treatment effect on heavy menstrual bleeding

General

By signing this form, I agree to participate in the above-mentioned study and study procedures as described in the Patient Information Sheet.

I understand that my decision to take part in the study is entirely voluntary. I am free to change my mind and withdraw from the study at any time, and without giving reasons. Such withdrawal will not affect the standard medical care I will receive.

I confirm that

- The study doctor or the physician delegated by the study doctor has explained the study to me comprehensively.
- I have had the opportunity to discuss the study with the study doctor and all my questions were answered.
- I have read and understood the Patient Information Sheet for the study.
- I understand that I will receive a copy of the Patient Information and Informed Consent Form once I have signed it.
- I understand that if I am using Mirena to control my heavy menstrual bleeding (HMB) (and as birth control) I am part of the HMB subgroup and there are additional procedures that I will complete. I have read and understood the additional procedures outlined in the Patient Information sheet above.
- I understand and agree if I become pregnant up to 3 months after the removal of Mirena, I will inform the study doctor.
- I understand and agree if I choose to prematurely discontinue my participation in the study due to a desire to become pregnant, my study doctor may contact me up to three (3) times within the year after Mirena is removed to see if I am pregnant.
- I understand that if I become pregnant at any point after I have signed this consent form, or within 3 months of Mirena removal (i.e. End of Treatment), the study doctor will ask me and my partner to sign an Informed Consent for permission to collect encoded data on my pregnancy, delivery and health of the child.

Handling of my data

Data Collection and Review

I understand and agree that during my participation in the study some of my personal data, will be collected and stored on paper and/or electronically in medical records at my study doctor’s office.

I understand and agree that my data, e.g. medical records, may be accessed and reviewed by competent authorities, ethics committees, the sponsor Bayer HealthCare Pharmaceuticals Inc. or contract services providers of the sponsor (who are obliged to keep my identity confidential) involved in monitoring and oversight activities in order to examine whether the study has been properly conducted and the collected data are correct.

Data Protection (coding) and Use

I understand and agree that in addition, my data will be furnished with a code, instead of my name, to keep my identity confidential. The list linking the code with my name is kept at my study doctor's office. This is hereinafter called encoded data.

I understand and agree that during and after the study my encoded data may be provided to the sponsor, its cooperation partners, which are involved in the research and development of Mirena, their group companies and their contract service providers (e.g. laboratories), to process and analyse the encoded data to determine the results of the study, publish the results in scientific articles or presentations (in which I will not be identified in person), submit them to competent authorities to help them decide if Mirena can be approved to be extended for use up to 8 years (currently approved for use up to 5 years). I understand and agree that in case of side effects, my encoded data may also be provided to the competent authorities and the ethic committees.

I understand and agree that after participation in the study, my encoded data might be used by competent authorities for further analyses, not directly related to the study or the study drug.

Some personal data will be transferred to third parties and U.S. government agencies as part of reporting requirements for Section 111 of the Medicare, Medicaid, and SCHIP Extension Act of 2007 (MMSEA).

Data Storage

I understand and agree that my data will be stored at the study doctor's site for at least the duration specified in local regulations for up to for 15 years.

I understand and agree that the encoded data may be stored and used for a longer duration.

I understand and agree that if I withdraw from the study, the data collected from me until the time of withdrawal will be kept, used and stored as described above.

Primary Care Doctor Notification:
I agree that my primary doctor can be told that I am taking part in this clinical research study (initial on the appropriate line).

Please tick and initial: _____ Yes _____ No

_____ Not applicable, I do NOT have a primary doctor

Heavy Menstrual Bleeding Subgroup:
I agree to take part in the Heavy Menstrual Bleeding (HMB) subgroup. I agree to allow the sponsor to test my menstrual blood loss to understand if Mirena remains effective or stays the same in lessening menstrual blood loss when used beyond 5 years for up to 8 years, as explained in this document. I understand that if I am using Mirena to control my HMB (and as birth control) I must consent to participate in the Heavy Menstrual Bleeding subgroup to participate in this study.

Please tick and initial: _____Yes _____No

_____Not applicable, I am not participating in the HMB Subgroup

Declaration of study subject related to participation in clinical study:

_____

Printed Name of Subject

_____

Signature of Subject **Date**

Declaration of Study Doctor/Study Personnel Delegated by the Study Doctor:
I have explained and discussed with the study subject in language he/she understood, the nature, purpose, requirements and risks of the study.

I have discussed alternative therapies / treatments.

I will ensure a copy of the patient information sheet and informed consent form is provided to the study subject.

_____

Printed Name of Person Obtaining Consent

_____

Signature of Person Obtaining Consent **Date**

INFORMED CONSENT FORM – PART B
(HANDLING OF SAMPLES)

Multi-center, open-label, uncontrolled study to assess contraceptive efficacy and safety of Mirena during extended use beyond 5 years in women 18 to 35 years of age including a subgroup evaluation of a treatment effect on heavy menstrual bleeding

Handling of my Samples

I understand and agree that samples of biological material (as described in the information sheet) will be collected during my participation in the study. These samples may be sent for evaluation to service providers of the sponsor during or after the study. Each sample will be labelled with a code instead of my name to keep my identity confidential.

