Official Title:	Multicenter, Randomized, Open-Label Trial in Children and Adolescents to Establish Optimal Number of Doses for HPV Vaccination in Children and Adolescents Living With HIV
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INFORMED CONSENT FOR PARENTS OR GUARDIANS OF CHILDREN AND ADOLESCENTS LIVING WITH HIV (9-13-year old)

'Multicenter, Randomized, Open-Label Trial in Children and Adolescents to Establish Optimal Number of Doses for HPV Vaccination in Children and Adolescents Living With HIV'

Official Study Title for Internet Search on http://www.ClinicalTrials.gov: 'Multicenter, Randomized, Open-Label Trial in Children and Adolescents to Establish Optimal Number of Doses for HPV Vaccination in Children and Adolescents Living With HIV'

Short title: OPTIMO

Protocol: ULACNet-301, version 4.2 19-August-2022

Funding Sponsor: National Cancer Institute (NCI), National Institutes of Health (NIH), USA.

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INTRODUCTION

Your child is invited to take part in a clinical research study authorized by the Peruvian National Institute of Health mainly because he/she lives with HIV and his/her current age is 9-13, which means he/she is eligible to be vaccinated against HPV (Human Papillomavirus). This form has information to help you decide if you would allow your child to participate in this study. Take the time you need, read this form carefully and ask the study physician any questions you may have.

You should not sign this form until you understand all the information included in the following pages and until your questions regarding the research have been answered satisfactorily.

- You can take an unsigned copy to read it again, if necessary, and talk about the study with your family, friends and/or doctor, if you wish.
- You can choose to allow your child to participate or not in the study and his/her rights will not be affected by your decision.
- You can stop your child's participation (or your child can stop participation) in the study at any time without explanation. This will not result in a loss of the benefits to which he/she would otherwise qualify.

Why is the study being done?

Study participants will include both children living with HIV and children who do not have HIV. This study is being done to determine the best number of HPV vaccine doses for children and adolescents living with HIV.

Human papillomavirus (HPV) is a common virus worldwide and is mainly spread through sexual contact. Most HPV infections occur early after sexual activity begins, typically between the ages of 14 and 24. Most HPV infections do not cause symptoms as the body is able to get rid of the virus on its own. However, when the body is unable to get rid of the virus, the infection can sometimes cause certain cancers as that of the cervix of the uterus, other parts of the external female genital organs such as the vaginal and vulvar region, the anus, as well as cancers of the back of the mouth and throat many years after the initial infection if it is not detected or treated early.

The OPTIMO study can help the investigators learn if one dose of the HPV vaccine Gardasil 9 is good against HPV infection. We will learn if one dose of the vaccine is able to induce a big enough response to HPV. If so, this could make HPV vaccination more practical and less expensive in the future. The reduction in the number of doses could help make sure all girls and boys living with HIV get vaccinated against HPV and reduce the impact of vaccine shortage.

Three vaccines against HPV are approved in Peru and other countries: Cervarix, Gardasil, and Gardasil 9, for women and men ages 9 to 26. In this study we will use Gardasil 9, the most recently approved vaccine. The Gardasil 9 vaccine protects against nine types of HPV (seven types that can cause cancer, and two that cause genital warts). These vaccines work by helping the body produce antibodies to fight HPV infections. When a vaccinated person encounters HPV, the antibodies in their blood combat the virus and prevent the infection from establishing. It usually takes several weeks after vaccination for the body to develop antibodies for protection. The HPV vaccine does not contain viruses; it just contains the outside coverings of the HPV virus. Therefore, it is not possible to become infected with HPV from receiving the HPV vaccine. The vaccine Gardasil 9 does not cause HPV infection or cancer.

Who can participate?

Your child may be eligible to participate in this study because he/she is living with HIV, is currently between 9 and 13 years old and hasn't had the HPV vaccine yet.

There could be reasons why your child may not be able to participate in this study. The study physician or study staff will discuss this with you.

What is the usual approach to HPV vaccination?

HPV vaccines have been given as a series of three shots over 6 months. In 2016, a 2-shot schedule with the second injection given 6-12 months after the first injection was recommended for children ages 9 through 14 years. Receiving 3 injections over 6 months or 2 injections with the second injection give 6-12 month after the first injection are considered the standard schedules.

In Brazil, the currently recommended vaccination for children/adolescents and/or adults living with HIV are three doses (0, 2 and 6 months).

