PATIENT INFORMATION SHEET

STUDY TITLE: "VACCINATION ADJUVED AGAINST HEPATITIS B IN SNS WORKERS TYPED AS NO RESPONDERS TO CONVENTIONAL VACCINES **"**

PROMOTER CODE: IBS-VACANTIB-1701

PROMOTER: Castilla y León Institute of Health Sciences Studies Foundation (IECSCYL) - Salamanca Biomedical Research Institute (IBSAL)

PRINCIPAL INVESTIGATOR:

CENTER:

INTRODUCTION

We are writing to you to inform you about a research study in which you are invited to participate. The study has been approved by an accredited Research Ethics Committee with medicines and by the Spanish Agency for Medicines and Health Products, in accordance with current legislation, Royal Decree 1090/2015 of December 4 and European Regulation 536 / 2014 of April 16, which regulates clinical trials with drugs.

Our intention is only that you receive correct and sufficient information so that you can evaluate and judge whether or not you want to participate in this study. To do this, read this information sheet carefully and we will clarify any doubts that may arise.

In addition, you can consult with the people you deem appropriate.

VOLUNTARY PARTICIPATION

We invite you to participate in the study that will be carried out among the workers of the National Health System (SNS) and the student staff of the health system that does not respond to conventional Hepatitis B vaccination, as is your case.

You should know that your participation in this study is voluntary and that you can decide NOT to participate. If you decide to participate, you can change your decision and withdraw your consent at any time, without thereby altering your relationship with your doctor or causing any harm to your health care.

THE PURPOSE OF THE STUDY

The health and non-health worker population of the SNS has a real risk of contracting a Hepatitis B infection, especially the unvaccinated groups and those classified as "non-responders"; understood as such, those people who, having received the conventional hepatitis B vaccine in a complete schedule (6 doses), do not present the antibody levels required to confirm their immunological protection against hepatitis B. The need arises to provide a solution to health and non-health workers in our environment, in whom conventional vaccination has not worked, and to offer them a vaccine alternative that they can benefit from and that is already authorized. It is an adjuvanted hepatitis B vaccine, but whose marketing authorization restricts its use to the immunization of patients with an immune response lower than that of healthy individuals.

Through this study, the aim is to benefit and provide NHS personnel with an additional protection tool against hepatitis B infection. So that the efficacy of the adjuvanted vaccine can be evaluated in healthy subjects who do not respond to the conventional antihepatitic B vaccine.

STUDY DESCRIPTION

It is a clinical trial that will be carried out in the Occupational Risk Prevention Services of the Health Areas of different autonomous communities, where SNS workers who do not respond to the conventional vaccine against Hepatitis B will participate. The initial estimate of subjects participants is a maximum of 80 among all centers.

STUDY ACTIVITIES

The subject participating in the study will make a series of visits to the responsible doctor to carry out the necessary tests, data collection and administration of the vaccine. The schedule to follow is shown in the following table. The total duration of the study will be 7 months from the moment the patient signs the informed consent form. After the administration of each of the doses, an analysis will be carried out to evaluate their response to the vaccine (approximately 30 days after the administration of each dose), making it clear that if optimal protection is achieved, the administration of successive doses. Pharmacological treatment will end at 6 months and then a follow-up visit is carried out one month after the last administration of the drug.

Visits	**Selection Visit**	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**Final visit**
Time		**Month 0**	**Month 1**	**Month 2**	**Month 6**	**Month 7**
Procedures and Tests						
Data collection and tests necessary for the study	**X**					
Analytics	**X**		**X**	**X**	**X**	**X**
Drug administration		**X**	**X**	**X**	**X**	
Data collection related to other medications and adverse events		**X**	**X**	**X**	**X**	**X**
Completion sheet						**X**

The blood samples collected for the analysis will be stored in the laboratories of each center and will remain there until the end of the study. Its subsequent destruction will be carried out according to the usual clinical practice of each center where the study is carried out.

RISKS AND HAZARDS DERIVED FROM YOUR PARTICIPATION IN THE STUDY

Fendrix® is a hepatitis B vaccine that contains a new adjuvant (a substance that, added to another, enhances its main effect) that has a greater immunogenic capacity than the conventional vaccine. Its use is only authorized in patients with renal failure, and it is intended to initiate a study of use outside the technical data sheet for its use in health workers and students of practices in health centers who have not responded to the previous vaccination.

Students in practices will only be included in those health centers where the instructions and measures for the adoption of risk prevention and occupational health allow it, according to current legislation.

A preliminary study based on research carried out with healthy individuals has been carried out at the University Hospital of Salamanca that supports the efficacy of this vaccine in the adult population.

Among the most frequent adverse effects that may occur during and after administration are: local pain, redness at the injection site, local swelling, fatigue, fever, intestinal disorders, headaches and general malaise. It is possible that other events unknown until now appear.

Once you have decided to participate and in order to facilitate the follow-up of the study, please follow certain indications:

- Compliance with study visits and activities
- Notify any adverse event that happens or changes in medication, warning that, except in an emergency, do not modify the medication you are taking or take other medications or "medicinal plants" without first consulting with the study doctor.

POSSIBLE BENEFITS

Participants will be able to benefit from one more tool to protect against hepatitis B infection. The data obtained from the study can support the use of this vaccine in more populations at risk.

WARNING REGARDING PREGNANCY

There are no data from the use of Fendrix® in pregnant women or during lactation or on fertility.

"In the event of a pregnancy during your participation in the study, you should inform your doctor immediately in order to receive adequate medical assistance." It will be requested, through a specific consent, the collection of data of the same and of health data of the baby for guarantee compliance with law 15/1999 LOPD.

