FREE AND INFORMED CONSENT (TCLE)

Basic Information

Study title: "Use of BCG Vaccine as a Preventive Measure for COVID-19 in Health Care Workers"

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Preliminary Data

You are being invited to participate in this research because you are a health professional of this Unit and we are studying the protective effect of BCG vaccination against Coronavirus infection, which is the causative germ of COVID-19, in health professionals. In this research we will vaccinate you with BCG or some serum and accompany you for 6 months after vaccination to check if you have been protected or not.

BCG, or *Bacillus de Calmete Guerin*, is a mandatory vaccine used in childhood to prevent severe cases of tuberculosis in this age group. It has a weakened part of a bacterium from the same family of the bacterium that causes tuberculosis. When this weakened part is applied to the body, it stimulates the body's defense cells to produce substances that fight the bacteria from tuberculosis. There are studies that show that these same cells and defense substances could also fight Coronavirus infection. This virus was identified in China in late 2019 and has spread around the world causing mild flu symptoms to severe life-threatening pneumonia. Healthcare professionals have been affected by this virus because they are in close contact with patients.

Recently, the regulatory institutions of Brazil (ANVISA) approved the use of specific vaccines against COVID-19, and the National Immunization Program has created a vaccination plan. The priority of the use of this vaccine includes health professionals, the elderly, people living in a long-term institution and indigenous people. The BCG vaccine is not a specific vaccine against this virus, however the Institute of Chest Diseases is working on this study to try to prove whether the BCG vaccine, in addition to preventing tuberculosis, can also prevent COVID-19 in health workers in the Brazilian population by increasing the capacity of the body's defense system and making the effect of the specific vaccine against COVID-19 more potent.

Participant's Rubric	Witness's Rubric	Researcher's Rubric

You can request a second opinion about participating in this study for your private or public physician if it brings you more security.

You are free to give up your participation in this research at any time without any prejudice to your service.

Goal

The purpose of this research is to evaluate whether BCG vaccination protects against Coronavirus infection in health workers.

This vaccine is already recommended by the National Immunization Program of the Ministry of Health to prevent tuberculosis in children. It is usually applied to newborn babies within the first 12 hours after birth, but can be applied to children up to 5 years of age.

What will happen in this Survey?

You will be one of approximately 1000 participants who will be included in this study.

You came to us to understand this study because you saw our call on the Internet, watched a lecture on this study, or were informed by some co-worker.

If you meet the requirements to enter this study you will be evaluated in five moments: at the time of recruitment, at the time of inclusion, 10 days, 90 and 180 days after vaccination. By participating in the recruitment, we will take tests that will assess whether you have or have ever had COVID-19, by collecting a secretion from inside your nose using a "swab", which looks like a toothpick with cotton wool on the tip, and by collecting blood tests. On that day we will also do tests that will test for HIV and pregnancy, in the case of women who may become pregnant. On the day of inclusion, if you have not submitted COVID-19, do not have HIV infection, and are not pregnant (in the case of women), you will receive the BCG vaccine or placebo (a product that mimics the vaccine but has no good or bad effect on your body). You will be asked about your work, symptoms of diseases, about your past illnesses and also lifestyle habits. You will also have some blood collected to assess how your body is and if you have ever had contact with the tuberculosis bacteria.

Over the course of 6 months, face-to-face visits, telephone contact/cell phone/email message and blood collection will be performed, and at the end of this period we will compare who took the BCG vaccine and who took placebo and evaluate whether there were fewer cases of COVID-19 among those who took BCG.

You can still participate in this research if you have received or are able to be vaccinated against COVID-19 using only vaccines approved by ANVISA and implemented by the National Immunization Program of Brazil. For this we will only need a period of 15 days between the use of the product we are investigating and the specific vaccination against COVID-19. The 15-day deadline is to ensure that there is no risk of interference between vaccines in accordance with what the Immunization Program advises.