Because we still do not know what the best number of vaccine doses is for children and adolescents living with HIV, all participants enrolling in this study will receive at least three doses of the vaccine by the end of the study (as shown in **Figure 1** next page), as is recommended by the Center for Disease Control (CDC) of the United States.

What are my child's other choices if he/she does not take part in this study?
If your child decides not to take part in this study, he/she may receive the standard HPV vaccination offered by the government health system or by a private provider. The study physician can talk to you about these options if your child does not participate in the study.

What are the study groups?
The study will include approximately 100 children (about 20 from Peru, 28 from Brazil and the rest from Haiti). This study will have a total of 4 groups. Three groups (about 75 children) are comprised of children living with HIV and the 4th group (about 25 children) is comprised of children without HIV infection.

The study groups are as follows (as shown in **Figure 1**) (the fourth group comprised of children and adolescents without HIV is in gray):
Group 1: receives 4 total doses of Gardasil 9, the first three doses are given within the first 6 months after enrolling in the study (baseline, 2 months and 6 months) and the fourth dose is a booster dose given 30 months after enrollment; includes 9-13 year-old children living with HIV.
Group 2: receives 3 total doses of Gardasil 9, the first two doses are given within the first 6 months after enrolling in the study (baseline and 6 months) and the third dose is a booster dose given 30 months after enrollment; includes 9-13 year-old children living with HIV.
Group 3: receives 3 total doses of Gardasil 9, one dose is given at the first study visit, then a booster dose is given 24 months later, and a final booster dose is given 30 months after enrollment; includes 9-11-year-old children living with HIV.
Group 4: receives 3 total doses of Gardasil 9, one dose is given at the first study visit, then a booster dose is given 24 months later, and a final booster dose is given 30 months after enrollment; includes 9-11-year-old HIV-negative children.

If you agree that your child will participate in this study, his/her study group will be randomly assigned (like throwing a dice), based on his/her age, but you will know which group he/she is assigned to before study initiation. Your child and the study staff will also know this information.

If your child is 9-11 years old, he/she will be assigned to Groups 1, 2 or 3. If your child is 12-13 years old, he/she will be assigned to Groups 1 or 2.

How is the vaccine administered?
The vaccine is administered as an injection (shot) given in the muscle of the the upper arm or thigh.

How long will my child participate in this study?
If your child participates in the study, he/she will be in the study for approximately 30-31 months starting from the first study visit, when he/she receives the first injection. He/she will be asked to visit the study center approximately 7-8 times over the course of the study based on the study group he/she will participate.

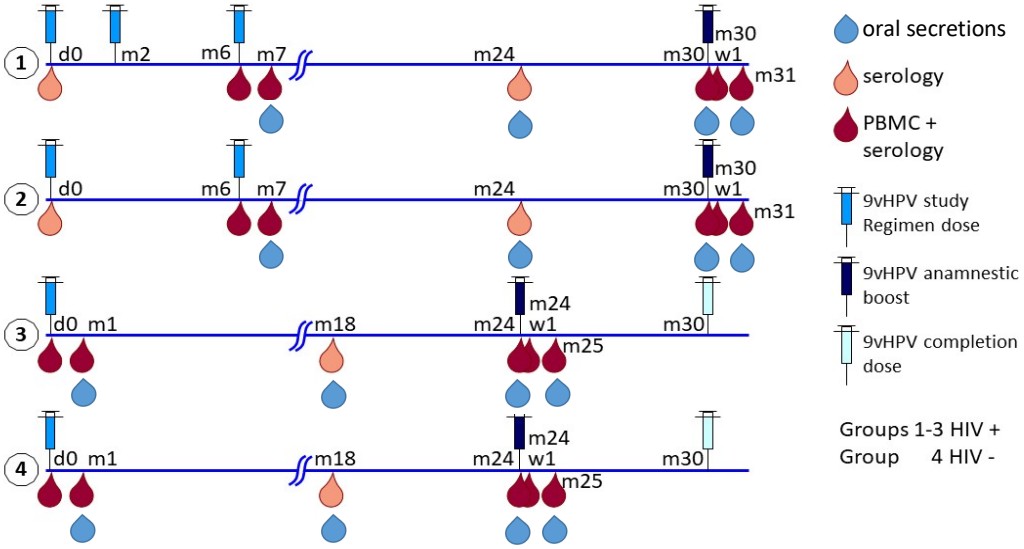

Figure 1. Study Design

What extra tests and procedures will I have if my child takes part in the study?
If you choose to have your child participate in the study, your child will need to have the following extra tests, and/or procedures to find out if s(he) can be in the study:

At the enrollment visit, the study physician will discuss this consent form with you and answer any questions you may have. Once you have signed it, the following procedures will be done.

