INFORMED CONSENT

Sponsor / Study Title:	**FHI 360 and National Institutes of Child Health and Human Development / "A multi-center, single-blind, randomized clinical trial to compare two copper IUDs: Mona Lisa NT Cu380 Mini and ParaGard"**
Protocol Number:	**CCN016**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Additional Contact(s): (Study Staff)	**«AdditionalStaffMemberContacts»**
Address:	**«PiLocations»**

The study site, FHI 360, and the Eunice Kennedy Shriver National Institute of Child Health and Human Development (NICHD) invite you to participate in a clinical trial. This clinical trial is an experimental research study using intrauterine devices (IUDs). Clinical trials involve people who volunteer to take part in a study. Take your time to decide if you want to be part of this experimental research study. If you want to know more about this study before volunteering, ask the study doctor or study staff.

If you are under the age of 18, your parent or guardian needs to give permission for you to be in the study. You do not have to be in this study if you don't want to be, even if your parent or guardian has already given permission.

If you are the parent or legal guardian of a child who may take part in this study, your permission and the permission of your child will be needed. When "you" appears in this form, it may refer to you or your child.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to find out:

- How well the experimental IUD prevents pregnancy
- How the experimental IUD compares to the currently-used IUD in the USA in terms of:
    - Subject satisfaction and continued use
    - Failure to successfully place the IUD, puncture of the uterus, or the IUD coming out of the uterus by itself
    - Side effects (vaginal bleeding, menstrual pain, pelvic pain)
    - Subjects' level of pain during and shortly after placement of the IUD
    - Ease of IUD placement

WHAT ARE THE STUDY PRODUCTS?

The study products are contraceptive intrauterine devices (IUDs) that are made of plastic and contain copper.

- The experimental IUD is the European-approved product called the Mona Lisa NT Cu380 Mini. It is used by many women in Europe. The study team has permission from the European company and the US Food and Drug Administration (FDA) to evaluate it here in the United States (US). The Mona Lisa NT has not been approved in the U.S. and is considered an experimental IUD.
- The second IUD is the ParaGard® product. It is approved by the US Food and Drug Administration (FDA). Currently, there are 5 approved IUDs available in the US. However, the ParaGard IUD is the only US-approved IUD that does not contain hormones.

The two copper IUDs in this study are different sizes. The ParaGard IUD is "T" shaped and is 32 mm by 36 mm in size. The Mona Lisa NT Cu380 Mini IUD is "T" shaped and is 24 mm by 30 mm in size (about 20% smaller than the ParaGard IUD).

WHAT DOES THE STUDY INVOLVE?

We expect that there will be about 1100 women participating at 16 clinics in the US. Women who join the study should be healthy, 16-40 years old, sexually active with a male partner at least once a month, and have regular menstrual periods every 21-35 days. They should understand what is required for them to do and be willing to meet the requirements of the study.

If you have decided to participate in the study, you will first sign and date this Informed Consent Form before any study procedures are done.

This is a randomized study and you will not know which IUD you receive, but your study doctor will know. Randomization means that you will be given a specific IUD by chance, like tossing a coin or rolling a die. If you are enrolled into the study you will have a 80% chance of being in the group that receives the Mona Lisa NT Cu380 Mini IUD and a 20% chance of being in the group that receives the ParaGard IUD. Your chance of getting the experimental IUD is four times higher than getting the ParaGard IUD.

The study will take approximately 39 months to complete. During this time, you will have to come to the clinic for approximately 7 visits; the exact number of visits will depend on when you are able to have the IUD placed. There is a possibility that the study will be extended, at that time, you will be asked if you consent for the additional participation time.

WHO SHOULD NOT TAKE PART IN THE STUDY?

If you have certain medical problems, take certain medicines, or are pregnant, you should not take part in this research study.
The study staff will ask you about these conditions to see if you are eligible to participate. You will not be enrolled if the study staff or your medical provider thinks it is not safe for you to use a copper IUD.

YOUR FIRST VISIT

If you choose to participate in the study, sign, and date this consent form, we will first make sure you meet the requirements to be in the study. Then the following will occur:

1. We will ask you your date of birth, ethnicity, race, medical and pregnancy history, and about any medication use.
2. We will measure your blood pressure, height and weight, and do a pelvic exam.
3. We will test you for sexually transmitted infections (STIs)/and reproductive tract infections (RTIs). If we learn that you have an infection, you will be treated with medications.
4. We will do a pap smear, unless you have had a recent test for which results can be provided or you are under 21 years of age.
5. We will test your urine for pregnancy.

