Southampton NIHR Clinical Research Facility
University Hospital Southampton NHS Foundation Trust
C Level West Wing, Mailpoint 218
Southampton
SO16 6YD
Tel: 023 8120 4989
Email: CRFstudyteam@uhs.nhs.uk
Website: www.southamptoncrf.nihr.ac.uk

Participant Information Sheet: Stablepharma Vaccine Study

Long title: A Phase 1, Randomised, Single-Blind Clinical Study to Evaluate the Safety, Immunogenicity and Tolerability of SPVX02, a Tetanus and Diphtheria Booster Vaccine, Against Two Comparator Vaccines in Healthy Adult Participants

Short title: A Phase I Study to assess the safety and immune response of a vaccine for tetanus and diphtheria which can be stored at room temperature

Protocol number: SPL-SPVX02-01

We would like to invite you to take part in a research study taking place at the Southampton NIHR Clinical Research Facility, University Hospital Southampton NHS Foundation Trust. Taking part in this research is entirely voluntary and before making a decision, it is important that you take the time to understand why the research is being done and what it would involve. Please read the following information carefully and discuss it with friends, relatives and your General Practitioner (GP) if you wish. Please ask us if there is anything that is not clear or if you would like more information.

What is the purpose of this study?

Most vaccines need to be constantly kept cold which means they are stored in fridges or freezers during transportation and storage in the clinic, before they are given to people. The World Health Organization (WHO) says that approximately 50% of vaccines worldwide go to waste each year because of problems encountered in keeping them cold enough during transportation and storage.

This need to keep vaccines cold is referred to as "The Cold Chain." In some parts of the world, the cold chain is not effective, for example, fridges may not be available or regular power cuts can stop fridges and freezers from working, resulting in wasted vaccines that cannot be used. Partly because of these problems, it is estimated that approximately 3 million children globally die each year from diseases that could be prevented with vaccines.

This wasted vaccine supply costs about $30 billion a year and also creates a big carbon footprint, which is bad for the environment. This is why it's so important to develop vaccines that don't need constant refrigeration or storage and transport in freezers.

The purpose of this study is to evaluate a new temperature stable, fridge-free, tetanus and diphtheria vaccine called SPVX02 to assess its safety and immune response in healthy adult participants. The study also aims to evaluate 2 existing, approved comparator vaccines so that the immune response seen with these 2 existing, approved vaccines can be compared to the immune response seen in the participants who have received the new vaccine, SPVX02. One of these 2

existing, approved vaccines is called Tetadif®. The new fridge-free vaccine, SPVX02 is a different form of Tetadif®. The other comparator approved vaccine is called diTeBooster.

This is the first study to use the SPVX02 fridge-free vaccine in human participants.

It is planned that a total of 60 volunteers will participate in the study.

In order to ensure the safety of all participants in the study, each of the first 3 participants receiving vaccine in the study will receive their vaccine at least 1 day apart. The first 3 participants (referred to as the sentinel group) will then have all of their study data from Day 1 to Day 7 (including e-diary card data) reviewed by the Local Safety Committee at the Southampton NIHR Clinical Research Facility.

Once the Local Safety Committee have reviewed the data from the first 3 participants in the study they will provide their written approval to the study doctors for the remaining 57 participants to be dosed. This approach is standard practice for studies where a vaccine is dosed for the first time in study participants.

Do I have to take part?
No. It is up to you to decide whether or not to take part. If you do decide to take part, you will be given this information sheet to keep and you will be asked to sign a consent form. You are free to withdraw at any time and without giving a reason, but you may be asked to return to the clinic for follow up visits to ensure your safety and wellbeing. If you are eligible to be involved in this study and you wish to participate, you will need to follow all instructions from the study doctor and research staff.

How long will the study last?
Your total participation in this study from the time you sign this consent form to your last visit is expected to be approximately 2-3 months . You should discuss with the study doctor any questions you have on the possible length of this study.

