Participant Information Sheet (16 year-olds): Com-COV3

Comparing COVID-19 Vaccine Schedule Combinations in adolescents

A single-blind, randomised, phase II multi-centre study to determine reactogenicity and immunogenicity of heterologous prime/boost COVID-19 vaccine schedules in adolescents

CONTENTS

Would you like to participate in a COVID-19 vaccine study?

We would like to invite you to take part in our COVID-19 vaccine study.

Taking part in research is entirely voluntary. You should only take part if you want to.

In this information sheet we explain the background for the study and describe what taking part would involve.

Before you make a decision, it is important you take the time to understand why we are doing this research and what it would involve. Please read the following information carefully and consider discussing it with friends and relatives.

Summary

- **Young people aged 12 – 16 years are invited to receive COVID-19 vaccine**
- **We would give the first and second dose or the second dose only**
- **5 or 6 visits over the next year**
- **5 or 6 blood tests in total, taking place in Children and Young Adults' Research Unit (Noah's Ark Children's Hospital for Wales).**
- **Complete an online diary for around 2 months**

IMPORTANT INFORMATION IF YOU ARE CONSIDERING TRAVELLING ABROAD

Many countries now require evidence of COVID-19 vaccination to allow travellers to enter. Taking part in this study may mean that you receive a combination of vaccines which is not recognised for travel to certain countries. Regulations vary between countries and are constantly changing.

If you are considering travelling abroad (especially in the next twelve months), please read the Appendix at the end of this information sheet. It contains information which will help you to decide whether or not to take part in this study.

Who is sponsoring, organising and funding the research?

The study is organised and sponsored by the University of Oxford. It is funded by the UK Vaccine Task Force and through financial support to the University of Oxford from the National Institute for Health Research (NIHR), which is a UK government funded research agency. Novavax is providing vaccines for the study. Neither your GP nor the researchers are paid for recruiting you into this study.

What is the purpose of this research study?

The purpose of this study is to test how well young people (aged 12-16 years) respond to two doses of COVID-19 vaccine, comparing three different vaccines.

Since early 2020, COVID-19 has spread around the world. It has killed over 130,000 people in the UK and over 4 million people worldwide (by August 2021). It has made many more people seriously unwell.

Widespread vaccination is helping to save lives, reduce severity of illness and reduce spread of the disease. Most adults in the UK have now been vaccinated. By early August 2021, over 88% of adults in the UK had received at least one dose of vaccine.

The vaccination programme in the UK has so far focussed on adults because older adults are more likely to suffer from severe disease or die from COVID-19 than younger people. Although children and young people usually do not become very unwell with COVID-19, some do develop serious illness and a few have died. Young people with COVID-19 occasionally develop a serious inflammatory condition called paediatric multisystem inflammatory syndrome (PIMS-TS). In England, in the first year of the pandemic (until the end of February 2021), 251 under 18-year-olds (about 20 per million) were admitted to intensive care with COVID-19, and 25 (about 2 per million) died; 309 (about 26 per million) developed PIMS-TS.

Vaccinating young people may reduce their risk of severe disease, reduce their chance of missing time in education whilst isolating, and reduce the chances of infecting others.

In the UK, healthy young people aged 12 to 17 are currently offered a single dose of the Pfizer-BioNTech vaccine. It is also recommended that children aged 12 to 15 years old with specific underlying health problems (such as Down's syndrome, severe neurodisability or immunosuppression), who are at particular risk of serious COVID-19, should be offered two doses of Pfizer-BioNTech vaccine, given 8 weeks apart, as should children in this age group who live with a person with impaired immunity.

There is very close surveillance of all vaccines to identify any rare, serious unwanted effects. The mRNA vaccines, Pfizer-BioNTech and Moderna, have now been given to many millions of people across the world. They are routinely given to young people under 18 years old in several countries, including the USA. Some very rare, but serious, side effects have been recorded, including myocarditis (inflammation of the heart muscle) and pericarditis (inflammation of the membrane around the heart). This has been observed more often after the second dose of mRNA vaccine, especially in young men (12-17 years). In the USA, in males

aged 12-17 years, myocarditis was reported in 9.8 per million first doses given, and in 67 per million second doses.

