Date: April 14, 2020
Principal Investigator: Stéphanie Gaillard, M.D.
Application No.: IRB00054202

[redacted]

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: **A Pilot Clinical Trial Assessing the Safety and Feasibility of Intramuscular Administration of the TA-CIN Vaccine as Adjuvant Therapy for Patients with History of HPV16 Associated Cervical Cancer**

Primary Study Consent

Application No.: IRB00054202

Sponsor: SPORE

Principal Investigator: Dr. Stéphanie Gaillard [redacted]

1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.

- 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.
- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.

2. Why is this research being done?

This research is being done to test whether it is safe to give the TA-CIN vaccine to women with cervical cancer who do not have disease recurrence after standard of care treatments.

Scientists have found that a family of viruses called the Human Papilloma Virus (HPV) can cause cervical cancer. Most cervical cancers are caused by a type of HPV called HPV16. This is the type of HPV that we target in this study. Other goals of the study are to learn more about how the immune system responds to the study drug given in the study. The study drug has been tested in humans in clinical trials.

The use of TA-CIN vaccine in this research study is investigational. The word "investigational" means that TA-CIN vaccine is not approved for marketing by the Food and Drug Administration (FDA). The FDA is allowing the use of TA-CIN vaccine in this study.

This is a Pilot study. Pilot studies are designed to see if a larger study can be done, with more participants. This pilot study will assess the safety of the TA-CIN vaccine in patients with the HPV16 virus. It will also look at whether TA-CIN works better if injected in the arm or leg.

What is TA-CIN?

TA-CIN is a vaccine. The vaccine is made up of three proteins from the HPV16 virus. The vaccine is comprised of HPV16 L2, E7 and E6 proteins. This study will test whether the vaccine can teach your body's immune system to recognize and get rid of the HPV16 virus. TA-CIN has been given alone or in combination with other vaccines in over 90 people.

Women with HPV16 positive cervical cancer who have completed standard of care treatment within the last 12 months and do not have disease recurrence are eligible for this study.

How many people will be in this study?

This research study plans to enroll up to 14 people at 2 centers in the United States. Up to 7 people are expected to take part in this study at Johns Hopkins.

3. What will happen if you join this study?

If you join the study we will ask you to do the following things:

The study will consist of the following parts:

- Screening evaluation
- Dosing period and response assessments
- Follow-up visits after last dose

Screening Evaluation

During the pre-study screening evaluation, you will be evaluated to see if you qualify for the study. This will occur before any study regimen can begin. The screening visit will be performed within 60 days of the first study drug administration visit.

The following tests will be performed as part of the screening visit. Some of these tests and procedures are likely to be part of regular cancer care and may be done even if it turns out that you do not take part in the research study. If you have had some of these tests or procedures recently, they may or may not have to be repeated:

- A complete medical history, including family history of cancer and a review of your current medications.
- Physical and pelvic exam, including vital signs (temperature, blood pressure, heart rate, breathing rate, height, and weight) and an assessment of your overall general health and ability to perform daily tasks (performance status).
- A computed tomography (CT), positron emission tomography (PET) scan and CT (PET/CT), or magnetic resonance imaging (MRI) scan will be done to evaluate your disease status during the study.
- Blood samples (about 2.5 tablespoons) will be taken in order to check blood cell counts (white and red blood cells, platelets), kidney and liver function, hepatitis, and HIV testing.
    - As part of being in this study, you will have a test for HIV virus (the virus that causes AIDS). You will be given the State of Maryland HIV consent form as part of that process. If this test is positive, it does not always mean that you are infected with the HIV virus. It means you will need further testing and you will receive counseling. The law requires us to report positive tests to the health department. Also as part of being in this study you will have a test for hepatitis (B or C or both). If the results of this test show that you have hepatitis (B or C or both), the law requires us to report this to the health department.
- HPV16 testing: We will use previously collected tumor sample (from a biopsy or surgery) to test for the presence of HPV16 (this will most likely already be done as part of the "Pre-Screening Consent" process)
- Archived (previously collected) tumor samples will be requested to assess tumor characteristics and the immune system.

The study team will check the results of these screening tests to see if you qualify to take part in the study. If you wish to continue to participate in the study, you must also agree to the following:

- You will agree to comply with the visit schedule and procedures.