If you are not ready or able to enroll on the day of screening but would still like to enroll, you will need to return within 60 days in order to be re-evaluated. When you return, the study doctor will make sure that you still meet the requirements to be in the study. If you previously had an infection, the study doctor will make sure that you were treated for the infection.

Visit 1 involves IUD placement. If you meet all the requirements to be in the study, you will have the IUD placed using standard procedures. The following will occur during Visit 1:

1. Before we place the IUD in your uterus (womb), we need to make sure your uterus is the proper size. We will use a slender tool (sound) passed through your cervix to measure your uterus.
2. If your uterus is the right size for an IUD, we will place the IUD in your uterus. A small plastic tube, containing the IUD, will be passed through your cervix. Then the IUD will be released from the tube into your uterus and the tube will be removed.
3. We will ask you to rely only on the IUD to prevent pregnancy. However, if you think you will be at risk for an STI, you should use a condom for protection while you are in the study.

4. We will collect information on the level of pain you experienced from IUD placement while you are in the office and we will provide a form to record your level of pain during the six days immediately following IUD placement.
5. We will provide paper diaries for daily recording of any vaginal bleeding or spotting. You will record this information each day for a full year. For every four-week period in the year-long study, you will record whether you used another type of contraceptive (including condoms). You will also record whether you had vaginal intercourse at least once in that period, whether you had any pelvic pain and if you did have pelvic pain, when it was relative to your period.

YOUR FOLLOW-UP VISITS AND PHONE CALLS

We will ask you to return to the clinic for follow up visits six (6) times after the IUD has been placed. We also will ask you to participate in four (4) phone calls.

The follow up visit schedule is as follows:

Visit 2	6 weeks after placement of the IUD
Visit 3	3 months after placement of the IUD
Visit 4	6 months after placement of the IUD
Phone Call 1	9 months after placement of the IUD
Visit 5	12 months after placement of the IUD
Phone Call 2	18 months after placement of the IUD
Visit 6	24 months after placement of the IUD
Phone Call 3	30 months after placement of the IUD
Visit 7 (Exit Visit)	37 months after placement of the IUD
Phone Call 4	17 days after removal of the IUD

During follow-up visits (study visits 2, 3, 4, 5, 6, and 7) the following will occur:

1. You will provide a urine sample to test for pregnancy.
2. We will check for the IUD string
    - If the IUD string is not present, we will do an ultrasound to make sure the IUD is in place. During the ultrasound, a small, thin instrument (probe) is placed in your vagina.
    - If an ultrasound is done because the IUD string is not present, for remaining visits you also will need an ultrasound to confirm the IUD is in place.
3. You will turn in your completed daily diaries during study visits 2, 3, 4, and 5. The research coordinator will review them with you to make sure that all the information is complete.
4. We will give you additional paper diaries during study visits 2, 3, and 4.
5. We will give you a paper form to record the use of any other contraceptive methods during study visits 5 and 6.
6. You will turn in your completed contraceptive use forms during study visits 6 and 7. The research coordinator will review them with you to make sure that all the information is complete.

7. We will ask you about your last menstrual period, satisfaction with the IUD, and any medications you may have taken since your last visit.
8. We will ask you about any health problems you may have experienced since your last visit.
9. We will provide a home pregnancy test to complete and report the results during each study phone call.

During phone calls 1, 2, and 3 the following will occur:

1. We will ask you if you think the IUD is in place.
2. We will ask you about your last menstrual period, satisfaction with the IUD, and any medication you may have taken since your last visit.
3. We will ask you about any health problems you may have experienced since your last visit.
4. We will ask you about the result of your home pregnancy test.
5. The research coordinator will review your completed contraceptive use forms with you during phone calls 2 and 3.

During visit 7 (exit visit) the following will also occur:

1. We will let you know which IUD you were using.
2. If you are using the experimental Mona Lisa IUD, we will remove it unless the study is extended as mentioned above and you consent to continue using the IUD.
3. If you are using the ParaGard IUD, you can continue to use it for an additional 7 years.
4. We will give you a home pregnancy test to complete 17 days after this exit visit.

During phone call 4 the following will occur:

1. We will ask you about the result of your home pregnancy test.
2. We will ask you about any ongoing health problems you may have experienced since your last visit.