Duration of Storage of and Blood Samples

I understand and agree that my and samples will be stored at the sponsor's representative for at least the duration specified in local regulations for up to 15 years.

I understand and agree that I can withdraw from this consent, related to the use and storage of samples collected during my participation in the study, at any time without giving a reason and without affecting my standard medical care.

Printed Name of Subject

Signature of Subject **Date**

Declaration of Study Doctor/Study Personnel Delegated by the Study Doctor:

I have explained and discussed with the study subject in language he/she understood, the sample encoding and storage condition.

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent **Date**

HIPAA AUTHORIZATION

Federal regulations give you certain rights related to your health information. These include the right to know who will receive the information and how it will be used. The study doctor must obtain your authorization (permission) to use or release any health information that might identify you.

What information may be used and shared?
The study doctor and study staff will use and share your health information as part of this research study. This may include your name, address, telephone number or other facts that could identify the health information as yours.

Examples of the information that may be used are:

- Medical records (from any doctor, hospital or other healthcare provider)
- Information created or collected during the research. This could include your medical history, and dates or results from any physical exams, laboratory tests or other tests.

Who will disclose, receive, and/or use the information?
This form will authorize the following person(s), class(es) of persons, and/or organization(s) to disclose, use, and receive the information:*

- Every research site for this study, including this institution, and including each site's research staff and medical staff
- Health care providers who provide services to you in connection with this study
- Laboratories and other individuals and organizations that analyze your health information in connection with this study, in accordance with the study's protocol
- The research sponsor for this study, Bayer HealthCare Pharmaceuticals Inc., and the people and companies that they use to monitor, administer, or conduct the research
- The United States Food and Drug Administration (FDA)
- The members and staff of Copernicus Group Independent Review Board (CGIRB) that reviews this study
- Principal Investigator and other Investigators working on this study

- Study Coordinator(s)
- Additional members of the Research Team
- Members of the institution's administrative staff responsible for administering clinical trials and other research activities
- A Contract Research Organization and its employees who are monitoring, administering and conducting the research on behalf of Bayer HealthCare Pharmaceuticals Inc. (A contract research organization is an independent entity with which a research sponsor contracts to oversee and facilitate various aspects of the clinical research process on the research sponsor's behalf.)
- Data and Safety Monitoring Boards and others authorized to monitor the conduct of the Study, for example a Clinical Events Committee
- The members and staff of the institution's affiliated Privacy Board (if such a board is used)
- Regulatory authorities in foreign jurisdictions
- Others (as described below)

* If, during the course of the research, one of the companies or institutions listed above merges with or is purchased by another company or institution, this authorization to use or disclose protected health information in the research will extend to the successor company or institution.

SPECIFIC UNDERSTANDINGS

By signing this research authorization form, you authorize the use and/or disclosure of your protected health information described above. The purpose for the uses and disclosures you are authorizing is to conduct the research project explained to you during the informed consent process and to ensure that the information relating to that research is available to all parties who may need it for research purposes. Your information may also be used as necessary for your research-related treatment, to collect payment for your research-related treatment (when applicable), and to run the business operations of the institution.

This information may be re-disclosed or used for other purposes if a recipient described on this form is not required by law to protect the privacy of the information. The investigator and institution for this study are required by law to protect the privacy of this information.

You have a right to refuse to sign this authorization. While your health care outside the study, the payment for your health care, and your health care benefits will not be affected if you do not sign this form, you will not be able to participate in the research described in this authorization and will not receive treatment as a study participant if you do not sign this form.

If you sign this authorization, you will have the right to revoke it at any time, except to the extent that the institution has already taken action based upon your authorization or needs the information to complete analysis and reports of data for this research. This authorization will never expire unless and until you revoke it. While your health care outside the study, the payment for your health care, and your health care benefits will not be affected if you revoke this authorization, you will not be able to continue participating in the research described in this authorization. To revoke this authorization, please write to the study doctor. The study doctor's contact information can be found below:

Michael L Twede MD, FACOG
Corner Canyon OB/GYN
11724 S State St Ste 200
Draper UT 84020

You will not be allowed to see or copy the study information collected about you described on this form as long as the research is in progress, but you have a right to see and copy the study information upon completion of the research in accordance with the institution's policies.

You have a right to receive a copy of this form after you have signed it.

The results from this study might be transferred to countries outside the US, for application for international registration in these countries. In that case your identity will still remain confidential.

If you agree, your primary physician/General Practitioner (GP) will be informed about your participation in the study. However, you may still take part if you choose for your doctor not to tell your physician/GP.

Will my authorization expire?
If you do not withdraw this Authorization, it will remain in effect.

If the research site is located in California, Delaware, Indiana, Washington, or Wisconsin, this authorization will expire on 31Dec2060.

There is no expiration of this authorization except for research conducted in the states listed above.

The study doctor will keep this Authorization for at least 6 years.

AUTHORIZATION
By signing this form, I allow the use or disclosure of my health information. I will receive a signed and dated copy of this Authorization.

Printed Name of Subject

Signature of Subject **Date**