Dosing Period

If you meet the study requirements during the screening period, you will then begin the dosing phase of this study.

TA-CIN will be given as a single injection in your muscle every 4 weeks for a maximum of 3 times. Where you receive the injection will depend on randomization. You will be randomized (like flipping a coin) into one of two groups. Group 1 will receive the vaccination in the arm. Group 2 will receive the vaccination in the leg. You will receive a numbing cream over the area where the injection will be done (lidocaine if you are not allergic) to reduce the pain from the injections. This will be done at least 1 hour before the injections. You will have to stay at the hospital or clinic for 60 minutes after the injections to see if you have any negative reactions to the study drug.

Below is a description of the tests and procedures that will be done during the dosing period:

- Physical and pelvic exam, including vital signs (temperature, blood pressure, heart rate, breathing rate, and weight) and an assessment of your overall general health and ability to perform daily tasks (performance status).
- A review of any medications you are taking or have taken since your last visit.
- A review of any side effects or other medical problems you have had since your last visit.
- Blood samples (about 3 teaspoons) will be taken in order to check blood cell counts (white and red blood cells and platelets) as well as kidney and liver function.
- Research blood sample about 5.5 tablespoons at the first visit and about 3 tablespoons at the second and third visits).

The study doctor will review the results of your physical exam and blood tests and decide if you should receive the study drug.

One week after you receive the study drug, the study nurse will call you to ask you about any reactions at the injection sites or other side effects that you are experiencing.

Follow-Up Period

Four follow-up evaluations will be performed during a clinic visit after your last dose of the study drug. These will take place at the following time points: (1) 1-3 weeks after your last dose of the study drug, (2) about 6 months after your last dose of the study drug, (3) about 12 months after your last dose of the study drug, and (4) about 24 months after your last dose of the study drug.

Below is a description of the tests and procedures that will be done during the follow-up visits:

- Physical and pelvic exam, including vital signs (temperature, blood pressure, heart rate, breathing rate, and weight) and an assessment of your overall general health and ability to perform daily tasks (performance status).
- A review of any medications you are taking or have taken since your last visit.
- A review of any side effects or other medical problems you have had since your last visit.
- Blood samples (about 3 teaspoons) will be taken in order to check blood cell counts (white and red blood cells and platelets) as well as kidney and liver function.
- Research blood sample will be about 5.5 tablespoons at the first visit and about 3 tablespoons at the second and third visits.

Request to collect and store biospecimens (tumor tissue and blood samples) for future research

As part of this research study, we would like to ask you to let us store your biospecimens and health information for future research. This research could include other diseases. The study doctor can provide you with additional information if you have questions. Also, further information about our use of your biospecimens can be found in this consent document under the heading *What happens to Data and Biospecimens that are collected in the study?*.

Will you allow us to store the biospecimens we collect for this study for use in future research?

YES ☐ _____
Signature of Participant

No ☐ _____
Signature of Participant

Future Contact
We would also like your permission to contact you about other studies that you may be eligible for in the future.

Will you allow us to contact you in the future for other research studies?

Yes ☐ _____ _____
Signature of Participant Date

No ☐ _____ _____
Signature of Participant Date

How long will you be in the study?
You will be in this study for 2 years.

4. What are the risks or discomforts of the study?

Any study has risks, which may include things that could make you feel sick, feel uncomfortable or harm you. You may experience side effects related to the TA-CIN vaccination while participating in the study. As with any investigational product, there may be serious risks that are not expected, including death.

TA-CIN
As of November 2014, about 98 patients and healthy volunteers have received TA-CIN (either by itself or in combination with other drugs). TA-CIN can cause side effects, although not everybody gets them. If you experience one or more side effects please speak with your study doctor.

Most common side effects (occurring in more than 20 out of 100 participants): Local vaccine site reactions (tenderness, pain, redness, bruising, itching, and swelling) and headache. The lidocaine cream that is used prior to each injection should help with pain at the time of injection. Some people experience allergic reactions to lidocaine which can include redness and/or rash of the skin, hives, swelling or pain.