It is likely that two doses of COVID-19 vaccine will provide better protection for young people against disease than a single dose. However, the advantage of better protection needs to be balanced against the potential risks of a second dose of vaccine.

We are therefore proposing to explore alternative vaccine strategies in this study. One possible strategy could be to use a different vaccine for the second dose. Another possible strategy could be to use a lower dose of Pfizer-BioNTech vaccine in the second immunisation.

It is currently unknown whether either of these strategies would produce an immune response in young people comparable to two standard doses of the Pfizer-BioNTech vaccine. Our study aims to answer this question.

If a lower dose of vaccine can be used for the second immunisation, then not only may adverse effects of vaccination be minimised, but it would also mean that more people can be vaccinated with the available supply of vaccine.

If a different vaccine can be used for the second immunisation, it allows flexibility in the immunisation schedule. If one vaccine were to be in short supply, then another could be used instead. Again, this would mean that more people can be vaccinated with the available supply of vaccine.

It is important to understand that this study will not be large enough to compare the risk of myocarditis in those receiving 2 full doses of an mRNA vaccine compared with the alternative schedules, since this is such a rare event. The study will provide valuable information on different vaccine combinations in adolescents, helping to identify those that produce the fewest common side effects and the best quality immune responses. We will also be measuring two blood proteins, known as Troponin and NT-proBNT, the levels of which can change if heart muscle is inflamed. These will be measured before and after immunisation, to learn more about the normal ranges of these tests in adolescents, and whether levels are affected by immunisation.

This study will provide useful information on the role for other vaccine options in adolescents more generally, helping to identify those that are most benign in terms of common side effects and those that produce the strongest and best quality immune responses to COVID-19.

What happens in the study?

This study will enrol young people aged 12 to 16 years from various sites in the UK.

All participants will receive first immunisation with a standard dose of Pfizer-BioNTech vaccine. This may be given in the study, or it may have been given in the community before enrolment in the study.

A second dose of COVID-19 vaccine will be given eight weeks after the first. The type and dose of vaccine given to each participant will be decided using a process called "randomisation".

The second dose of vaccine will be one of the following four possibilities:

1. A full standard dose of Pfizer-BioNTec vaccine
2. A half standard dose of Pfizer-BioNTec vaccine
3. A half standard dose of Moderna vaccine
4. A standard dose of Novavax vaccine

The chance of being allocated to each of these is the same (25%). Participants (and their parents/guardians) will **not** be informed which of these vaccines they will receive until one month after their second dose of vaccine. This is because one of the aspects of the study is to investigate the side-effects associated with the vaccines and we do not want reporting to be biased.

Each participant who receives their **first vaccine in the study** will have a total of six blood tests during the course of the study to assess their immune response to the vaccines. These will be before the first vaccine; before the second vaccine; approximately two and four weeks after the second vaccine; approximately six and twelve months after the first vaccine.

Each participant who receives their **first vaccine in the community** will have a total of five blood tests during the course of the study. These will be before the second vaccine; approximately two and four weeks after the second vaccine; approximately six and twelve months after the first vaccine.

Participants at some sites would be asked to provide saliva samples and have a sample of nasal fluid taken before and after the vaccines, but this is completely optional. Participants will not be informed of the results of their blood tests (or saliva and nasal fluid tests).

Visits will take place at the Children and Young Adult's Research Unit, at Noah's Ark Children's Hospital for Wales, Cardiff.

Participants will be given a diary to record symptoms for 28 days after each immunisation.

Participants remain enrolled in the study for one year.

What vaccines are we testing?

This study uses three different vaccines: Pfizer-BioNTech, Moderna and Novavax.

Pfizer-BioNTech COVID-19 vaccine (BNT162b2) was the first COVID-19 vaccine to be granted regulatory approval by the UK medicines regulator MHRA on 2nd December 2020. The approval was extended to include children aged 12 -15 years on 4th June 2021.