- A review of your child's medical history and current medications, including any symptoms s(he) may be currently experiencing. We will ask questions about your child such as demographics and school attendance.
- A physical exam will be performed that includes your child's vital signs (pulse, blood pressure, temperature, and breathing rate), height and weight.
- Urine samples for pregnancy testing will be obtained from your daughter, if she has started her period. It is unlikely that she will be pregnant but if so, she will not be able to be in the study. In this case, we will talk to and support you and your daughter and refer you to the appropriate care.
- Blood will be collected at this first enrollment visit, to test for the presence of specific antibodies* against the HPV types in the vaccine and to measure memory B cells (cells that form as a result of an infection or vaccination). If your child is in group 1 or 2, we will collect 16.5 mL (about 1.1 tablespoon) of blood at this visit: 8.5 mL will be used to test for the presence of HPV antibodies and 8 mL will be used for HIV viral load (6 mL) testing and CD4/CD8 T cell counts testing (2 mL). If your child is in group 3 we will collect 34 mL of blood (2.3 tablespoons): 26 mL will be used to test both for the presence of HPV antibodies and to measure memory B cells (cells that form as a result of an infection or vaccine) against the HPV types in

the vaccine. 8 mL will be used for HIV viral load testing (6 mL) and CD4/CD8 T cell counts testing (2 mL).

- **Optional:** In this visit we will also collect two types of samples for your child's mouth:
  - Saliva: we will ask your child to provide about 10 mL of saliva by spitting into a device connected to collection tubes where the saliva will be dripping into. Saliva will be used to test for the presence of oral specific antibodies against the HPV types in the vaccine.
  - Mouth gargle: we will ask your child to gargle with 15 mL of mouthwash for 15 sec and then swish the mouthwash around inside his/her mouth for 15 more second seconds. We will then ask for your child to spit the mouthwash into a collection cup. Mouth gargle will be used to look for antibodies against the HPV types in the vaccine and to look for the HPV virus (HPV DNA) itself that can be found if infected naturally.
- The first dose of the study vaccine schedule will be administered. Your child will be asked to stay in the clinic at least 30 minutes after he/she receives the injection to make sure s(he) does not have any negative reaction to the study vaccine.

What will happen at other visits during the study?
If your child is eligible to continue in the study, some or all the following procedures will happen at the visits during the study:

Group 1:
Your child will return to the clinic at least six more times at 2 months, 6 months, 7 months, 24 months, 30 months, and 30 months plus 1 week after the enrollment visit (as shown in **Figure 1** and **Table 1**).

At these *follow-up study visits*, all or some of the following procedures will happen:

- A review of your child's medical history and current medications, including any symptoms s(he) may be currently experiencing. We will ask about all side effects (serious and non-serious) your child may have experienced.
- A physical exam will be performed that includes your child's vital signs (pulse, blood pressure, temperature, and breathing rate), height and weight.
- Urine samples for pregnancy testing will be obtained from your daughter, if she has started her period. If your daughter becomes pregnant during the study, her study vaccinations will be stopped until the pregnancy is completed. Similarly, participants in the study who are breastfeeding will not receive the vaccine. If your daughter becomes pregnant during the study, we will support you and your daughter and refer you to the appropriate care.
- Blood will be collected as follows:
  - At the 24 months visit, 8.5 mL of blood (less than 1 tablespoon) will be collected and tested for the presence of HPV antibodies.
  - On all other visits where blood is drawn (5 visits), 26 mL of blood (1.8 tablespoons) will be collected as shown in **Table 1** to test for the presence of antibodies and to measure memory B cells (cells that form after an infection or vaccination).
- **Optional:** Both saliva (10 mL) and gargle rinse (15 mL) will be collected at the following study visits where blood is to be collected: 7-month, 24-month, 30-month, and 31-month.
- Administration of the study vaccine doses will be done on the upper arm or the thigh following the study vaccine schedule shown in **Figure 1** and **Table 1** for group 1. A booster vaccine dose will be administered at the 30 months follow-up study visit. At each visit in which a vaccine dose is administered your child will be asked to stay in the clinic at least 30 minutes after he/she receives the injection to make sure s(he) does not have any negative reaction to the study vaccine.