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Visit for participant recruitment

- The entire study will be explained to you by a nurse and, if you agree to participate, you will sign this document called the Free and Informed Consent Form (TCLE), stating that you agree. You will also receive a pathway of this term.
- The nurse will ask you some questions about your disease history to see if you can participate in the research. You will also be asked about the use of specific vaccines against COVID-19 and to participate in the study you should:
  - Have not received a specific vaccine against COVID-19 **OR**,
  - If vaccinated, have received only vaccines approved by ANVISA and implemented by the National Immunization Program (including the second dose) within a minimum of 15 days prior to the date of inclusion in the **STUDY OR**,
  - If you have not received a specific vaccine against COVID-19 approved by ANVISA, know that you can only receive them 15 days after bcg vaccination used in this study.
- Next, you will be assisted by a nursing technician. It will collect approximately 10 ml of blood that corresponds to about 2 teaspoons. This blood will be used to assess whether you have or have had contact with Coronavirus. Part of this blood will also be used for HIV testing, and in case women still able to get pregnant, the pregnancy test. These two tests are important because the BCG vaccine should not be applied to patients who have HIV infection or in pregnant women. Soon after, a secretion will be collected from inside your nose using a "swab" to search for if you have Coronavirus.
- After collecting the exams you will have a new visit scheduled within 10 days after, for the evaluation of the results;
- If you experience symptoms of COVID-19 in this 10-day period you will be invited to repeat the exam that collects the secretion from your nose;
- In case of indeterminate results, you will be invited to take the exam again once again. If your HIV serology test is positive, we will refer you for evaluation and follow-up by the Infectious Diseases Specialist.

Participant inclusion visit:

- The nurse will assist you with the results of the examinations performed during the recruitment visit. If you have not submitted COVID-19, do not have HIV infection, and are not pregnant (in the case of women), you may be included in the study. The nurse will ask about other questions related to the study and if you continue to agree to participate you will be referred for a medical evaluation.
- The research physician will ask about their work, symptoms of diseases, about their past illnesses and also life habits.
- Next, you will be assisted by a nursing technician. It will measure your weight and height and collect approximately 35 ml of blood that corresponds to about 2 and a half tablespoons. This blood will be used to assess how your body is before any vaccination or disease and assess whether you have ever had contact with the tuberculosis bacteria. Finally, he/she will apply a product just below the skin of his right arm. This product may be the BCG vaccine or some saline, which is an industrial product based on the mixture of water and salt, usually used to offer liquids to someone dehydrated.

Participant's Rubric	Witness's Rubric	Researcher's Rubric

- In case of altered test results, you will be evaluated by the study physician and if necessary we will refer you to a specialist physician at this hospital.

- If there is a problem in the laboratory in performing the test that evaluates whether you have had contact with the tuberculosis bacteria we will summon you to collect the blood again for this test.

Participant follow-up visits

- Between 10 and 14 days after vaccination you will have a scheduled visit in the study laboratory for blood collection to assess how your body is after vaccination. The collected blood will be used to assess whether you have ever had contact with Coronavirus and assess how your body is after vaccination. About 35 ml of blood will be collected, which corresponds to about 2 and a half tablespoons.
- Once a week after vaccination you will receive a telephone contact, text message by phone (SMS) and/or email with a link to a questionnaire with questions about whether you are presenting signs or symptoms of COVID-19. This contact will occur every week until you complete 3 months after vaccination and later each month. At each contact we will ask you to attach in the questionnaire a photo of the site where the injection was performed to assess whether the lesion is evolving in normal.
- 90 days after vaccination you will have a scheduled visit at the research center for evaluation by the clinical team of the study and for blood collection to assess how your body is after vaccination and also test whether you have or have had contact with coronavirus. About 35 ml of blood will be collected, which corresponds to about 2 and a half tablespoons.
- After 180 days of vaccination, we will schedule your last visit with the doctor or nurse of the study and you will be asked about your work, if you are having any symptoms, about your history of diseases and also lifestyle habits. In addition, you will be asked about any reaction after vaccination. Your arm will also be examined to see if any lesions have arisen at the vaccination site. After this evaluation you will be attended by the nursing technician to measure weight and to collect blood, which will serve to test if you have or have had contact with the coronavirus. About 5 ml of blood will be collected, corresponding to 1 teaspoon.
- If you do not attend follow-up appointments, we will contact you by phone to understand the reason for the no-show. In case I have been diagnosed with COVID-19 we will do the evaluation by phone with yourself or some family member.

COVID-19 diagnostic visit

- If at some point between the day you were included and 6 months later, you have any symptoms of COVID-19 you should look for the HUCFF's Division of Worker's Health and flag the study team at 3938 6220. We will make a telephone assessment with you or your next of kin, maintaining social leave care as directed by the Ministry of Health and the World Health Organization.

