Short study title: A Phase 1 Vaccine Study in Healthy and Chronic Hepatitis B Participants

Sponsor: Vaccitech Ltd **EudraCT No.: 2019-003420-20**

REC: South Central Berkshire **REC Ref. No.: 19/SC/04**

PARTICIPANT INFORMATION AND CONSENT FORM FOR HEALTHY VOLUNTEERS

You are invited to take part in a study to test a new vaccine against Chronic Hepatitis B (CHB) infection. Before you decide to take part, it is important that we explain why this research is being done and what it will involve.

The participants in the study should be aged 18-65 years, without prior infection with Hepatitis B, Hepatitis C and HIV. Women who are interested in participating should not be pregnant or intending to become pregnant during the study period.

Participating in this trial does not mean that you will be protected against Hepatitis B Virus (HBV). It is important that you continue to protect yourself against Hepatitis B infection.

Please take time to read the following information carefully and discuss it with friends, relatives or your GP if you wish. Please ask us if there is anything that is not clear or if you would like more information.

Why is this study being done?

Hepatitis B virus (HBV) is one of the most common forms of liver infection worldwide. The World Health Organisation estimates that there are approximately 240 million people with long term hepatitis B infection called "chronic hepatitis B (CHB)". Left untreated CHB may cause severe liver disease, liver inflammation (hepatitis) and liver cancer.

Once CHB infection is established, drugs can be given that reduce the virus in the blood and prevent damage to the liver, but these drugs do not cure patients completely of the infection. When the drugs are stopped the virus returns, so that most patients require lifelong treatment. In this study we are aiming to develop a new vaccine that will eradicate the virus in patients after they have developed CHB infection (a therapeutic vaccine). This is the first time that this particular vaccine is being given to humans. This new vaccine is different to the existing HBV vaccine that is established in clinical practice, and which prevents Hepatitis B infection in the first place (a prophylactic vaccine).

The purpose of this study is to confirm if the study vaccine can be given safely to healthy adults and to adult patients with CHB.

This study will also look at your immune response (body's defense mechanism) generated by the study vaccine. The study will include 10 healthy adults and 12 patients with CHB. This Participant information sheet is designed specifically for Healthy Volunteers.

What is the vaccine being tested in this study?

The study vaccine is called Chimpanzee Adenovirus-vectored Hepatitis B Virus Vaccine (ChAdOx1-HBV).

The vaccine being tested in this study consist of three parts:

1) The first part is known as a carrier (also called a 'vector'). The carrier is a Chimpanzee Adenovirus called 'ChAd' which does not cause disease in people. This type of vector has been safely used in research vaccine studies against many different infections at Oxford University (e.g. Influenza, Middle East Respiratory Syndrome (MERS), Malaria, Tuberculosis (TB) and Prostate cancer).

2) The second part of the vaccine contains segments (also known as antigens) of the HBV. The HBV components of the vaccines are synthetic and do not contain live Hepatitis B. The vaccine used in this study cannot infect people with HBV.

The third part of the vaccine consists of a small segment (a gene called "invariant chain" or "SIi") that is thought to improve the immune response to the vaccine. This part of the vaccine has already been safely given to humans participating in a malaria vaccine study by leading researchers at Oxford University

Who can take part?

We are looking for Healthy Volunteers who are:

- Willing and able to take part – i.e. able to attend all visits required to complete the study
- Aged between 18 and 65 years old
- Willing to use effective contraception after signing this consent form and for 2 months after vaccination
- Willing to allow us to communicate with your GP and/or medical consultant:
    - to notify them of enrolment into the study
    - to check your medical history (including accessing your Electronic Patient Record, if applicable)

You would <u>not</u> be able to take part in the study if you:

- Have medical conditions including (but not limited to) heart, liver, lung, kidney, neurological, psychiatric, and / or immune disease and cancer
- Have been diagnosed with autoimmune disease e.g. Type 1 diabetes, Graves' Disease, Systemic Lupus Erythematosus (SLE)
- Have an Immune deficit
- Have Hepatitis B, Hepatitis C or HIV infection
- Are pregnant or breastfeeding, if you are female
- Are currently taking part in another clinical study where you have/will receive an investigational medicine/vaccine within 3 months prior to first study visit (screening)

- Have received or plan on receiving a vaccine within 14 days prior to the vaccination in this study (in the case of a live vaccine, this would be 30 days).
- If you have ever received any adenoviral vaccine.
- Have allergies to any of the components of the study vaccine used in the study
- Have received any immunoglobulins or other blood product transfusion within 3 months prior to screening
- Have received prolonged therapy with any corticosteroids or biologics within 3 months prior to screening
- Have current alcohol or drug abuse as per your doctor's evaluation
- Have had any other finding that in the opinion of the doctor, deems you not suitable.