At the *End of study visit* (31 months after the first visit) we will collect 26 mL of blood (1.8 tablespoons) to test for the presence of antibodies and to measure memory B cells (cells that form after an infection or vaccination).

Group 2:
Your child will return to the clinic at least five more times at 6 months, 7 months, 24 months, 30 months and 30 months plus 1 week after the enrollment visit (as shown in **Figure 1** and **Table 1**).

At these *follow-up study visits*, all or some of the following procedures will happen:

- A review of your child medical history and current medications, including any symptoms s(he) may be currently experiencing. We will ask about all side effects (serious and non-serious) your child may have experienced.
- A physical exam will be performed that includes your child's vital signs (pulse, blood pressure, temperature, and breathing rate), height and weight.
- Urine samples for pregnancy testing will be obtained from your daughter, if she has started her period. If your daughter becomes pregnant during the study, her study vaccinations will be stopped until the pregnancy is completed. Similarly, participants in the study who are breastfeeding will not receive the vaccine. If your daughter becomes pregnant during the study, we will support you and your daughter and refer you to the appropriate care.
- Blood will be collected as follows:
  - At the 24 months visit, 8.5 mL of blood (less than 1 tablespoon) will be used to test for the presence of HPV antibodies.
  - On all other visits where blood is drawn (6 visits), 26 mL of blood (1.8 tablespoons) will be collected as shown in **Table 1** to test for the presence of antibodies and to measure memory B cells (cells that recall an infection or vaccination).
- Optional: Both saliva (10 mL) and gargle rinse (15 mL) will be collected at the following study visits where blood is to be collected: 7-month, 24-month, 30-month, and 31-month.
- Receive an injection of the study vaccine on the upper arm or the thigh, following the vaccine study schedule indicated in **Figure 1** and **Table 1** for group 2**.** Each time your child receives a vaccine dose we will ask that s(he) stay in the clinic at least 30 minutes after the injection to make sure s(he) does not have any negative reaction to the study vaccine.

At the *End of study visit* (31 months after the first visit) your child will provide 26 mL of blood (1.8 tablespoons) to test for the presence of antibodies and to measure memory B cells (cells that recall an infection or vaccination).

Group 3:
Your child will return to the clinic at least five more times at 1 month, 18 months, 24 months, 24 months plus 1 week and 30 months after the enrollment visit (as shown in **Figure 1** and **Table 1**).

At these *follow-up study visits*, all or some of the following procedures will happen:

- A review of your child medical history and current medications, including any symptoms s(he) may be currently experiencing. We will ask about all side effects (serious and non-serious) your child may have experienced.
- A physical exam will be performed that includes your child's vital signs (pulse, blood pressure, temperature, and breathing rate), height and weight.

- Urine samples for pregnancy testing will be obtained from your daughter, if she has started her period. If your daughter becomes pregnant during the study, her study vaccinations will be stopped until the pregnancy is completed. Similarly, participants in the study who are breastfeeding will not receive the vaccine. If your daughter becomes pregnant during the study, we will support you and your daughter and refer you to the appropriate care.
- Blood will be collected as follows:
  - At the 18 months visit, 8.5 mL of blood (less than 1 tablespoon) will be used to test for the presence of HPV antibodies.
  - On all other visits where blood is drawn (4 visits), 26 mL of blood (1.8 tablespoons) will be collected as shown in **Table 1** to test for the presence of antibodies and to measure memory B cells (cells that recall an infection or vaccination).
- **Optional:** Both saliva (10 mL) and gargle rinse (15 mL) will be collected at the following study visits where blood is to be collected: 1-month, 18-month, 24-month, and 25-month.
- Receive an injection of the study vaccine on the upper arm or the thigh (at the 24 months visit, as indicated in **Figure 1** and **Table 1** for group 3)**.** After your child receives the vaccine dose, we will ask that s(he) stay in the clinic at least 30 minutes after the injection to make sure s(he) does not have any negative reaction to the study vaccine.

At *the End of study visit* (30 months after the first visit) your child will receive a final vaccine dose. We will ask your child to stay in the clinic at least 30 minutes after he/she receives the injection.

The results of the pregnancy tests that will be done on your child will be explained to you verbally by the clinical team at each of the study visits. You will also receive a copy of the results.