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- If necessary, you can be attended to in person by the emergency department of the HUCFF and will be hospitalized if necessary. You are also free to seek care from your private doctor if you find it more convenient. We only ask you to contact us as the phone above so we can ask questions about your symptoms and your diagnosis.
- When you are without any symptoms of the disease and at least 14-30 days after the onset of these symptoms we will schedule a face-to-face visit. On this visit we will ask you to take the tests performed if you have been attended by any medical service. In addition, we will collect approximately 35 ml of blood corresponding to about 2 and a half tablespoons to assess how your body responded to COVID-19 infection.

Risks and discomforts

Risks on laboratory tests

Blood collection may result in some pain or small local redness associated with using the needle to obtain blood (60 ml, equivalent to a maximum of 4 tablespoons). All material used for collection will be new and disposable. During the collection of the examination, the needle used may leave the correct position and there will be a need for a new placement of the needle. In such cases there may be a small purple spot on the spot.

The collection of the material from the nose generates a slight discomfort to introduce the swab into the nosh. After collection, sneezing and a small nosebleed may occur.

If you have any questions about the risks call the phone at the initial part of this TCLE that will be available for contact 24 hours. If you have any problems directly or indirectly related to your participation in this study, you will receive support from the doctor responsible at the center where you work and in the absence of this, another professional of the research team will assume the responsibility of performing the medical care.

You will be guaranteed full and free assistance due to direct/indirect and immediate/late damages related to your participation in this study and for as long as necessary.

Risks of bcg or placebo vaccination

The BCG vaccine is applied to newborn babies or children up to 5 years and is well tolerated unless the small bruise that forms on the skin at the site of application and means that the body has reacted and produced cells and defense substances.

After applying the vaccine, you may experience a little pain or discomfort in the site and over the weeks a bruise will arise as follows:

- 3 to 4 weeks after a small lump appears on site

- between 4 to 5 weeks after the lump progresses to a small wound with pus

- then evolves into a small open wound

- between 6 to 12 weeks, finally, form a wound with bark to then heal it

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It may also be that you feel a little fever and that a small lump arises in the left armpit. Both situations mean that your body has recognized the vaccine and is starting production of cells and defense substances. Other possible but less common reactions are ulcer suppurating in diameter greater than 1 cm, cold subcutaneous abscess, hot subcutaneous abscess, granuloma, unsuppurated regional lymphadenopathy greater than 3 cm, suppurated regional lymphadenopathy, cheloid scar, lupoid reaction, or BCG ostheitis, and localized reactions on the skin, joints, or ganglia. Generalized BCG infection is described in the literature as a very rare event (0.19-1.56 cases/ 1 million vaccinated) and is usually related to people with diseases that lead to reduced immunity, so people with this type of disease will not be included in this study.

As this is a clinical study, other unforeseen adverse events may occur. If you have any questions or feel something different you can contact us at this outpatient clinic or call 3938 6220.

Applying serum as placebo can cause a small pain or discomfort and local redness soon after application. Differently than BCG we will not have the formation of the lump, wound or scar. Similarly, if you have any questions or feel something different you can contact us at this outpatient clinic or call 3938 6220.

You won't know if you received the vaccine or placebo, but still, if you have any questions or feel anything different you can come to us at this outpatient clinic or call 3938 6220.

If you agree to participate in this study, you will receive the BCG/placebo vaccine in addition to the specific COVID-19 vaccine. It is important that you know that vaccines should be applied only at intervals of 15 days as directed by the National Immunization Program, in order to avoid any interaction between vaccines and any unforeseen adverse effects. If you have any questions or feel something different you can contact us at this outpatient clinic or call 3938 6220.

Risks on the use of the specific vaccine against COVID-19:

The study team took care to follow the guidelines of the Ministry of Health and will only vaccinate with BCG/placebo who took all doses of the COVID-19 vaccine at least 15 days apart between the two vaccines. With this we will avoid any confusion of side effects of bcg vaccine or COVID-19 vaccine.

Risk of breach of confidentiality

The study team will take all steps to keep the documentation that has your name written (such as consent form, data collection forms and test results performed) in key locked locations and study documents will not contain your name, upon entering the study you will receive a number and this is how you will be identified in the study.

Our team will take great care to preserve your confidentiality and keep all documentation in key locked lockers under the guard of the study team.

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Benefits

You will not receive any direct benefit for participating in this study. Their participation in this study can help researchers discover a way to prevent COVID-19 for healthcare professionals.

Costs

There are no costs for you to participate in this study.

Payment

You will not receive financial compensation for participating in this survey. But if it is necessary to travel to situations related to the study, will be guaranteed the reimbursements of your expenses and your companion. These expenses, in addition to transportation and food, will also be related to any expense that occurs as a consequence of participation in the study.