Less common side effects (occurring in 3 to 20 out of 100 participants): abdominal pain, dizziness, fatigue (tiredness), muscle aches (myalgias), skin redness, and runny nose (rhinitis).

Rare side effects (occurring in 3 or fewer out of 100 participants): loss of appetite (anorexia), arm pain or weakness, abnormal dreams, drowsiness, dry mouth, menstrual disorder, flu-like symptoms, general discomfort or uneasiness (malaise), syncope, nausea, anaphylaxis (severe allergic reactions), bronchospasm (difficulty breathing because the airways have narrowed), swelling of larynx due to fluid accumulation, generalized collapse.

Blood Sampling
Taking blood may cause some discomfort, bleeding or bruising where the needle enters the body, and in rare cases, it may result in fainting. There is a small risk of infection. Some people have not felt well

when having their blood taken. Some people have felt dizzy while having their blood drawn or after. Let the nurse know if you would prefer to lie down while you have your blood drawn.

Additional Side Effects

It is possible that there may be side effects and discomforts that are not yet known or that the known side effects may be more severe. You will be told about any new risks that become known during this research study.

5. Are there risks related to pregnancy?

Women who are capable of becoming pregnant will be excluded from this study.
It is not known if TA-CIN may affect an embryo, fetus, or nursing baby. A woman who has experienced natural menopause with absence of a menstrual period for more than 12 months is considered postmenopausal. In the majority of cases, treatment for cervical cancer (either with hysterectomy or radiation or chemotherapy) will render women unable to become pregnant. If you have any questions regarding your menopausal status or your potential to become pregnant, please discuss them with your study doctor prior to signing this consent. Your doctor may perform a blood test to make sure that you are postmenopausal.

6. Are there benefits to being in the study?

There is no direct benefit to you from being in this study.

If you take part in this study, you may help others in the future.

7. What are your options if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment. All options have risks and benefits that you should discuss with your study doctor.

You do not have to join this study. If you do not join, your care at Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).
- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

If you are eligible for and enroll in this study you will be offered:

- $25 per completed visit in appreciation of you time
- Parking voucher

You may be required to provide your Social Security number to be paid. If your payment for study participation exceeds $600 per year, this information must be reported to the Internal Revenue Service.

10. Can you leave the study early?

- You can agree to be in the study now and change your mind later.
- If you wish to stop, please tell us right away.
- Leaving this study early will not stop you from getting regular medical care.

If you leave the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential – but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. You may be asked to give us a list of other health care providers that you use.

14. What does a conflict of interest mean to you as a participant in this study?

A researcher and Johns Hopkins have a financial or other interest in this study.

In some situations, the results of this study may lead to a financial gain for the researcher and/or Johns Hopkins. This financial interest has been reviewed in keeping with Johns Hopkins' policies. It has been approved with certain conditions, which are intended to guard against bias and to protect participants.

If you have any questions about this financial interest, please talk to Dr. Stéphanie Gaillard at [redacted]. This person is a member of the study team, but does not have a financial interest related to the study. You may also call the Office of Policy Coordination ([redacted]) for more information. The Office of Policy Coordination reviews financial interests of investigators and/or Johns Hopkins.

15. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

- If you have health insurance: The costs for any treatment or hospital care you receive as the result of a study-related injury will be billed to your health insurer. Any costs that are not paid for by your health insurer will be billed to you.

- If you do not have health insurance: You will be billed for the costs of any treatment or hospital care you receive as the result of a study-related injury.

By signing this form you will not give up any rights you have to seek compensation for injury.

16. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is [redacted]. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

b. What do you do if you have questions about the study?

Call the principal investigator, Dr. Stéphanie Gaillard at [redacted]. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at [redacted].

c. What should you do if you are injured or ill as a result of being in this study?

If you think you are injured or ill because of this study, call Dr. Stéphanie Gaillard at [redacted] during regular office hours.

If you have an urgent medical problem related to your taking part in this study, call Dr. Stéphanie Gaillard at [redacted] during regular office hours and the on-call physician at [redacted] (24-hour clinic number) after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?

Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

17. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time
Signature of Person Obtaining Consent	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO [redacted]; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time
Signature of Participant	(Print Name)	Date/Time
Signature of Witness to Consent Procedures (optional unless IRB or Sponsor required)	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO [redacted]; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

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