During the study, you will receive follow-up phone calls from study staff every three months to ask how your child is doing.

If your child start having sex after entering the study, your child must agree to use suitable contraception during the remainder of the study. The study physician will discuss appropriate contraception with you and your child. The method chosen to be effective for your child will be provided for free until the end of the study.

All participants will receive the Gardasil 9 HPV vaccine.

Do the HPV vaccines work?

All HPV vaccines are effective against the types of HPV for which they are designed. Protection can be expected to last long. In different studies, almost all participants who received the vaccines were protected from HPV infection and the diseases it causes. In countries where HPV vaccination is offered, the number of HPV infections and diseases that HPV causes have decreased over the past 11 years.

Are the HPV vaccines dangerous?

HPV vaccines are generally very safe. More than 100 million doses of HPV vaccine have been administered in the last 11 years and the best evidence to date shows no increase in reactions compared to other vaccines.

Gardasil 9, also known as the 9-valent HPV vaccine, is an approved vaccine (injection) in many countries. In Brazil, this vaccine was approved by ANVISA (Health Surveillance Agency) to provide protection against anal and genital diseases caused by nine types of HPV. The U.S. Drug Regulatory Authorities (FDA) and the European Medical Agency (EMA) have authorized the use of Gardasil 9.

Will my girl need cervical testing later in life, even if she is vaccinated? (this question does not apply for boys)
Yes. HPV vaccines protect against the most common HPV types, but people can become infected with other types of HPV not included in the vaccine.

What effects might the study tests have on my child?
Your child may feel discomfort during some of these tests, and some procedures may even involve risks, such as:

Possible risks of vaccination: Your child may experience pain in his or her arm (or thigh) and may develop a bruise, pain, or swelling at the injection site. Severe reactions are very rare. If they occur, the research center team will be here to help you immediately.

Possible risks of having blood drawn: Drawing blood from your child's arm can cause pain, a bruise, dizziness and, rarely, infection. The clinical team will be present to help your child if any reaction to blood draw occurs.

Table 1. Study Visit Schedule and Procedures												
Study Visits (Months)	**ENR (0)**	**1**	**2**	**6**	**7**	**18**	**24**	**24 + 1 Wk**	**25**	**30**	**30 + 1 Wk**	**31**
Visit type: Group 1 & 2	Enrollment visit	Follow-up study visits										End of study
Visit type: Group 3	Enrollment visit	Follow-up study visits								End of study visit	NA	NA
Obtain Consent and Assent	All											
Determine Eligibility	All											
Randomization	All											
Study Medical History	All											
Medical Chart Review	All									3		1,2
Questionnaires	All	3	1	1	1,2	3	All	3	3	All	1,2	1,2
Physical Exam	All						All			All		
Urine Pregnancy Test (females only)	All		1	1,2			3			All		
HIV Viral Load	All											
CD4/CD8	All											
Vaccination												
Group 1	V1		V2	V3						Boost		
Group 2	V1			V2						Boost		
Group 3	V1						Boost			Last Dose		
Blood Draw	All	3		1,2	1,2	3	All	3	3	1,2	1,2	1,2
Saliva and gargle	All	2			1,2	3	All		3	1,2		1,2

Blood volumens will be collected as follows:
Group 1 and 2: 16.5 mL at the enrollment visit, 8.5 mL at 24 months visit and 26 mL in all other visits in which blood is to be collected
Group 3: 34 mL at the enrollment visit. 8.5 mL at the 18 months visit and 26 mL in all other visits in which blood is to be collected
ENR, enrollment; **V**, vaccine; **NA**, not applicable. The numbers inside the table indicate the study groups shown in Figure 1.

What should I know about the study vaccine and its side effects?

As with any other vaccination, your child may have a pain in the arm (or thigh) and have redness, pain, or swelling at the injection site. Other reactions that may occur, usually within a day or two, include:

- Headache
- Fever (feeling hot)
- Nausea (feeling sick) without vomiting
- Dizziness
- General discomfort (not feeling well, in pain)

Rarely, a severe allergic reaction (anaphylaxis) may occur after vaccination (in 3 out of a million people vaccinated), usually minutes after vaccination. Also, fainting can occur after vaccination and sometimes results in falls with injuries. Clinical staff are trained to help with a reaction of this kind. A doctor will observe your child for 30 minutes after vaccination. This is the routine procedure after each vaccination.