Confidentiality

We will do our best to keep your information safe. However, we cannot guarantee confidentiality in certain situations. If state and federal agencies are required by law or are involved in research oversights, they can access information about you in that study. But we will keep all your medical information as private as possible as required by law.

Still, all measures will be maintained so that you and your data are protected. These measures include the assurance that no information will be used that leads to any harm to you and/or your community, including in terms of self-esteem, prestige and/or economic and financial aspects. We will also ensure that your data and privacy are kept confidential during all phases of this research by keeping all documents containing your name and identification in locked files kept in closed rooms of our research laboratories.

Participant Rights

Your participation in this study does not eliminate your legal rights. Consent means that you received information about this study and agreed to participate in this research. You will have guaranteed your right to seek compensation for recurring damages from this research.

Similarly, the researcher responsible for this study will allow access to information about the results of the tests performed by you to your doctor or yourself, whenever requested and/or indicated.

You will have direct astoifis whether you are part of the group that received the BCG vaccine or placebo at any time in the study, provided that you decide to withdraw from the research and thus withdraw consent. However, this will not affect any benefit you are entitled to.
You will receive a signed and dated via this Free and Informed Consent Form.

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If you do not agree to participate in this study or if at any time you wish to withdraw from this study you will not suffer any penalty or lose any benefit you are entitled to. This participation is your decision and will not affect your ability to get assistance. Similarly, your decision will not affect your enrollment in any health plan or benefits you may acquire.

You may also decide to remove the blood and secretion collected from your nose that we collected throughout the study and that will be stored in our laboratory at any time and without any harm to your treatment or follow-up. All you have to do is make this request in writing and sign the order. This request will apply immediately from the moment such communication is made.

During this study, we may discover some factor that makes you no longer want to participate in this study. If this happens, you will be informed as soon as possible.

In the case of women, if you become pregnant between the day of vaccination and 30 days after, we will follow the entire pregnancy and also the baby after birth. You and the baby will have all the guarantees of medical follow-up at the study hospital. If pregnancy occurs after 30 days of vaccination there is no risk to the baby.

We may decide to remove you from the study even if you choose to remain if, for example, the study is terminated. This can happen only after the due analysis and approval of the CEP/CONEP System, unless in cases of urgency for the benefit of its participants. In this case, the CEP should be communicated at the first opportunity.

Issues

The researcher or a member of the research team will try to answer all your questions. If you have questions or concerns at any time, please contact Dr. Fernanda Mello at 21 3938 2426. You can also call if you need to report any damage while participating in this survey to 21 3938 6220**.** If no one answers this number make sure you are calling during business hours.

If you have any consideration or doubt about the ethics of research, please contact the Research Ethics Committee (CEP) of the Clementino Fraga Filho University Hospital/HUCFF/UFRJ. The CEP is a committee of professionals that exists in institutions that conduct research involving human beings in Brazil, created to defend the interests of study participants in their integrity and dignity and to contribute to the development of research within ethical standards.

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The ZIP Code of the University Hospital Clementino Fraga Filho/HUCFF/UFRJ is located at R. Prof. Rodolpho Paulo Rocco, n. 255, Cidade Dúvidas contact the CEP/HUCFF/FM/UFRJ from Monday to Friday from 8am to 4pm. E-mail: cep@hucff.ufrj.br - Tel.: 3938-2480 and FAX: 3938-2481. You can also contact the National Research Ethics Commission located at: SRTV 701, Via W 5 Norte, lot D - Building PO 700, 3rd floor - Asa Norte ZIP Code: 70719-040, Brasília/DF.

Participant: _____

Printed participant name

By signing this Informed Consent Form (TCLE), you are indicating that you have read this term (or been read to you), that your questions have been answered, and that you voluntarily agree to participate in this research study.

_____Data and time:_____
Participant signature

Researcher: _____

Printed name of the professional who is conducting the consent discussion

I personally explained the survey to the participant mentioned above and answered all questions. I believe that he/she understands what is involved in the study and voluntarily agrees to participate in the research.

_____

Signature of the professional who is conducting the discussion of consent

The rest should be completed by a witness if the researcher reads this term to the participant.

This Informed Consent Form (TCLE) was read and apparently understood by the participant in my presence,

Witness: _____

Printed name of the witness (a person not associated with the study)

_____

Signature of the witness (a person not associated with the study)