What is the vaccine being tested?
Scientists at a company called Stablepharma based in the UK have developed a technology called StablevaX™ that allows them to reformulate existing approved vaccines into fridge-free forms, enabling distribution and storage in the NHS or even in the most inhospitable parts of the world, without any need for the cold chain.

Using this technology, they have reformulated a vaccine called Tetadif, a WHO-prequalified liquid combined tetanus and diphtheria (Td) vaccine into SPVX02 (the study vaccine).

SPVX02 has the same ingredients as Tetadif®, except for the addition of trehalose. Trehalose is a type of sugar that is used in many products, including some other medicines and is generally recognised as safe. Trehalose is a key component of the vaccine and is needed to stabilise the vaccine, which eliminates any requirement for the cold chain.

In this study, participants will receive a single of dose of either SPVX02 (study vaccine), Tetadif® (comparator vaccine) or diTeBooster (comparator vaccine). All 3 of these vaccines aim to prevent

tetanus and diphtheria infection. All 3 vaccines (SPVX02 , Tetadif® and diTeBooster) contain small, harmless parts of the diphtheria and tetanus toxins, called toxoids. These toxoids are made so they can't cause disease but still look like the real toxins to your immune system.

All 3 vaccines also contain something called an adjuvant (aluminium hydroxide). This is an ingredient that boosts your immune system's response to the vaccine, helping your body learn faster and remember longer. When you get the vaccine, your immune system spots the toxoids and reacts as if they were dangerous. It sends out special cells to study and "remember" the toxoids. Your immune system then makes proteins called antibodies that are specifically designed to fight diphtheria and tetanus toxins. These antibodies stay in your system, ready to act if the real toxins ever show up. After the vaccine, if the real diphtheria or tetanus toxins ever enter your body, your immune system will recognize them immediately. The antibodies will attack and neutralize the toxins before they can make you sick.

To participate in this study it is important that you have had a diphtheria or tetanus vaccine in the past. In order to receive a vaccine in the study it is important that you don't have tetanus antibodies over a certain level in your blood that might make it hard for us to see if the study vaccines work. Whether you can receive the study vaccines or not will be decided as part of the trial itself.

Am I eligible to take part?

<u>In order to take part in this study you must be:</u>

- 18-55 years of age with a body mass index (BMI) equal to or less than 30 kg/m^2
- able to provide informed consent indicating that you are willing to participate and that you understand the purpose of the study and the assessments you are required to undergo as part of your involvement in the study
- in good health with no current conditions that may significantly impair your safety or influence the study results, as determined by the Study Doctor
- not have any medical condition that causes immunodeficiency
- able to provide history or documentation of any previous primary or booster immunisation with diphtheria and tetanus vaccines
- participants of child-bearing potential must not be pregnant or breastfeeding and must also be willing to practice continuous effective contraception during the study. This will be discussed with you at the screening visit if you choose to take part
- male participants must be surgically sterile or willing to use barrier contraception method upon enrolment and during the study. This will be discussed with you at the screening visit if you choose to take part

You might not be able to take part in this study if you:

- have a serious and uncontrolled chronic disease (i.e., cardiac, pulmonary, renal, neurologic, metabolic, rheumatologic, etc.)
- have known or suspected autoimmune disease or impairment of immunological function of any cause
- have been given immunoglobulin or other blood products within the last three months or have recently been given steroids (injected or oral) or other immunomodulatory therapy.
- live with HIV, hepatitis C virus or hepatitis B virus infection
- have received any vaccine in the last 30 days