What are the expected benefits of participating in this study?
Your child will benefit from this study by receiving human papillomavirus (HPV) vaccination. Specifically, he/she will receive protection against the 9 types of HPV of vaccine Gardasil 9. The vaccine routinely available in Peru protects against only 4 types of HPV.

What if new information comes up after I decided that my child will participate in the study?
You will be informed in a timely manner of important new information that could affect your child's participation in the study.

What if my child is injured in the study?
If your child suffers any harm as a result of participating in the study, we will ensure that get, at no cost, full and immediate treatment at the INI, which works 24 hours a day, comprehensive assistance and follow-up for as long as necessary, during and after the study.
By signing this consent form, you or your child will not be giving up any of legal rights, guaranteed in the Brazilian regulation of research involving human beings, being one of the rights to request compensation.

Will I get paid?
You will not be paid for your child's participation in this study. However, you will receive reimbursement to cover the costs of transportation to the study center and food and/or a snack during each study visit.

Will I have to pay?

You will not need to pay anything for your child to participate in this study. There will be no expense on your part. The researcher and the sponsor are responsible for all expenses related to the care routine (exams and procedures) necessary after signing this free and informed consent. All materials, research vaccines, samples and tests that are part of this study will be provided free of charge to your son/daughter. All expenses necessary for the participation in the study concerning your child and his/her companion, including transportation and food, will be reimbursed on all study visits.

What if I want my child to stop receiving the study vaccine, stop study procedures, or withdraw from the study?

You are free to choose to have your child NOT participate in this study and leave the study at any time. Your child's care will not be affected, and you will not lose any benefits or rights you would normally have if you do not agree to your child participating in this study, or if you decide that your child will not continue after he/she has entered the study. To opt out, you can inform or call any member of the research team at any time and tell them that you do not want your child to participate further in this study. You can also send a written note to the study researcher and this will cancel all your child's study appointments in the future.

If your child withdraws from the study before receiving at least three doses of the vaccine, we will recommend that your child receive the pending injections through the health system.

Researchers may use the information and/or specimens collected before you or your child decide to discontinue participation in the study.

Researchers could terminate your child's participation in the study, if necessary. Possible reasons include:

- The study could be interrupted by the sponsor or some of the institutions or authorities in charge of regulating its execution.
- The study physician or researchers might determine that it is a risk for your child to continue in the study.
- Your child might not want or could be unable to follow the instructions of the study.

If your child decides not to participate or if he/ she decides to leave the study, this will not damage the relationship with his/her doctors or with this study clinic or any of the staff of the study clinic.

Will my child's privacy be protected?

If your child participates in this study, he/she will be assigned a unique code. All information collected will be identified only with that code. The information linking his/her name with the code will be kept in a separate file. His/her personal information will be kept on a secure computer in a password-protected file in a closed office with restricted access. Both computers and files are password protected. His/her personal information will be used only for this study and only staff working on this study will have access to the information.

Any identifiable information we obtain for this study will remain confidential. When the results are published or discussed in conferences, no information that could reveal your child's identity will be included. Some of the information collected may be shared anonymously with other researchers.

The collected information will be stored during the study and up to five years after it is finished. After that time, it will be destroyed or de-identified, i.e. any information that identifies your child will be replaced with a unique code that does not directly identify him/her.

Who will see my child's medical information?

There are organizations that may inspect your child's records or information from the study. These organizations are required to make sure your information is kept private. Some of these organizations are:

- The study sponsor, the National Cancer Institute (NCI) and NCI agents and partners.
- The National Cancer Institute will obtain information for this clinical trial under data collection authority Title 42 U.S.C. 285T
- The Food and Drug Administration in the US.
- The Office of Human Research Protection (OHRP)
- Study team members of the Fred Hutchinson Cancer Research Center, Seattle, USA and the INI-FIOCRUZ.
- Members of the study Data and Safety Monitoring Board.
- The Ministry of Health

- INI-FIOCRUZ Institutional Research Ethics Commmittee (CEP) as well as other ethical institutions that guarantee good study practices
- Every health care personnel who provides services in connection with this study.
- Any laboratories, other individuals/organizations that analyze your health information in connection with this study as defined by protocol.

You and your child may withdraw permission to use and share your child's health information at any time by written request to the study doctor or by calling the study personnel. If this is the case, your child will not be able to remain in this study. After that date, no new information that identifies your child will be collected. However, information about your child's health that was previously collected may continue to be used and provided to third parties, as mentioned above. When the study is complete, you and your child can write to the study physician to ask for access to his/her health information that was collected as part of the study.