WILL I STILL HAVE PERIODS?

You will still have periods while the IUD is in place. You may have an irregular bleeding pattern the first month after placement of the IUD. Your periods also may be heavier, or more crampy. Please write down on the diary every time you have any bleeding and/or spotting. If your bleeding is heavier than usual, please get in touch with the study staff.

HOW DO I USE THE DIARY CARDS?

You will have diary cards to fill out for the first 12 months after the IUD has been placed. You will use the cards every day and check-off whether bleeding or spotting occurred or not. You will also use the diary card to note if you had intercourse, if you used a condom or any other type of contraception, and if you had any pelvic pain and when the pain occurred.

The study staff will review your diary cards with you at Visits 2, 3, 4, and 5. Please ask us if you are not sure how to use your diary card.

WHAT IF THE IUD COMES OUT?
Call the study center **right away to report if the IUD comes out.** The study staff will schedule you for a clinic visit as soon as possible. The IUD will not protect you from pregnancy if it is not in place. So, if you have sex before you come back to the clinic, you should use another kind of birth control.

WHAT HAPPENS IF I THINK I AM PREGNANT WHILE USING THE IUD?
You should contact the study staff right away if you think you may be pregnant. We will ask you to return to the clinic as soon as possible for a urine pregnancy test.
If your urine pregnancy test is positive, we may collect a blood sample of approximately 4 teaspoons for a blood pregnancy test. If the blood test also confirms pregnancy, you will have an ultrasound to determine when you got pregnant and to see if the IUD is still in your uterus.

The study staff will discuss options with you if you become pregnant. Please see the possible adverse events associated with pregnancy that occurs with the IUD in place in the Risks of Using the IUD section, below.

WHAT HAPPENS IF I DECIDE THAT I WANT TO BECOME PREGNANT WHILE USING THE IUD?
If you want to get pregnant while in the study, you should contact the study staff. You will be scheduled to come into the clinic to have the IUD removed. You will be asked to complete the Study Exit Visit procedures at the time that the IUD is removed. You will be asked to have a urine pregnancy test. You will no longer be a part of the study after the IUD is removed; however, you will be asked to let the study staff know if you become pregnant within 17 days after the IUD is removed and what happens to the pregnancy.

WHAT ARE THE RISKS OF USING THE IUD?
Infection:

The IUD does not protect again HIV, AIDS, or STIs like herpes, gonorrhea and Chlamydia. One of the risks is an infection of the uterus called pelvic inflammatory disease (PID). This is uncommon (less than one in 100 women). PID can develop when bacteria that cause sexually transmitted infections (STIs) move into the uterus. This could happen on its own, but also at the time when the IUD is placed. To reduce the risk of PID, we will test for STIs at screening. Women testing positive for STIs will be treated as soon as possible. If untreated, PID can lead to ectopic pregnancy or infertility, or in rare cases, lead to hysterectomy, or cause death.

Pregnancy:

There is a chance you may become pregnant during this study. If you do get pregnant, the pregnancy could be outside the uterus (ectopic). Ectopic pregnancy is very rare (less than one in 1,000 women using IUDs). If you are pregnant with an IUD in place, an ultrasound will be done as soon as possible to assess the IUD and the pregnancy.

With the ParaGard IUD, the chance of pregnancy is less than 1 per 100 women per year. With the Mona Lisa IUD, the chance of pregnancy has not been measured. However, the Mona Lisa IUD was approved in Europe because it is similar to other products (such as ParaGard) that are known to be highly effective.

You should consider the possibility of pregnancy before you decide to take part in this study. Talk to the study staff about what you might do if you become pregnant and do not wish to continue the pregnancy. You should understand your options before you give consent to take part in this research study.

If pregnancy should occur with the study IUD in place, the IUD should be removed. However, removal or manipulation of the IUD may also result in pregnancy loss.

The following may occur if you become pregnant with the IUD in place:

- Miscarriage, infection, preterm birth, or other pregnancy complications
- If the IUD cannot be removed or you choose not to have it removed, you will have a higher risk of miscarriage, preterm labor or preterm birth than if the IUD was removed.
- When pregnancy continues with the IUD in place, long-term effects on the offspring are unknown.

Uterine Perforation:

The copper IUD or sound may pierce (make a small hole) in the wall of your womb (rare – less than one in 500 women). If this happens, you may need surgery to remove the study device from your pelvis (abdomen).