What would I be vaccinated with?

During this study, 10 healthy volunteers will receive one study vaccine dose each. As described in the table below, the first 5 participants will receive a low dose of the study vaccine, and the next 5 participants will receive a high dose of the study vaccine.

Healthy Volunteers (10)	Group 1	N=5	Low dose study vaccine
	Group 2	N=5	High dose study vaccine

Do I have to take part?

No, it is entirely your decision as to whether or not to take part. If you do decide to participate in the study, you will be asked to sign a consent form. After you have done so, you are still free to withdraw at any time and without giving a reason. Choosing to withdraw from the study will not affect your current or future medical care or legal rights.

How often do I need to attend visits?

You will be asked to attend 9 study visits over a period of 8 months. There will be one screening visit, one vaccination visit, 6 face to face follow up visits, and 1 follow up telephone call.

The chart below gives a summary of the visits involved in the study:

Number of visits	9 (i.e. 8 clinic visits and 1 telephone call)
Duration of study	Up to 8 months
Visits	Screening, day 0 (vaccination), follow ups on days 1*, 7, 14, 28, 56, 84, 168

Blood samples	Screening visit, visits on days 0, 7, 14, 28, 56, 84, 168

***At Day 1 participants will be followed up with a phone call. If deemed necessary, they will attend a face to face visit, at the discretion of the investigator.**

What do I have to do if I agree to take part?

Screening Visit

On the first visit (screening visit) the study doctor or nurse will discuss the study in detail with you to make sure that you fully understand what the study is about and what is involved if you decide to take part, and that you agree to take part.

If you decide to take part, you will be asked to give a written confirmation (consent) to take part in the study. We will give you a copy of the consent form that you have signed which you can keep for your records together with this information sheet. We will give you an appointment schedule for the study visits. For female participants, we will ask you to ensure that you use effective contraception throughout the study.

We will ask you questions about your health and any medications you are taking. A complete physical examination will be performed. We will also ask questions to ensure that you are not at risk of Hepatitis B infection. A blood sample will be taken in order to confirm that you are eligible to take part in this study. This will include tests for HIV, Hepatitis C and Hepatitis B infections. Feel free to ask questions about those tests.

If we identify any reason that would prevent you from taking part in this study, this will be explained. If something abnormal is noted on a screening blood test, a repeat test might be required to check it.

With your permission, we will inform your GP of your participation in the study and request a copy of your medical summary from your GP. The information will be used to confirm if you have any reason to be excluded from the study. You will be asked to sign a letter addressed to your GP in order to allow them to release relevant medical information about you to the study doctor. You will be notified within two weeks to let you know if you are eligible to take part.

We will ask you not to take part in other clinical studies at the same time. In addition we will register you on the TOPS database (www.tops.org.uk), which is a confidential national database of healthy volunteers that identifies volunteers participating in studies, to minimise the risks that can come from over-volunteering. We will enter into the database:

- your National Insurance number (if you are a UK resident);
- your passport number and country of origin (if you are not a UK resident);
- the date of your study vaccination

Screening visit can last up to 2 hours.

Vaccination Visit

On the vaccination visit you will be given an injection into the muscle of your non-dominant arm. We will monitor you for between 30 minutes and 1 hour at the clinic to ensure that there is no serious reaction to the vaccine.

Before going home, you will be given the login for a web based electronic diary that you will be asked to fill in daily for the first three days after vaccination. You will be asked to keep a daily record of your temperature and any 'flu-like' symptoms that you might experience. We will give you a telephone number (s) to call the doctor or nurse in case you have any side effects or concerns about the vaccine.

If you experience unexpected events or become in any way concerned you can use this to contact one of the study doctors at any time. We will ask you to record these symptoms too.

Other Visits

There will be 8 clinic visits and 1 telephone call. On all visits we will ask questions about your health and, if necessary, we will carry out a physical examination. Blood will be taken at each visit. The amount of blood taken at each visit will vary as different amounts are required to assess your response to the vaccine over time. At each visit, the amount of blood taken will vary between 10 and 100 ml (roughly 1½ – 6 tablespoons) with a total amount of approximately 771 ml taken over a period of 8 months. 771 ml is less than the amount that would be taken from regular blood donors at a Blood Donation Centre during an 8-month period.

There might be a case in which your blood or urine need to be retested to confirm test results. If this happens, the study staff will take another sample of your blood or collect a urine sample, as needed. This may happen during a scheduled visit or you may need to come back to the clinic for an additional visit.