This is a messenger RNA (mRNA) vaccine. This vaccine uses a small amount of the genetic coding material (mRNA) of the SARS-CoV-2 (COVID-19 virus) spike protein packaged inside tiny fatty particles (lipid nanoparticles). After injection, these fatty particles are taken up by human cells, which start producing the spike protein. The immune system then makes a protective immune reaction to the spike protein. The original mRNA is broken down within a few days and cannot be incorporated into human genes.

This vaccine has been shown to be very effective at preventing severe COVID-19 disease and reducing transmission of infection. Millions of doses of this vaccine have now been given in the UK.

The following are recognised side effects of this vaccine:

Very common (may affect more than 1 in 10 people): injection site pain or swelling; tiredness; headache; muscle pain; joint pain; chills; diarrhoea; fever.

Common (may affect up to 1 in 10 people): injection site redness; nausea; vomiting.

Uncommon (may affect up to 1 in 100 people): enlarged lymph nodes; feeling unwell; arm pain; insomnia; injection site itching; allergic reactions such as rash or itching.

Rare (may affect up to 1 in 1000 people): temporary one-sided facial drooping; allergic reactions such as hives or swelling of the face.

Very rare: severe allergic reaction; pericarditis or myocarditis (as described above in the section "What is the purpose of this study?").

The characteristic symptoms of myocarditis are:

- a stabbing pain and/or tightness in the chest (which may spread across the body)
- pain in the neck that may spread across the shoulders and/or arms
- shortness of breath when lightly exercising or walking; or difficulty breathing when resting; or feeling light headed
- palpitations (the feeling of an abnormal heart rhythm).

Young people experiencing these symptoms after receiving a COVID-19 vaccine are advised to ring 111 or see their GP.

Moderna COVID-19 vaccine was granted regulatory approval by the UK medicines regulator MHRA on 8th January 2021. The approval was extended to include children aged 12 -17 years on 17th August 2021.

Like the Pfizer BIoNTech vaccine, it is a messenger RNA (mRNA) vaccine and uses a small amount of the genetic coding material (mRNA) of the SARS-CoV-2 (COVID-19 virus) spike protein packaged inside lipid nanoparticles.

This vaccine has also been shown to be very effective at preventing severe COVID-19 disease and reducing transmission of infection, and hundreds of millions of doses have been given worldwide.

The following are recognised side effects of this vaccine:

Very common (may affect more than 1 in 10 people): Swelling/tenderness of the underarm glands on the same side as the injection site; headache; nausea; vomiting; muscle ache, joint aches or stiffness; pain or swelling at the injection site; tiredness; chills; fever.

Common (may affect up to 1 in 10 people): rash; injection site rash, redness or hives.

Uncommon (may affect up to 1 in 100 people): injection site itching.

Rare (may affect up to 1 in 1000 people): temporary one-sided facial drooping; swelling of the face; dizziness; decreased sense of touch.

Very rare: severe allergic reaction; hypersensitivity; pericarditis or myocarditis.

Novavax (NVXCoV2373) is an investigational medical product. It is not currently licensed for general use outside medical studies. It has been given to tens of thousands of people within medical studies, including about 1400 adolescents, and so far no safety concerns have been raised. In clinical trials in the UK, the US and South Africa, this vaccine has been shown to be very effective at preventing symptomatic COVID-19 infection and severe COVID-19 disease. The manufacturer has now applied for regulatory approval of the vaccine by both the UK regulator (the MHRA) and the European Medicines Agency (EMA). A decision is expected in the next few months, but it is possible that the vaccine may not be approved for general use before this study begins.

This vaccine is based on the spike protein from the SARS-CoV-2 virus in combination with an adjuvant, a substance that increases the response of the immune system to the protein. The adjuvant is called "Matrix-M1™" and consists of saponin (which is derived from the soapbark tree) and natural fats.

There is less information available about the incidence of side effects than for the Pfizer-BioNTech vaccine. However, the common minor side effects of Novavax are likely to be similar to those shown above for Pfizer-BioNTech. In a recent study in adults over 50 years old, we found that those given Novavax tended to experience similar rates of generalised effects (such as fever, tiredness, muscle aches, etc.) as those given Pfizer-BioNTec, but lower rates of effects at the injection site (such as swelling, redness, soreness or tenderness).