Will information about this study be included in a registry or database?
A description of this clinical study will be available on the http://www.ClinicalTrials.gov page. This website will not include information that can identify your child. At most, the website will include a summary of the results. You can search this website at any time.

Information from this clinical trial will also be available on the REBEC website (Registration of Brazilian Clinical Trials) at http://www.ensaiosclinicos.gov.br. This site does not include any information that can identify your son/daughter.

Who to call if you have questions about...?

- The Study or Study-Related Injuries: Contact Study Investigator Dr. Beatriz Grinsztejn, 24 hours a day, 7 days a week, by phone (021) 2270-7064 or at STD and AIDS Clinical Research Laboratory at INI/Fiocruz – Avenida Brasil, 4365 – Manguinhos – Rio de Janeiro
- Child rights as a study participant: if you have any questions about the rights of your son/daughter as a participant or about the ethics of the study, you can contact the CEP INI-FIOCRUZ, at (021) 3865-9585 or at Avenida Brasil, 4365 –Manguinhos – Rio de Janeiro, National Institute of Infectious Diseases Evandro Chagas. An Ethics Committee is composed of a group of people from scientific and non-scientific areas who carry out an initial and periodic review of the research study to ensure safety and protectparticipants' rights.

Upon completion of this research protocol your study physician will receive the results of the research when available. At your request, your doctor may provide you with information related to these results, unless otherwise indicated.

Sample Storage
During the study, we will collect medical and other anonymized information and blood samples that will be stored and analyzed to answer study-related questions. The remaining samples that can be useful in future research, seran almacenadas a largo plazo. Stored samples can help researchers how to better understand the immune responses of children and adolescents living with HIV can help immunity children against HPV in children and adolescents living with HIV. The stored samples may

be shared with researchers in the United States and other countries for the exclusive use described for this study.

You can withdraw your consent for future use of stored samples anytime, and this will not affect your son/daughter's participation in the main study.

How will samples be obtained for future studies and long-term storage?

No additional samples will be collected. You only need to authorize the use of the remaining samples (whole blood in RNALater, plasma and PBMC) that will be obtained as part of the main study.

Where will the samples be stored?

The remaining samples that can be used in future studies will be labeled with a code of the study. The samples will be collected, processed and stored in the INI-FIOCRUZ laboratory. The final destination of the samples will be the study's central laboratory at Fred Hutchinson Cancer Research Center in Seattle, United States.

How long will the samples be stored?

The collected samples can be stored for a period of 10 years and this period can be renewed for another 10 years, if approved by the CEP.

The benefit of studies with stored samples and data includes knowing more about the immune response to the vaccination against HPV infection. The analyzes that will be carried out with the samples will only be for research purposes.

Storage of samples will not incur additional expenses for you or your child. The stored samples and data for future use will be anonymized, i.e. will not include information that can identify the child, in order to maintain privacy and the right to confidentiality.

Future use of biological samples:

If you agree, a portion of your son/daughter's biological samples that are remaining after the tests in this study will be stored in freezers, in a place called a biorepository, approved by the local authorities, for eventual use in future research related to HPV. The benefit of studies with stored samples and data includes knowing more about the immune response to vaccination against HPV infection. The analyzes that will be carried out with the samples will only be for research purposes.

These samples will not be identified with the child's name and will receive a special study code, called a personal identification number. The documents that allow identifying this special code and the child's personal data will be kept by the researchers in a secure place, preserving their identity, in order to maintain privacy and the right to confidentiality. The biological samples that are stored in the biorepository of this study can only be accessed by approved researchers and people who work in the institution and maintain control of the samples.

Storage of samples will not incur additional expenses for you or your child, and the samples will not be sold or used directly to produce commercial products.

In the future, if a researcher wants to carry out a new study with your biological samples, that have been stored, he will write a project proposal that will be analyzed by the local regulatory bodies for research on human beings, also called the Ethics Committee (CEP) and, if necessary, by the National Research Ethics Commission (CONEP). Ethics committees will ensure that the new study is relevant

and related to the type of research you have agreed to participate in. Your samples can only be used when the researcher's proposal for a new study is approved by the CEP. You may be required to sign a new informed consent form, and you have a right to know what is being done with your samples and test results. To receive this type of information, you must notify the study team of any changes to your address or telephone number.