What will happen to the blood samples that I give?

The blood tests will include a full blood count (measures the cells that make up your blood), and blood chemistry (measures amounts of certain chemicals in a sample of blood) and liver function tests at selected visits. These tests are needed to detect any underlying medical condition and to understand the impact of the vaccine on your health.

In addition, a blood sample will be taken at each visit to measure your immune response to the vaccine. Blood samples will be labelled with your unique study code only, before sending to the appropriate laboratory for analysis.

With your permission, we would like to store any remaining blood from your samples when the study ends. These remaining samples may be stored in a biobank facility and used in future research approved by an ethics committee. You can withdraw your consent for the storage and future testing of these left over samples at any time by contacting the study team or the biobank directly. Samples stored for use in another research project would remain anonymised (had all personal identifiers removed).

If you choose not to allow the future use of your remaining samples, you may still take part in this study and your samples will be destroyed at the end of the study, in accordance with local procedures and the Human Tissue Act (established by the Health Authorities to regulate activities concerning the removal, storage, use and disposal of human tissue).

The blood samples collected during this study will be stored and analysed in the Oxford University Hospital and University of Oxford research laboratories. However, as part of this project, and maybe in the future for studies approved by an Ethics Committee, samples will be sent to other laboratories both within and outside the UK. These samples will be stored in an anonymised form. The samples could be kept for up to 20 years and may at any time be transferred to a biobank in a fully anonymised form for use in ethically approved research studies.

If you choose to withdraw from the study, no further samples will be taken. All the samples collected before withdrawal will be analysed.

What are the risks of taking part?

There may be unknown risks associated with your taking part in this study, including risks related to the vaccine being tested, and/or, the procedures or tests planned in this study.

If you participate in this study, you or your friends/family members should tell the study doctor or his/her study staff immediately if you have any unusual health problems, injuries or side effects, even if you think these problems are not caused by the study vaccine or by the study procedures.

Ask the study doctor if you have questions about the signs or symptoms, or any side effects that you read about in this consent form.

What are the likely risks with the study vaccines?

There are potential known and unknown risks associated with any vaccine, including licensed ones, and there is a rare risk of severe allergic reaction ("anaphylaxis") which can be fatal.

This is the first study to assess this particular vaccine, ChAdOx1-HBV. However, based on our previous experience with similar ChAd vaccines, we know that it is likely that you will experience some local or general side effects from vaccination. You may, or may not, have the same side effects. Side effects previously reported with similar vaccines are generally mild or moderate in severity and they are typically short lived (1-2 days). They include:

- Vaccination reactions at the site of injection: pain, swelling, warmth, redness
- General adverse events: feverishness, chills, muscle pain, tiredness, headache, nausea, joint pain, malaise (a general feeling of being unwell), fever (high temperature)

Side effects of Vaccination

This is the first study to assess this particular vaccine. However, based on our previous experience with similar adenoviral vaccines, we know that it is likely that you will experience some local or general side effects from vaccination.

Local reactions

After the vaccination, we expect you will see a reaction around the area where you were injected as this happens to most people (about 75% of people). Local pain, redness, warmth, and swelling are the most likely local reactions. In general, these side effects are expected to be mild and expected to get better without needing to do anything.

General Reactions

The most common general reactions based on previous studies (using similar ChAd vaccines) include fatigue (40% of people experience this event), headache (30% of people experience this event) and malaise (20% of people experience this event). Other symptoms include fever, chills, joint and muscular pain. Most of these reactions were mild to moderate in severity and resolved within a few days after the vaccination.

The risk of severe reactions in this study is expected to be low. However, unexpected outcomes are possible.

There have been no serious adverse events in any similar ChAd vaccine studies related to the vaccine. However, with any vaccination, there is a risk of rare serious adverse events, which may be related to the nervous system, or the immune system, like an allergic reaction. An allergic reaction can be recognized by itchy skin rash, swelling of the face, difficulties in breathing and swallowing or by a sudden drop in blood pressure. If such reactions occur, they usually start very soon after vaccination. That is why it is important that you stay at the study site for at least 30 to 60 minutes after vaccination, where all medical equipment and personnel are available to treat an allergic reaction.

This is the first study using ChAdOx1-HBV and there is no information available on the effect in humans. The side effects of using the ChAdOx1-HBV study vaccine are currently unknown. Please discuss any concerns you may have with the study doctor. If you experience unexpected events, or become in any way concerned you should contact the Investigator using the contact details listed on page 10 of 11 under 'who can I contact for more information'. Should you have any side effects, you will be asked to inform your study doctor.