Do I have to take part?

No. It is up to you to decide whether or not to take part. You will not be penalised in any way if you decide not to participate. Your decision will not affect your standard medical care. If you do decide to take part, you will be given this information sheet to keep (or be sent it electronically) and will be asked to sign a consent form. You are free to withdraw at any time and without giving a reason, but we may request a follow up appointment for safety reasons.

Can I take part?

To take part in this study you must:

- Be aged between 12 and 16 years.
- Be able and willing (in the investigator's opinion) to comply with all study requirements.
- Allow the Investigators to discuss your medical history with your GP and access all medical records.
- Provide written informed consent. If you are 16 years or older, you can provide consent for yourself. However, your parents/guardians should also be involved in your decision to take part.

You cannot participate in this study if any of the following apply:

- You have received any vaccine (licensed or investigational) less than 7 days before enrolment (or intend to receive any vaccine less than seven days after receiving the study COVID-19 vaccines).

- You have previously received two doses of COVID-19 vaccine, or one dose of a COVID-19 vaccine other than Pfizer BioNTech.
- You are a close family member of someone working at the study sites.
- You belong to a group already advised by the JCVI to receive two doses of COVID-19 vaccine, e.g. if you have specific underlying health problems (such as Down's syndrome, severe neurodisability or immunosuppression), or if you live with an immunosuppressed person. (The full details can be found in the "Green Book").
- You have received immunoglobulins or blood products within 3 months of enrolment.
- You have any confirmed or suspected significant problems with your immune system.
- Your spleen has been removed or is not functional.
- You have recurrent severe infections.
- You have used immunosuppressant medication within the past 6 months (except topical steroids or short-term oral steroids for under 14 days).
- You have a history of anaphylaxis, allergic disease or reactions likely to be worsened by any component of study vaccines, or if you are allergic to latex or polyethylene glycol/macrogol (PEG).
- You are pregnant or breast feeding, or intending to become pregnant within three months of the second dose of vaccine.
- You have had a malignant disease requiring chemotherapy or radiotherapy for malignancy within the past 6 months.
- You have a bleeding disorder, or prior history of significant bleeding or bruising following IM injections or blood tests.
- You are prescribed anticoagulants (such as warfarin, apixaban, rivaroxaban, dabigatran and edoxaban).
- You have any serious chronic illness requiring hospital specialist supervision.
- You have congenital heart disease.
- You have severe and/or uncontrolled respiratory disease, gastrointestinal disease, liver disease, renal disease, rheumatological disease, endocrine disorder or neurological illness (If you have mild to moderate, well controlled conditions you may participate in the study).
- You have a history of active or previous auto-immune neurological disorders (e.g. multiple sclerosis, Guillain-Barre syndrome, transverse myelitis).
- You have significant kidney or liver impairment.
- You have elective surgery requiring overnight admission and/or general anaesthetic scheduled during the study.
- You have participated in another research study involving an investigational product in the past 12 weeks.
- Your ability to understand English is insufficient to undertake all study requirements, in the opinion of the investigators.

Mild conditions that are well-controlled would not automatically exclude you from participating. If you are unclear whether you are eligible to be involved in the study, you can contact the study team who will be able to advise you.

If you have previously had confirmed or suspected COVID-19 infection, you may still take part in the study.

What will happen if I decide to take part?

If you decide to take part in the study, you should complete the short online questionnaire to check that you are eligible. At the end of this, you will be asked if you agree to a researcher contacting you by phone to ask questions about your current health and discuss details of your medical history, if required. You will also be asked to agree to allow us to contact your GP for further information, if necessary. If you are eligible, you will be invited to a face-to-face visit where you will be asked to sign the consent form in person.

What happens next will depend on whether you have already received your first dose of COVID-19 vaccine in the community.

IF YOU HAVE NOT ALREADY RECEIVED A COVID-19 VACCINE IN THE COMMUNITY: You would visit us six times over the course of a year. All visits will be arranged to take place outside of school hours.

What happens at each visit is summarised in this table and then described in more detail below.