- are planning to receive any other vaccine in the 30 days following administration of the study vaccine
- are planning to donate blood during your participation in the study
- have a history of allergic reaction (including anaphylaxis or Arthus-type hypersensitivity reaction) to vaccines or any of the components of the vaccines used in this study
- are enrolled in another interventional clinical study or have participated in an interventional clinical study in the last 6 months
- have any condition that, in the opinion of the study doctors, would pose a health risk to you or interfere with the evaluation of any of the study vaccines
- have a history of Guillain-Barré syndrome
- have received a tetanus or diphtheria vaccination within the last 10 years and your tetanus antibody levels are too high to take part in the study
- have a previous history of diphtheria or tetanus disease within the last 25 years
- have a history of alcohol or substance abuse
- have had significant psychiatric illness in the last 2 years
- have permanent body art on both right and left upper arms that would obstruct the ability to observe local reactions at the injection site
- unable to attend scheduled visits or unable to comply with the study procedures

What will happen if I decide to take part?
If you decide to take part in the study, you will come to the Southampton NIHR Clinical Research Facility (Southampton NIHR CRF) for 4 scheduled visits. All participants will attend a screening visit. During this visit the study team will collect information on your medical background, examine you physically, and perform tests (including blood and urine tests).

Following the screening visit if you are eligible for the study, you will be invited for another visit during which a single dose of vaccine will be given. You will have a randomly assigned to receive a dose of vaccine which will either be SPVX02 (the study vaccine), or a comparator vaccine (either Tetadif® or diTeBooster). The comparator vaccines are both approved vaccines for the prevention of diphtheria and tetanus in the European Union but not in the UK. You will not be told at this stage of the study which of the vaccines you have received.

During this visit you will have another physical examination by a study doctor and more tests will be performed. After being vaccinated you will be asked to complete an electronic diary over the next 7 days, recording any symptoms that may be related to having had the vaccine. On the day after you have received the vaccine, a member of the study team will call you by telephone. You will have two more visits; one will be 7 days after vaccination; the other will be 28 days after vaccination – this will be your final scheduled visit.

The study timetable is summarised in the table below, note that items marked with * will only be performed if your study deems them necessary

	Screening	Vaccine	Phone Call	Follow Up	Follow Up
		Day 1	Day 2	Day 7	Day 28
Consent	x				
Medical History	x				
Physical Exam	x			(X)*	(X)*
Blood Test	x	x			x
Urine Test	x	x			x
Pregnancy Test	x	x			
Vaccination		x			
Provide Diary		x			
Review Diary			x	x	
Physical Observations	x	x		x	x
Estimated Visit Duration	2 hours	3-5 hours	20 minutes	1 hour	1 hour

Screening Visit – Determining Eligibility

If you are interested in taking part in this study, we will arrange for a pre-screening telephone call to take place where we will ask you some questions to see if you may be eligible to take part.

You will then be invited to attend a screening appointment at the NIHR Southampton Clinical Research Facility at Southampton General Hospital. The purpose of the screening visit will be to determine whether you are eligible to take part in the study. This visit will last approximately two hours. We will discuss the trial with you, and you will be given the opportunity to ask any questions that you have.

If you decide to participate then we will ask you to sign a consent form to confirm that you have read and understood the information in this document. You can still change your mind at any time after you have signed the consent form. Providing consent at the screening visit does not prevent you from leaving the trial if you change your mind later on.

Once you have signed the consent form, we will check that you do not have any health conditions that affect your eligibility for the study or that make the study unsafe for you. One of the study doctors will ask you some medical questions and perform some examinations. We will collect some blood samples through a vein in your arm (including a blood pregnancy test for participants of childbearing potential) and we will perform tests on a urine sample. We will also record your heart rate, respiratory rate and blood pressure. We will check your heart rate using an ECG, which involves

placing electrodes (sticky pads, similar to plasters) on your chest, arms and legs. We will also measure your height and weight.

As part of the consent process, we will ask for your permission for a letter to be sent to your GP asking them to confirm your medical history. This is so that we can check that it is safe for you to take part in the study. We will provide your GP with information about what the study involves and the criteria for enrolment.

Vaccination Visit

At the vaccination visit (Day 1) we will check that you are still happy to continue in the study and that your medical history hasn't changed. Before giving you the study vaccination, we will take some blood samples and record your body temperature. We will also take a urine sample and participants of childbearing potential will also undergo a urine pregnancy test. You will then be vaccinated with either SPVX02 (the study vaccine) or a comparator vaccine (either Tetadif® or diTeBooster). The vaccine you are given will be selected at random, and you will not be told which vaccine you have been given at this point of the study.