Risks of taking blood samples (venepuncture)

Having blood taken may cause discomfort, pain, bleeding or bruising where the needle enters the body and, in rare cases, light-headedness and fainting.

We do not foresee that the amount of blood taken during the study will cause harm to your health. It would not be expected for this amount of blood taken to cause anaemia. However, we will check for anaemia at regular intervals during the study.

Incidental findings

We will notify your GP that you are taking part in this study. If unusual results or undiagnosed conditions are found in the course of the study, these will be discussed with you and, if you agree, your GP will be informed of these results to arrange further follow-up (we would not report them to anyone else without your permission). In addition, your GP may be required to pass on details of any adverse event to the study investigators

If, at screening or any time during the study, a blood sample shows an unusual result, we will take a second sample to confirm this result. If the test result is confirmed, we may need to withdraw you from the study and discuss what this might mean for you before referring you for treatment and/or further support.

False positive results on Hep B tests

As a result of vaccination with the study vaccine you may develop antibodies against Hepatitis B and these antibodies may persist in the future. This is as a result of vaccination and NOT because of Hepatitis B infection. There is a simple blood test which can tell if you have contracted Hepatitis B before and after the study. We will do these tests to be sure that you are not infected with the HBV. If you develop antibodies against the HBV as a result of vaccination, we will give you a formal letter, that you may use in the future as evidence that you did not have Hepatitis B infection during the study and that you developed antibodies as a result of the study vaccine.

Social harms

The research team will keep your participation in this study confidential. However, it is possible that others may think you are at risk of Hepatitis B infection or disapprove if you decide to let them know about your involvement in the study. If you have any concerns or difficulties, study staff will provide assistance and support.

Will the study benefit me?

You will not receive any direct benefit from this study. **The study vaccine will not protect you from Hepatitis B infection and it is important that you continue to protect yourself against Hepatitis B infection.** HBV can be contracted from unsafe blood products (including injecting drug use) and through sexual transmission. However, knowledge gained from this study is needed for future research to see if this vaccine can safely treat an existing Hepatitis B infection.

Can I take part in this study if I am pregnant?

If you are trying to or are planning on becoming pregnant, or if you are breast-feeding, you are not able to take part in this study. The risks associated with the use of the vaccine in pregnant women and during breastfeeding is not known.

You will be asked to use an effective method of contraception during the study. You will be given guidance on what is an effective method of contraception in this study. Contraception will need to be continued throughout your time in of the study.

If you become pregnant during the study, you should tell us immediately. Should this happen you will withdraw from the study. However, we would like to collect some information about your pregnancy until after delivery, if you agree.

Will I be able to participate in other studies in the future if I have received this vaccine?

Probably, but it depends on the specific criteria of each study and it would need to be discussed on an individual basis.

Will the information from the study be confidential?

Yes, all your records will be kept confidential. In addition to the doctors and nurses that you meet, other study staff involved who have access to your records are equally bound to respect your confidentiality – as is your GP, who will be made aware that you are taking part in the study. Any data collected will be kept in accordance with the Data Protection Act 2018 and will be coded, which means that your name will not be used on any research report or samples collected during the study. Your identifiable information, such as your consent form, will be kept in a locked cupboard within the University of Oxford facilities and will be stored separately to the anonymised data collected during the study. Your anonymised personal and medical information may be checked by the sponsor, study team or regulators. We may need to check anonymised personal data in case there is something about your individual experience in the study that requires us to check back to find a cause. This is to make sure that the study is being run properly. Besides that, only the study site staff can use information that identifies you (such as name and address) and only for the purpose of the study. In line with the Medicines for Human Use (Clinical Study's) Amendment Regulations 2006, the University of Oxford requires that all original paper documents be retained for at least 15 years after the completion of Clinical Research.

Anonymised data collected during the study (from screening until the final visit, or until the end of your follow-up) may be passed onto other organisations, which may include commercial organisations.

What if new information becomes available?

Sometimes new information may become available during a study about the study vaccine, including information that could potentially impact your health. If this happens, we will tell you about it and discuss whether you want to, or should, continue in the study. If you decide to continue to take part you may be asked to sign an updated consent form. On receiving new information, we may consider it to be in your best interests to withdraw you from the study.

Who reviews the study?

The study procedures have been reviewed and approved by the South Central Berkshire Research Ethics Committee (REC).

Additionally, a committee of experts (called the Data Safety Monitoring Committee) who are independent from the study team and from the sponsor, will monitor the data collected for events that could have an impact on the health of the participants.

What happens to the results at the end of the study?

One of the study doctors will inform you of the results of the study. The anonymised data collected from the study will be submitted for publication in scientific journals. In addition, we may produce reports for the general public which would be published via the web and other media. You will not be identified in any report or publication.