Visit	D0	D56	D70	D84	D182	D364
Week	0	8	10	12	26	52
Eligibility	✓					
Consent	✓					
Blood test	✓	✓	✓	✓	✓	✓
Saliva sample/nasal fluid sample (at some sites only, and optional)	✓	✓	✓			
Vaccine	✓	✓				
Diary	✓	✓				

At **the first visit (D0)**, we will re-check that you are eligible to take part. Your temperature will be recorded. If it is above 37.8°C, or if you have symptoms of a respiratory tract infection, the visit will be rescheduled. Your heart rate, and height and weight will be checked. A doctor may need to do a physical examination such as listening to your heart and lungs or feeling your abdomen. It is important that females who take part in the study are not pregnant and do not become pregnant during the course of the study (until at least three months after the second vaccination). Anyone who could possibly be pregnant (considered to be any female aged 12 and above) must provide a urine sample to check before they receive a vaccination (at the first and second visits). We also ask that all female participants who have started their periods should avoid becoming pregnant during the study (for example using effective contraception if they are sexually active).

You may be shown a video, describing the study. You will have the opportunity to ask any questions you want before being asked to sign the consent form for the study.

You will have a blood test. If you want your skin numbed with local anaesthetic cream, this can be provided. Your blood will be sent for analysis to measure various markers of immunity

to COVID-19 (antibodies and T-cells). Blood samples from the first three visits will also be analysed for a substance called troponin (levels of which can rise in myocarditis).

We would also (at some sites) ask to take nasal fluid and saliva samples which are to look at the immune response in the lining of the airways. These tests would be repeated at subsequent visits if you had them at the first visit. You can say no to these tests and still take part in this study.

You will be given your first dose of COVID-19 vaccine (full standard dose of Pfizer-BioNTech) by injection into the muscle your upper arm (deltoid). You will need to stay for at least 15 minutes after your vaccination.

You will be given a link to an e-diary to record any symptoms you experience after the vaccination. A back up paper version can be given instead, if you are experiencing difficulties with internet; to allow the study team to view the entries on a regular basis we would prefer you to complete the diary online. You will also be given a thermometer and paper tape measure. You will be asked to record local symptoms at the injection site (pain, tenderness, redness, warmth, itch, swelling and hardness) each day for seven days after your vaccination. Similarly, you will be asked to record general symptoms (fever, chills, joint pains, muscle pains, fatigue, headache, malaise, nausea, vomiting, diarrhoea) each day for seven days. You will also be asked to record any other symptoms you experience in the 28 days after your vaccination.

Your first visit is likely to take up to two hours. The other visits will be shorter.

At **the second visit (D56)**, about 8 weeks later, you will have another brief health check. We will take a second blood test (and saliva/nasal fluid sample if this was taken at the first visit).

You will then be "randomised" to decide which vaccine you will receive for the second dose (Pfizer-BioNTech, Moderna or Novavax) and whether you will receive a full or half standard dose. You will not be told which it will be.

We will give you your second dose of COVID-19 vaccine, according to what is determined by the randomisation. You will again need to stay for at least 15 minutes after your vaccination.

We will look at what you have recorded in your symptom diary and ask you to record your symptoms after the second vaccination. We will ask you for the same information as after the first vaccination. This visit will last up to one hour.

At the third, fourth, fifth and sixth visits (D70, D84, D182 and D364) only require you to have a brief health check, and blood test (and a further saliva/nasal fluid sample will be taken at the third visit, if this was taken at previous visits). They will be scheduled at about 10, 12, 26 and 52 weeks after your first visit. These visits will last about half an hour.

IF YOU HAVE ALREADY RECEIVED A COVID-19 VACCINE IN THE COMMUNITY:
You would visit us five or six times over the course of a year. All visits will be arranged to take place outside of school hours.

What happens at each visit is summarised in this table and then described in more detail below.

Visit	**S**creening	**D56**	**D70**	**D84**	**D182**	**D364**

Eligibility	✓					
Consent	✓					
Blood test		✓	✓	✓	✓	✓
Saliva sample/nasal fluid sample (at some sites only, and optional)		✓	✓			
Vaccine		✓				
Diary		✓				

The screening and D56 visits may be scheduled separately or may be combined to occur at the same time.