The vaccine will be given into the deltoid muscle (upper arm) in your non-dominant arm unless there is a medical reason to give the vaccine into your dominant arm instead (e.g. you have a tattoo which covers the vaccination site). Following the vaccination, you will be asked to remain at the NIHR Clinical Research Facility for at least one hour so that we can check that you experience no immediate side effects. You will be assessed again before leaving and we will ask you to record any symptoms, any medications that you take and any redness at the vaccination site, in a diary every day for 7 days. You will be given an emergency contact card should you have any concerns and wish to get in contact with us following your vaccination. This card will let you know what number you need to call during and out of office hours if you wish to speak to one of the study doctors.

Follow Up Visits

There will be follow up visits after the vaccination visit on Day 7 and Day 28 (2 in total). There will also be a telephone call on Day 2, where the study team will call you to review the diary with you and ask how you are doing. The days on which you will need to return are shown in the table above. At these visits we will ask if you have experienced any adverse reactions, check if you have had to take any medications at home and review the diary that you will have been completing at home. On the Day 28 visit (the last visit) we will also carry out some blood and urine tests.

During the course of the study, you may be asked to attend for an extra visit, for example if a blood test needs to be repeated. You will be compensated financially for the time and inconvenience of all study visits, including any extra visits. Details of the compensation provided are available towards the end of this information sheet.

What are the potential benefits of taking part?

Information gained from the study may help to develop vaccines that can be deployed in areas of the world most affected by vaccine-preventable diseases and reduce the global financial and environmental burden of vaccine wastage caused by failings in the cold chain.

You may benefit personally by receiving one of the comparator vaccines that has already been shown to boost protection to diphtheria and tetanus. It is hoped that the study vaccine will also boost protection to diphtheria and tetanus, and demonstrating this is one of the aims of the study.

What are the potential disadvantages and risks of taking part?
Some procedures in the study may cause discomfort or symptoms. It is important that you understand what these are before signing the informed consent form.

Vaccine Associated Risks: SPVX02 has not previously been studied in human participants and not all potential side effects of the vaccine are known. However, all the ingredients of the vaccine have been tested extensively in previous studies, and most have been used in approved diphtheria and tetanus vaccines (including the Tetadif® and diTeBooster vaccines) for many years. We can therefore predict from past experience what the potential risks and side effects might be. We don't expect any side effects or symptoms that have not previously been seen in other diphtheria and tetanus vaccines. Most symptoms are expected to be mild, although some effects may also be moderate or severe.

It is important to remember that the SPVX02 vaccine is in the early stages of development and the amount of safety data available is limited, which is part of the reason this study is being conducted. There is a possibility you could experience a side effect that is more severe than those described below:

Side effects of vaccine administration can include but are not limited to:

1) Local Reactions
Discomfort at the site where the injection is given. This usually gets better within a few minutes. Later, you might experience pain resulting in some difficulty moving your arm, but this should resolve within a few days. In addition to pain, you may experience redness, swelling, itching or warmth at the injection site.

2) General Reactions
You may experience flu-like symptoms such as muscle aches, joint aches, feverishness, chills, headache, nausea, tiredness and/or feeling generally unwell in the first 24-48 hours after the injection. We would expect these symptoms to resolve within a few days. You are encouraged to take over-the-counter medications such as paracetamol (providing you are not allergic to these medicines) as soon as you experience these symptoms as this is likely to reduce the intensity of any symptoms you have. We will make a note of any medications you have used in the diary and discuss them with the Study Doctor at your follow up visits.