Side effects may include:

- Anemia (low iron in the blood)
- Back pain
- Dysmenorrhea (pain during your period that interferes with your daily life)
- Dyspareunia (pain during intercourse)
- Embedment (the IUD becomes fixed into the wall of your uterus, and may require surgical removal of the IUD)
- Expulsion, partial or complete (the study device moves part way into your vagina or all the way out of your body)
- Fainting or light headedness after IUD placement
- Leukorrhea (whitish or yellowish discharge from your vagina)
- Menstrual flow that is heavier or for more days than usual
- Menstrual spotting
- Movement of study device during MRI (magnetic resonance imaging)
- Pain and cramping
- Skin rash
- Vaginitis (inflamed vagina that can result in discharge, itching or burning feeling)

There may also be risks that are unknown at this time. It is important that you promptly report any complications or changes in health.

Risks from study procedures:

It is not expected that the severity or frequency of the following events will be any different for the Mona Lisa IUD compared to ParaGard.

Pelvic exams
Pelvic exams may cause discomfort or cramping. Some women may experience temporary spotting or bleeding afterward. Some women are embarrassed during these exams.

Ultrasound
There are no known harmful effects of ultrasound. You may experience slight vaginal discomfort, but the instrument used for the ultrasound is small.

Diary and medical history questions
Some of the questions you will be asked may be personal or embarrassing. They may upset you. You may refuse to answer any of the questions that you do not wish to answer.

Although we have made efforts to protect your identity, there is a small risk of loss of confidentiality.

WHEN SHOULD YOU CONTACT YOUR STUDY DOCTOR?
Contact the study doctor if you experience any of the following symptoms:

- If you have severe or persistent pain, swelling or tenderness in your abdomen;
- If you have a sudden fever (101 °F +), chills, vomiting, diarrhea, dizziness, fainting or a sunburn-like rash on your face or body;
- If you think you might have become pregnant; or
- If you think the IUD may have come part-way or all of the way out of your uterus.

HOW WILL THE STUDY HELP ME OR OTHERS?
You may get no direct benefit if you are enrolled in this study. However, this study may lead to the approval of a new IUD here in the USA.

HOW LONG DOES THE STUDY LAST?
You will take part in the study for up to 37months after IUD placement. Including the screening process before and the follow up process after IUD placement, the total time you may participate in the study could be up to 39 months. If we extend the study, we will ask if you wish to continue participating in the study.

WHO IS WORKING ON THIS STUDY?
The study is supported by funds from FHI 360 and the National Institute of Child Health and Human Development (NICHD) of the National Institutes of Health (NIH). FHI 360 and NICHD are leading the conduct of the study and are sponsors.

WILL I BE PAID FOR THE STUDY?
You may be reimbursed for time and travel. You will receive $_____ for each study visit you complete. You will be reimbursed at the end of each study visit / monthly for completed study visits / quarterly (every 3 months) for completed study visits. If you do not finish the study, you will only be reimbursed for the visits you completed.

COSTS OF BEING IN THE STUDY
The study device and all tests, procedures and visits required by the study are provided at no cost to you. The sponsors, FHI 360 and National Institutes of Child Health and Human Development, pay for them.

WHAT HAPPENS IF I NEED MEDICAL TREATMENT?
If you become ill or are hurt while you are in the study, obtain the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study.

If you get hurt because of the study and you need medical care, the study doctor will help you get the care you need right away. You will not have to pay for any emergency care expenses that are directly related to conditions caused by the study. The study will not be obligated to pay for any other medical care. The study doctor will talk with you about any medical problems you may have. He or she may send you to other doctors for medical care.

If you have questions, talk with your study doctor at the number listed on the first page of this form.

Emergency contact: If you are having a serious medical problem as a result of the study, call the study doctor at the number listed on the first page of this form. These study doctors need to know you have a serious medical problem.

You will be given a card to keep in your wallet that will have emergency contact information on it. The card also has information on it about the study drug. Keep the card with you at all times and call the number on the card immediately if you are admitted to the hospital or if any other important health events happen.

In no way does signing and dating this consent form waive your legal rights nor does it relieve the investigators, Sponsors or involved institutions from their legal and professional responsibilities

IS MY PARTICIPATION IN THIS RESEARCH STUDY VOLUNTARY?
Participation in this study is voluntary. If you do not want to be in this study, you will still receive any of the services and alternative treatments otherwise available to you at this study site. Your study doctor can discuss the alternatives and the risks and benefits of these alternatives with you.