At the screening visit, we will check that you are eligible to take part. You may be shown a video, describing the study. You will have the opportunity to ask any questions you want before being asked to sign the consent form for the study.

At the D56 visit, at least 8 weeks after your first vaccination, you will have a brief health check. Your temperature will be recorded. If it is above 37.8°C, or if you have symptoms of a respiratory tract infection, the visit will be rescheduled. Your heart rate and height and weight will be checked. Anyone who could possibly be pregnant (considered to be any female aged 11 and above) must provide a urine sample to check before they receive a vaccination.

You will have a blood test. If you want your skin numbed with local anaesthetic cream, this can be provided. Your blood will be sent for analysis to measure various markers of immunity to COVID-19 (antibodies and T-cells). Blood samples from the D56 and D70 visits will also be analysed for a substance called troponin (levels of which can rise in myocarditis).

We would also (at some sites) ask to take nasal fluid and saliva samples which are to look at the immune response in the lining of the airways. These tests would be repeated at subsequent visits if you had them at the first visit. You can say no to these tests and still take part in this study.

You will then be "randomised" to decide which vaccine you will receive for the second dose (Pfizer-BioNTech, Moderna or Novavax) and whether you will receive a full or half standard dose. You will not be told which it will be.

We will give you your second dose of COVID-19 vaccine, according to what is determined by the randomisation. You will need to stay for at least 15 minutes after your vaccination.

You will be given a link to an e-diary to record any symptoms you experience after the vaccination. A back up paper version can be given instead, if you are experiencing difficulties with internet; to allow the study team to view the entries on a regular basis we would prefer you to complete the diary online. You will also be given a thermometer and tape measure. You will be asked to record local symptoms at the injection site (pain, tenderness, redness, warmth, itch, swelling and hardness) each day for seven days after your vaccination. Similarly, you will be asked to record general symptoms (fever, chills, joint pains, muscle pains, fatigue, headache, malaise, nausea, vomiting, diarrhoea) each day for seven days. You will also be asked to record any other symptoms you experience in the 28 days after your vaccination.

This visit is likely to take up to two hours. The other visits will be shorter.

The remainder of the visits (D70, D84, D182 and D364) will only require you to have a brief health check, and blood test (and a further saliva/nasal fluid sample will be taken at the D70 visit,

if this was taken previously). They will be scheduled at about 2, 4, 18 and 44 weeks after your D56 visit. These visits will last about half an hour.

What should I avoid during the study?

You should not take part in other studies that involve the administration of drugs or vaccines, or studies testing other interventions for COVID-19. If you need to receive any vaccinations while enrolled in this study you should inform the research team beforehand, so we can discuss with you the most appropriate time to receive them.

It is important that females do not become pregnant from the start of the study until at least three months after the second vaccination. This is partly because the effects of a new vaccine on the unborn child are unknown, but also because if a participant is pregnant, this might affect the results of the study. Females who have started their periods should avoid becoming pregnant during the study (for example using effective contraception if they are sexually active).

You should not give blood whilst you are in the study. (The Blood Transfusion Service only accepts donations from people aged 17 years or above. Participants in this study whose 17th birthday falls during the study, should not give blood until after their last study visit.)

Are there any risks from taking part in the study?

1. **Vaccination side effects**

All vaccines can potentially cause side effects. Most side effects are likely to be mild or moderate in severity and resolve within a few days. Details of possible side effects for the Pfizer-BioNTech and Moderna vaccines are given above in the section "What vaccines are we testing?".

Novavax is still an investigational medical product, so less detailed information is available. It is likely to have the same common side effects as other vaccines. Very rare side effects may not be recognised until a vaccine has been given to very large numbers of people.

Severe allergic reactions (anaphylaxis) after vaccination are extremely rare. If they occur, they do so within minutes of the injection. This is why we ask you to stay for at least 15 minutes after your vaccination. The study staff are trained and equipped to recognise and treat anaphylaxis.