3) Serious Reactions
With any vaccination there is a risk of rare serious reactions, which may be related to the nervous system or the immune system. Severe allergic reactions to vaccines (anaphylaxis) are rare but can be fatal. Reactions in the nervous system are also extremely rare following vaccination and can cause an illness called Guillain-Barré syndrome. Guillain-Barré syndrome is an illness in which people can develop severe weakness and can also be fatal.

Autoimmune diseases are a class of diseases resulting from a disordered attack of the immune system on the body's own organs and tissues. Such diseases have very occasionally been reported in individuals who have received adjuvanted vaccines like SPVX02, Tetadif® and diTeBooster. The relationship of the SPVX02, or any of its components, to these events has not been established but cannot be excluded.

The investigators are contactable at any time if you are concerned about any possible vaccine side effects.

Blood Sampling Associated Risks:
The total volume of blood taken during the study for participants is approximately 60 ml (12 teaspoons) over approximately 2-3 months. The amount taken on one day will vary between 30 ml (approximately 5 teaspoon) to 15 ml (approximately 3 teaspoons).

The volume of blood being taken over the course of the trial should not cause any problems for healthy adults. There may be some temporary mild discomfort, such as bruising and tenderness at the site where the blood samples are taken. You may experience faintness as a result of the blood test. We will give you a copy of your blood test results if you request them and will only send the results to your GP if you wish us to.

If abnormal results or undiagnosed conditions are found during the course of the study these will be discussed with you and, if you agree, your GP (or a hospital specialist, if more appropriate) will be informed. Any newly diagnosed conditions (e.g. hepatitis B or HIV) will be looked after within the National Health Service (NHS) and you will be referred to your GP or specialist team within the hospital for further assessment and follow up as required as per local standard of care guidelines. The hospital teams also have a responsibility to report newly diagnosed cases of notifiable diseases (e.g. acute infectious hepatitis) to the UK Health Security Agency.

Considerations

Pregnancy
If you are pregnant, breastfeeding or planning to become pregnant during the study period you will not be allowed to take part in the study.

Before being included in the study, participants of childbearing potential must be either:

a) Practicing an acceptable effective method of contraception (if of childbearing potential) for the duration of the study. Acceptable methods for this study include:

- hormonal contraception (use of hormonal contraception should start at least 28 days before the first administration of the study vaccine).
- intrauterine device (IUD).
- intrauterine hormone-releasing system (IUS).
- male or female condom with or without spermicide.
- cap, diaphragm or sponge with a vaginal spermicide.
- vasectomised partner (the vasectomised partner should be the sole partner for that volunteer)

- sexual abstinence (sexual abstinence is considered an effective method only if defined as refraining from heterosexual intercourse from signing the consent form until the end of the study)

b) Not of childbearing potential defined as:

- Postmenopausal: amenorrhea (no menstrual periods) for at least 12 months without alternative medical cause.
- Permanently sterile: permanent sterilization methods include hysterectomy (removal of the womb), bilateral salpingectomy (surgical removal of the fallopian tubes), bilateral tubal occlusion/ligation procedures, and bilateral oophorectomy (surgical removal of both ovaries).

If you were to become pregnant during the trial you must tell us immediately and you will be withdrawn from the study, although we will ask to follow you up for safety reasons.

Private Insurance

If you have private medical or travel insurance you are advised to contact your insurance company before participating in this trial, as involvement may affect the cover provided.

Expenses and Payments

A payment of up to £525 will be made on completion of the study for your time, expenses and to compensate for any inconvenience (see table below). If any repeat visits are required e.g., for extra blood samples you will be paid for these visit(s) too.

If you are enrolled onto the study but withdraw prior to completion, you will be paid on a pro-rata basis. You should be aware that data collected up to the point at which you have withdrawn from the study may be used. If you do not adhere to study procedures on which the pro-rata payment is based, your payment may be reduced accordingly.

If you are screened for the study but are found to be unsuitable, or you attend the unit and are not dosed, you will receive a pro-rata compensation payment. Reserve participants will receive payment on a pro-rata basis.