CAN I QUIT THE STUDY EARLY?
You may refuse to participate or quit the study at any time. If you decide to quit, you will still be able to receive any of the services and alternative treatments otherwise available to you at this study site. Any non-study treatment will be at your cost or provided through your usual coverage.

If you decide to quit, you will need to notify the site and complete the final visit to the clinic to have the IUD removed. You will also be asked to have a pelvic exam, urine pregnancy test, and safety assessments. Your last diary cards will be collected and you will be asked about use of any medications. The IUD will be removed.

There is no penalty and you will not lose any benefits you have earned up to the time you quit. Your medical care from the study hospital or clinic will not change. You can get copies of your medical records and lab results to take to your own hospital or doctor.

If you leave the study early, you will be reimbursed only for your time in the study. Your compensation for time and travel will stop after you quit the study.

During the study, your study doctor will tell you about any new information that may change the risks of the study or may change your decision to be in it.

CAN I BE REMOVED FROM THE STUDY WITHOUT MY CONSENT?
The study doctor may decide that you cannot stay in the study. He or she may not think it is best for you to be in the study. He or she may not allow you to continue in the study if you cannot do what the study requires such as coming to your scheduled clinic visits.

The Sponsor, IRB, Food and Drug Administration (FDA), or other regulatory agency may stop the study at any time for any reason.

WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser: Pro00020530.

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.

HOW WILL MY PRIVACY BE PROTECTED?

The results of this research may be published to inform other physicians and scientists. Your name or your records will not be given out without your consent unless there are extreme circumstances. Your records may also be reviewed by the Food and Drug Administration (FDA), the Institutional Review Board (IRB) or its staff and the sponsors of this study or their designees. All of these people are required to keep your personal information private. You will be told if the researcher has any current personal interest, such as any economic interest, related to performing the proposed research.

Your study doctor and his or her study staff will collect information about you. This information, called data, will be entered, without your name, on a report form. On all those report forms, a code number will replace your name, so your name is not used. All the data collected will be kept confidential. Authorized personnel will enter the data into the sponsor's computer database. The data might be transferred to other sponsor locations within the European Union, the United States or other countries for review or analysis by authorized personnel. The data collected will be used for the evaluation of the study, and may be used in the future in related or other studies. The data may be submitted to health authorities for registration purposes. Members of health authorities, the Food and Drug Administration, Institutional Review Board, the sponsors or other persons required by law may review the data provided. These data may also be used in publications about the IUD.

We will do everything we can to keep others from learning about your participation in this study. To further help us protect your privacy, we have obtained a Certificate of Confidentiality from the United States Department of Health and Human Services (DHHS).

With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below.

You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study.

If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

Disclosure will be necessary, however, upon request of DHHS for the purpose of audit or evaluation, and is limited only to DHHS employees involved in the review.

The Privacy Act of 1974, as amended, applies to Federal data that is retrieved by your name or an identifier assigned to you. The documents you complete and provide to the study site will be safeguarded in a record system covered by Privacy Act System Notice 09-25-0200 which applies to clinical, basic, and population-based research studies at the National Institutes of Health.

We will in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself, children, or others. For example, in the case of child abuse or neglect.

Adult Subject's or Minor's Assent statement:

I _____ (print your name) have been told the benefits and risks of the study. I have read and understood this Informed Consent and talked with study staff. They told me whom to contact in case of an emergency. I had the chance to ask questions. All my questions have been clearly answered. I understand participation is completely voluntary and that I can stop at any time. I agree to take part in this research study.

_____ _____

Date ***Sign your name here***

Parental/Guardian Permission statement (if applicable):

I _____ (print your name) have been told the benefits and risks of the study. I have read and understood this Informed Consent and talked with study staff. They told me whom to contact in case my child should have an emergency. I had the chance to ask questions. All my questions have been clearly answered. I agree for my child to take part in this research study.

_____ _____

Date ***Sign your name here***

Investigator's statement:

I, _____ (printed name), the undersigned, have explained to the subject or their parent/legal guardian in her native language the procedures to be followed in this study and the risks and benefits involved.

_____ _____

Date ***Signature of Investigator or Designee***

<u>Please keep a signed and dated copy of this document for your records.</u>