Who sponsors, organises and funds the study?

The study is sponsored and funded by Vaccitech Ltd, The Schrodinger Building, Heatley Road, The Oxford Science Park, Oxford OX4 4GE. The Chief Investigator for this study is Professor Eleanor Barnes, Professor of Hepatology at University of Oxford.

Financial disclosures:

For full disclosure, the Chief Investigator and other members of the study team invented this HBV vaccine and therefore have intellectual property rights in relation to this vaccine. The Sponsor and other members of the study team may benefit financially if this vaccine is commercialised in the future.

Research-Related Injury

We do not expect you to suffer any injury as a result of participating in this study. Medical care will be organised in the unlikely event that an injury related to the vaccine or the study does occur.

Vaccitech Ltd, as Sponsor, has appropriate insurance in place for the event that you suffer any harm as a direct consequence of your participation in this study.

The insurance for the study provides “No Fault” cover and provides compensation for you if you suffer harm while taking part in this clinical study.

Will I be paid for taking part in this study?

Study participants will be reimbursed for their time, travel and inconvenience of taking part in the study. The reimbursement for any volunteer who completes the whole study is up to **£345.** You will be reimbursed £25 for the screening visit. For the other visits you will be reimbursed for your time, travel and the inconvenience based on the following figures:

- Travel expenses: £10 per visit
- Inconvenience of blood tests: £10 per blood donation
- Time required for visit: £20 per follow up visit and £40 for the vaccination visit

The sum reimbursed is on a ***pro rata*** basis. So, if for example, you choose to withdraw half way through the study we will calculate your reimbursement based on the visits you have attended and samples that have been taken.

You may also receive reimbursement for any unscheduled visits attended (if blood tests must be repeated or if you are asked to perform a face to face visit after the day 1 phone call).

You will be reimbursed **£40** for every unplanned visit. Any payments made to you because you have taken part in the study may need to be declared for tax and benefit purposes

What happens if I have a complaint?

If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the Chief Investigator, Professor Eleanor Barnes, on 01865 281547. For any queries regarding your personal data protection, you may contact the information commissioner's office on 01625 545 745 or by email at international.team@ico.org.uk. The information commissioner's office is your supervisory data protection authority. More information about how your information will be used can be found on www.hra.nhs.uk/information-about-patients/

Who can I contact for more information?

For questions about this study please contact:

Dr Paola Cicconi (Principal Investigator): Email paola.cicconi@ndm.ox.ac.uk, Tel. 01865 611413

Professor Eleanor Barnes (Chief Investigator): Email ellie.barnes@ndm.ox.ac.uk, Tel. 01865 281547

If you have any questions you would prefer to discuss with a staff member who is not directly involved in this research, please contact:

Dr Susanne Hodgson susanne.hodgson@ndm.ox.ac.uk, Tel. 01865 611385

Short study title: A Phase 1 Vaccine Study in Healthy and Chronic Hepatitis B Participants

CONSENT FORM FOR HEALTHY VOLUNTEERS

Rec Ref. No.:19/SC/0419 Chief Investigator: Prof. Eleanor Barnes

Participant identification number for this study: …… *Please initial the boxes:*

1. I confirm that I have read and understood the information sheet dated …… (version ……) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily. ☐
2. I understand that my participation is voluntary and I am free to withdraw at any time without giving reason, and without my medical care or legal rights being affected. If I choose to withdraw, I agree to the use of any anonymised sample(s) or data that have been collected prior to withdrawal. ☐
3. I understand that the data collected during the study and relevant sections of my research study notes may be looked at by members of the University of Oxford and the Host institution(s) who are involved in the running of the study, or other regulatory authorities, for the purposes of auditing and monitoring. I give permission for these individuals to have access to my records. ☐
4. I understand that my anonymised data and samples collected during the course of the study may be passed on to other organisations, which may include commercial organisations, as part of this research. ☐
5. I understand that all samples will be considered a gift to the University of Oxford and I will not gain any direct personal benefit from this. ☐
6. I agree to my GP being informed of my intended participation in this study and I give permission for the study team to ask my GP and/or medical consultant to verify the medical history (including verifying my medical history by accessing my Electronic Patient Record, if applicable) ☐
7. I agree to have my leftover samples stored for future research in the UK or abroad in an approved biobank (optional) ☐
8. I agree to take part in the HBV-001 study

_____	_____	_____
Name of patient	Signature	Date
_____	_____	_____
Name of person taking consent	Signature	Date

When completed, 1 copy to be given to the volunteer and 1 copy to be kept in the site file.