The payments that will be made to you include any travels costs, you will not be reimbursed separately for your travel costs. However, if you need one you will receive a parking ticket from the hospital during each study visit so you will not be required to pay for car parking.

The total potential compensation for participation is shown in the table below. Compensation for this study is calculated as follows:

Study Related Activity	**Participant Compensation**
Screening Visit Attendance	£75.00
Day 1 Visit Attendance	£140.00
Day 2 Telephone Call	£20.00
Diary card completion for a 7-day period	£50.00
Day 7 Visit Attendance	£75.00

Day 28 Visit Attendance	£75.00
Additional fee for completing all study visits, including the Day 2 telephone call, and completing the 7-day diary card	£90.00
Total participant payment for completing the 7 day diary card, attending 4 study visits and participating in 1 telephone call	£525.00

Note that extra visits, if required, will be reimbursed using the criteria detailed in the table above.

Participants who withdraw from the study prior to its completion will be offered financial re-imbursement corresponding to the number of visits or days attended.

Reimbursement will be issued to volunteers after the last scheduled visit for each participant. Reimbursement for any unscheduled visits will be issued following the unscheduled visit. Please note that reimbursements can take up to four to six weeks to be processed and will be paid by bank transfer. In order for the reimbursement to be processed, we will request the following information from you nearer the time: name of the bank, bank account number and sort code. Members of the study team and hospital finance teams will require access to this data in order to process the reimbursement request. It will not be shared outside of these departments. You are responsible for paying tax on this payment if this is appropriate to your circumstances. If you receive a means-tested benefit of any kind, you should check whether participating in this study will have any effects on the benefits you receive.

Involvement of your General Practitioner (GP) / Family Doctor
In order to take part in this study, you will be required to sign a form, documenting that you consent to us contacting your GP. This is to inform them that you are interested in being involved in the study and to check that there are no medical reasons that they are aware of why your participation would be inadvisable. The researchers will not enrol you in the trial if they have any concerns about your eligibility or safety. We will write to your GP to let them know whether or not you are enrolled onto the study, and whether or not you completed the study, so that they can update your medical records accordingly.

Will my taking part in this study be kept confidential?
The study site will record basic personal details about you, including your name, contact details, gender, height, weight and ethnicity (to be used only for clinical purposes), as well as information on your medical history and clinical data collected about your participation in the study. The following people may also access these records:

- Study monitors and auditors, who may work for Stablepharma or its authorised agents, who check that the study is being performed correctly and that the information collected about you is accurate.
- Individuals from the study team responsible for the conduct of the study.
- National and international regulatory authorities involved in keeping research safe for participants.

To ensure privacy, your name and other directly identifying information will not be attached to records or samples released to Stablepharma and its service providers for research purposes. Instead, you will only be identified by a code. Only the Study Doctor and authorised personnel will

be able to connect this code to your name, by a list that will be kept securely by the study site for at least 15 years. Your date of birth may also be recorded to help identify your study record. Your coded data will be forwarded to Stablepharma and its service providers for activities related to the study, such as laboratory and data analysis. A list of companies to whom your coded information is transferred is available from Stablepharma via your Study Doctor.

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained which includes data from blood samples that have already been analysed.

Following the study, the researchers may share anonymised results of the study with other researchers to aid shared understanding. Results may be used to guide research in the future. You will not be identified in any of the shared or published data.

For further information on how health researchers use information from patients, please see Appendix 1. You can find out more about how we use your information by contacting Professor Saul Faust, Chief Investigator, using the contact details for the site on the first page.

What will happen to the blood samples that I give during the study
We take blood tests as part of the screening visit and at the study visits in order for us to assess your general health, immune response to the vaccine and for safety reasons. If you would like them, we can give you the results of your blood tests when they are available.