ALTERNATIVE TREATMENTS

In the event of a biological accident with risk of infection, the subject will be administered the specific anti-hepatitis B Gamma globulin, but it would be logical to offer a vaccine alternative that protects workers from possible infection.

The study doctor will give you more information if you want.

SAFE

This clinical trial has been classified as a low-intervention clinical trial by the Research Ethics Committee evaluating the study, this implies that the expected coverage of the study that covers the impairment of your health or injuries that may occur in relation to Your participation in the study is included in the civil / property liability insurance of the Hospital Centers where the study is carried out. This policy, which complies with current legislation (Royal Decree 1090/2015), will provide you with compensation and compensation in the event of impairment of your health or injuries that may occur in relation to your participation in the study,

For more information regarding this section, please consult the principal investigator of the study at your site.

We inform you that it is possible that your participation in this clinical trial may modify the general and conditions (coverage) of your insurance policies (life, health, accident ...). Therefore, we recommend that you contact your insurer to determine if participation in this study will affect your current insurance policy.

CONFIDENTIALITY

The promoter undertakes to comply with Regulation (EU) 2016/679 of the European Parliament and of the Council of April 27, 2016 on Data Protection (RGPD) and Organic Law 15/1999, of December 13, on data protection of a personal nature and the Royal Decree that develops it (RD 1720/2007). Both the Center and the Promoter are respectively responsible for the processing of your data and undertake to comply with the data protection regulations in force. The data collected for the study will be identified by a code, so that it does not include information that can identify you, and only your study doctor / collaborators will be able to relate said data to you and to your medical history. Therefore, your identity will not be revealed to any other person except the health authorities. The Research Ethics Committees, the representatives of the Health Authority in inspection matters and the personnel authorized by the Sponsor, may only access to verify personal data, clinical study procedures and compliance with the rules of good clinical practice. (always keeping the information confidential).

The Researcher and the Sponsor are obliged to keep the data collected for the study for at least 25 years after its completion. Subsequently, your personal information will only be kept by the center for the care of your health and by the sponsor for other scientific research purposes if you have given your consent to do so, and if this is permitted by law and applicable ethical requirements.

The data will be collected in a center research file and will be processed solely and exclusively within the framework of your participation in this study.

In accordance with the provisions of the data protection legislation, you can exercise the rights of access, modification, opposition and cancellation of data, for which you should contact your study doctor. You can also limit the processing of data that are incorrect,

request a copy or transfer to a third party (portability) the data that you have provided for the study. To exercise your rights, contact the principal investigator of the study. We remind you that the data cannot be deleted even if you stop participating in the trial / study to ensure the validity of the research and to comply with legal duties and drug authorization requirements. You also have the right to contact the Data Protection Agency if you are not satisfied.

If you decide to withdraw your consent to participate in this study, no new data will be added to the database, but those that have already been collected will be used.

If we transfer your encrypted data outside the EU to our group entities, service providers or scientific researchers who collaborate with us, your data will be protected with safeguards such as contracts or other mechanisms by the data protection authorities. If the participant wants to know more about it, he / she can contact the promoter Data Protection Delegate at comunicacion@ibsal.es.

EXPENSES AND FINANCIAL COMPENSATION

The promoter of the study is responsible for managing the financing of the study. To carry out the study, the promoter has signed a contract with the study doctor and the center where it will be carried out.

You will not have to pay for drugs or specific study tests. Your participation in the study will not incur any expense.

OTHER RELEVANT INFORMATION

A description of this clinical trial will be available at http://reec.aemps.es, as required by Spanish legislation.

Any new information regarding the drugs used in the study and that may affect your willingness to participate in the study, which is discovered during your participation, will be communicated to you by your doctor as soon as possible.

You should know that you can be excluded from the study if the promoter or the study investigators consider it appropriate, either for safety reasons, for any adverse event that occurs due to the study medication or because they consider that you are not complying with the established procedures. . In either case, you will receive an adequate explanation of the reason for your withdrawal from the study.

By signing the attached consent form, you agree to comply with the study procedures that have been set forth to you.

If the study is suspended or terminated while you are being treated with Fendrix®, the evolution of the parameters under study will be followed.

CONTACT IN CASE OF DOUBTS

If you have any questions during your participation or need more information, please contact:

Dr. José Lorenzo Bravo Grande
National coordinating investigator of the clinical trial
Tel. 639438852

INFORMED CONSENT

Study title:

"Vaccination adjuved against hepatitis b in SNS workers typed as no responders to conventional vaccines". Protocol code: IBS-VACANTIB-2017

I, (name and surname of the participant) .....

- I have read the information sheet given to me about the study.
- I have been able to ask questions about the study.
- I have received enough information about the study.
- I have spoken with: (name of researcher) .....
- I understand that my participation is voluntary.
- I understand that I can withdraw from the study:
  - Whenever you want.
  - Without having to explain.
  - Without this affecting my medical care.

- I freely give my consent to participate in the study.

Participant name	Investigator's name
Participant signature	Investigator's signature
Date: ____/____/____	Date: ____/____/____

I want the information to be communicated to me derived from research that may be relevant to my health:

☐ YES ☐ DO NOT

Participant signature	Investigator's signature
Date: ____/____/____	Date: ____/____/____

REVOCATION OF CONSENT

I_____ of legal age, and as the subject of the IBS-VACANTIB-2017 study, I revoke the consent given on _____

Patient signature_____date (day / month / year)

Investigator Signature_____date (day / month / year)