If you agree to have your stored samples used for future research, you should know that these samples will be stored for a period of ten (10) years, and this term may be renewed for another ten years if the CEP and, if applicable, CONEP approve.

You may decide that you do not want your son/daughter's samples stored for future research. If you decide that you do not want the remaining samples to be stored for future use, the child can still participate in the OPTIMO study and any remaining samples after completion of the study specific tests will be destroyed. If you decide to authorize the storage of samples for future research, you can change your mind at any time. If you change your mind, you should contact the study team and let them know that you no longer want the child's samples to be stored for future research.
If, in the future, you decide to withdraw your consent, the stored samples that have not been used will be destroyed. However, information obtained from samples prior to revoking consent will not be deleted. If you withdraw your consent to store the samples for future use, your son/daughter will continue to participate in the study and will not lose any benefits, medical treatment or legal rights to which he/she is entitled.

Read the following statement and then check your option by putting an X in the appropriate space:
( ) I AGREE that my son/daughter's biological samples collected during the study be stored for use in future HPV-related research, regularly approved by local and national agencies for human research.

( ) I DO NOT AGREE that my son/daughter's biological samples collected during the study be stored for use in future HPV-related research, regularly approved by local and national agencies for human research.

Samples for genetic testing
Samples from some participants in this study may be selected for further genetic testing. We plan to perform genetic analysis to better understand the immune (or defense) response to HPV and the use of the HPV vaccine. Therefore, we would like you to be well informed about genetic research. Below are some brief explanations. Please let us know at any time if you want or need more information to understand:

The DNA is the material that controls the inheritance of many human characteristics, such as hair and eye color or risk for some diseases. DNA is contained in most of the cells that compose the body's tissues. The DNA carries the instructions for your organism's development and functions. A piece of DNA that determines the specific function of a cell is called a "gene". Abnormalities in the information of a gene can lead to a disease or modify the response to a disease. All of your unique genetic material, made up of DNA, is known as a "genome". All the cells in our body have our DNA, some genes are activated or not in the cells depending on their function in our organism. One of the types of defense cell is called a B lymphocyte.
These cells, called memory B lymphocytes, can sit still in the body and be activated when needed.
We hope to compare the memory B lymphocyte genes between the different study groups.

The study team can provide you more information if you wish. You can also get professional genetic counseling before consenting to genetic testing. As the tests will be done for research purposes only and collectively (globally) without a personal identification, individual results will not be available. However, if you are interested in knowing the overall results of genetic tests, you may receive explanations from the team about these results when they are ready and available for release. After the results are released, you will receive genetic counseling and clinical follow-up, free of charge. Our goal is exclusively to relate the global genetic variations found with the immune (defense) response to HPV and HPV vaccination.

Read the following statement and then check your option by putting an X in the appropriate space.
( ) **I AGREE that my child's biological samples collected during the study be stored for use in additional genetic testing related to HPV.**

Regarding the results of additional genetic tests related to HPV:
( ) I WOULD LIKE to be informed about the results of additional HPV-related genetic testing.
( ) I DO NOT LIKE to be informed about the results of additional HPV-related genetic testing.

( ) I DO NOT AGREE that my child's biological samples collected during the study be stored for use in additional genetic testing related to HPV."

If you have read this consent form (or someone has explained it to you), if any questions you had have been clarified and if you agree to participate in this study, please sign below. This ICF will also be signed, and all pages of the form will also be initialed by the member of the study team that discussed this document with you.

I received a signed and dated copy of this free and informed consent form.

Consent for collection of oral specimens:
I understand that collection of oral specimens is optional and that my decision will not affect my child's participation in this study
_____ **Yes**, I accept collection of oral specimens from my child
_____ **No**, I do not accept collection of oral specimens from my child

SIGNATURE PAGE

Minor name: _____

Mother's Name or Guardian's name (in legible letters):

_____

Mother's or Guardian's signature:

_____

Date and time: ___ /___ /___ ____:____

Father's Name or Guardian's name (in legible letters):

_____

Father's or Guardian's signature:

_____

Date and time: ___ /___ /___ ____:____

Name of Witness (in legible letters):

_____

Witness's signature:

_____

Date and time: ___ /___ /___ ____:____

Name of Study Physician (in legible letters):

_____

Physician signature:

_____

Date and time: ___ /___ /___ ____:____