Coded blood samples will be stored after testing, and, if you consent, may be used in future research . Giving your consent to the use of your coded blood samples for future research is optional for all participants and you can still participate in the trial even if you do not give your consent to the use of your coded blood samples in future research. You will be asked to consent specifically for blood to be stored and used in future research and you are free to withdraw this consent at any point if you change your mind. Your study visit blood tests will be analysed in the hospital laboratories and in United Kingdom Health Security Agency (UKHSA) laboratories. Any samples or data sent to UKHSA laboratories, or any other laboratory, would be anonymous.

The blood tests we will take may include measures of:

Blood test	Purpose of test
• Red and white blood cell counts • Clotting function • Liver, kidney and thyroid function • Blood-borne viruses (HIV, hepatitis B & hepatitis C)	Eligibility screening and patient health assessment
• Immune responses to vaccines	To assess and compare the immune response to the different vaccines

Will any genetic tests be done?
No genetic tests will be performed as part of this study.

What if any new relevant information becomes available?
Sometimes during the course of a study, new information becomes available about the vaccine being studied. 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 will 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.

What will happen if I no longer want to take part in the study?
Taking part in this study is your choice. You can choose to participate in this study and then you can change your mind at any point. This trial is not part of routine NHS care, which will not be affected.

The Study Doctor may decide to remove you from this study without your permission for different reasons:

- If you do not follow the procedures required by the study.
- If the study procedures are found to be unsafe.
- If the study procedures are found to be ineffective.
- If the study is closed.

It is important that you tell the Study Doctor if you want to withdraw from the study, so that they can plan an appropriate visit to discuss withdrawal and follow up to monitor your safety and wellbeing. For example, you choose to attend all follow up visits, but you may not want any further blood tests to be carried out for the purpose of the study. Unless you state otherwise, any blood taken for the study will continue to be stored and used for research as detailed above. You are free to request that your blood samples are destroyed at any time during or after the study. Your medical care will not be affected if you choose to withdraw from the study.

What if there is a problem?

- If you have a concern about any aspect of this study, you should ask to speak with the research staff who will do their best to answer your questions.
- If you remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from your local hospital.
- If you are harmed due to someone's negligence, then you may have grounds for legal action.

If you wish to complain or have any concerns about any aspect of the way you have been approached or treated during the course of this study, the normal National Health Service complaints mechanisms will be available to you.

If you think you have an injury or illness related to this study, please call the study team and seek immediate medical attention if it is required We will provide compensation for any injury caused by taking part in this study in accordance with the guidelines of the Association of the British Pharmaceutical Industry (ABPI).

We will pay compensation where the injury probably resulted from:

- A drug being tested or administered as part of the trial protocol
- Any test or procedure you received as part of the trial

Any payment would be without legal commitment. (Please ask if you wish more information on this). We would not be bound by these guidelines to pay compensation where:

- The injury resulted from a drug or procedure outside the trial protocol - The protocol was not followed."

The offer to provide the payment described above does not mean that the illness or injury is the fault of the Study Doctor/hospital. In no way does signing the consent form waive your legal rights. It also does not relieve the investigators, sponsors, or involved institutions from their legal and professional responsibilities.

What will happen to the results of the research study?

The results of the study will be presented at relevant conferences and meetings and published in relevant medical and scientific journals once the data has been reviewed by the researchers. The results will also be made available to you via your study team (upon request) and through accessing the European Clinical Trial Database. The results may also be reviewed by the Ethics Committee and the Medicines and Healthcare product Regulatory Agency (MHRA) at the end of the study.

Who is organising and funding this study?

This research is being organised by the University Hospital Southampton NHS Foundation Trust. The study is funded by Stablepharma (Sponsor). In addition, some of the funding for the trial has been provided to Stablepharma and University Hospital Southampton NHS Foundation Trust by Innovate UK, a UK Government funder of trials of new medicines and technologies. Your Study Doctor and University Hospital Southampton NHS Foundation Trust do not have any financial interest in the outcome of the study.

Who has reviewed this study?
This study has been reviewed and approved by the London Bridge Research Ethics Committee and the Health Research Authority (HRA). The Medicines and Healthcare products Regulatory Agency (MHRA) which regulates the use of all medicines in the UK, has reviewed the study design and has granted permission to use SPVX02 vaccine, and the 2 comparator vaccines, in this clinical study.

Prevention of 'Over Volunteering'
Participants taking part in this study must not be receiving medications or vaccines in another study at the same time. In order to check this, you will be asked to provide your national insurance or passport number (if you do not have a NI number). This will be entered on to a national database, which helps prevent participants from taking part in too many clinical trials at once. More information can be found at www.tops.org.uk. Your national insurance or passport number is also required to allow processing of compensation payments. The study team will remind you to bring a copy of your photographic ID and proof of your national insurance number (e.g. NI card) to your screening visit.

Contacts for further information
If you are interested in taking part in this study or have any questions, please contact the study team on:

Email: CRFstudyteam@uhs.nhs.uk
Tel: 023 8120 4989

In the event that you wish to discuss this project with an independent third party, please contact the hospital's Patient Advice and Liaison service (PALS) (available 8.30am to 4.30pm Monday to Friday).

Patient Advice and Liaison service
C Level Centre Block, Mailpoint 81
Southampton General Hospital
Tremona Road
Southampton
SO16 6YD
Tel no. 023 81 20 6325
Email: PatientSupportService@uhs.nhs.uk

APPENDIX 1

This document explains how health researchers use information from patients. If you are asked to take part in research, you can ask what will happen in the study.

How will we use information about you?

We will need to use information from you and from your GP medical records for this clinical trial (research project).

This information will include your name, NHS number, contact details and bank details (so we can pay your study compensation by BACS transfer).

People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead.

Stablepharma is the sponsor of this research, and is responsible for looking after your information. We will keep all information about you safe and secure by:

- University Hospital Southampton NHS Foundation Trust will collect information from you and your medical records for this research study in accordance with our instructions.

- University Hospital Southampton NHS Foundation Trust will keep your name, NHS number, contact details and bank details confidential and will not pass this information to Stablepharma.

- University Hospital Southampton NHS Foundation Trust will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study.

- Certain individuals from Stablepharma and regulatory organisations may look at your medical and research records to check the accuracy of the research study. Stablepharma will only receive coded information, they will not receive any identifying information.

- The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number, contact details or bank details.

- All of the documents and information you provide to us will be stored safely and securely in confidential conditions.

International transfers

We may share data about you outside the UK for research related purposes to:

- The analysis of your coded blood samples for future research purposes

If this happens, we will only share anonymous data as needed. We will also make sure you can't be identified from the data that is shared where possible. This may not be possible under certain circumstances – for instance, if you have a rare illness, it may still be possible to identify you.

If your data is shared outside the UK, it will be with the following sorts of organisations:

- Stablepharma R&D laboratory or partner laboratory facilities in Spain or other countries within the European Union.

We will make sure your data is protected. Anyone who accesses your data outside the UK must do what we tell them so that your data has a similar level of protection as it does under UK law.
We will make sure your data is safe outside the UK by doing the following:

- (some of) the countries your data will be shared with have an adequacy decision in place. This means that we know their laws offer a similar level of protection to data protection laws in the UK

- we do not allow those who access your data outside the UK to use it for anything other than what our written contract with them says.

Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

We will keep your study data for a maximum of 15 years. The study data will then be fully anonymized and securely archived or destroyed.

What are your choices about how your information is used?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

You have the right to ask us to remove, change or delete data we hold about you for the purposes of the study. We might not always be able to do this if it means we cannot use your data to do the research. If so, we will tell you why we cannot do this.

Where can you find out more about how your information is used?

You can find out more about how we use your information, including the specific mechanism used by us when transferring your personal data out of the UK.

- our leaflet (www.hra.nhs.uk/patientdataandresearch)
- by asking one of the research team

- by sending an email to Sponsor's Data Protection Officer [nchild@stablepharma.com],
- by ringing us on 02381 204989.

Thank you for taking the time to read this information sheet.