2. **Blood tests**

Having blood taken may cause slight pain, although we will use anaesthetic cream to numb the skin if requested. You may feel light-headed or even faint. You may notice a bruise afterwards. Taking blood can sometimes be difficult. If we are unable to obtain the blood sample first time, we may ask your permission for a second attempt.

3. **Saliva and nasal fluid sampling (selected sites only, and optional)**

Collecting nasal fluid samples involves insertion of a small swab of soft synthetic material about 2cm into your nostril and leaving it in there, pressed up against the inside of your nose for about one minute. This can cause some eye-watering, but should not cause any damage

to the nostrils. Some people might have more sensitive nostril linings and this might rarely cause a small amount of bleeding. To collect a small amount of saliva we use a funnel and collection tube. Participants may find the saliva collection process unsavoury as it is involves drooling and spitting into a collection device. We would ask participants who are giving saliva samples not to eat, drink, smoke, chew gum, brush their teeth or use mouthwash for at least 30 minutes prior to their appointment.

4. Unwanted media attention

The media are very interested in reporting news about COVID-19. They sometimes approach study participants for "their story". We can give you advice about avoiding unwanted media attention if needed.

5. Implications for travel and attending events

If you are planning to travel abroad, please read the Appendix at the bottom of this information sheet. This will help you to decide whether to take part.

What are the advantages of taking part?

All 16- and 17- year-olds are now going to be offered one dose of Pfizer-BioNTech vaccine. By taking part in this study, you will receive a second dose of a COVID-19 vaccine. It is expected that two doses of COVID-19 vaccine will provide better protection for young people against disease than a single dose. It is also possible that by receiving two doses you are less likely to transmit COVID-19 to other people than if you receive only one dose.

The results of this study may be used to guide future decisions about how best to vaccinate young people against COVID-19. By taking part in the study, you will have contributed to this.

What should I do if I believe I may have developed COVID-19 during the study?

The vaccinations you would receive in this study do not guarantee protection from COVID-19. Participants in the study should continue to follow all current government advice on COVID-19.
If you are unwell then contact the NHS 111 service or phone 999.

If you have a positive swab performed in the community or are diagnosed as having COVID-19 disease while in the study then you must contact the study team on 02921 847816.

If you are admitted to hospital during the study (for any reason), then you should inform the medical or nursing staff that you are taking part in this study. We will provide a contact card for you to give to these staff.

It is important that you understand that if you become seriously unwell and need to be admitted to hospital, the standard referral routes within the NHS will be used. Participants will be treated the same way as the general population in this context of the COVID-19 pandemic. We are unable to offer extra medical support outside what is available within the NHS for the general public.

If you have been diagnosed with COVID-19, or if you think you may have COVID-19, you should not come to any scheduled visit until you have fully recovered. Similarly, you should not attend during any period of self-isolation or quarantine. If you are unable to attend for any of these reasons, please telephone us.

What if I am eligible for routine immunisation against COVID-19, or become eligible whilst enrolled in the trial?

Any adolescent who is currently eligible for two doses of COVID-19 vaccine should not take part in this study. (This applies to adolescents at high risk of COVID-19 disease, or those living with someone with a poorly functioning immune system). At present, 16- to 17- year- olds in the UK are eligible to get a single dose of the Pfizer COVID-19 vaccine, and by taking part in this study they will receive this first dose, as well as a second dose of a vaccine (which is expected to improve protection against COVID-19 disease). However, it is important to note that participants in this trial will not know which vaccine schedule they have received until after the D84 visit.

If the recommendation for routine immunisation changes, then we will seek advice from the study trial steering committee. They will consider what vaccines are required routinely and the immune responses observed in this study, before deciding about further immunisations in the study. You may not require additional vaccines.

Will I be compensated for taking part?

Yes, we are able to reimburse you at a rate of £10 for each study visit, to help towards your travel and other expenses. This may be given as vouchers. These may not be given at each visit (for example, we may give you a £20 voucher at every second visit). The exact arrangements for reimbursement may vary between sites.

What if new information becomes available during the study?

Sometimes during the course of a study, relevant new information becomes available. If this happens, we would tell you about it. We would 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 from the study. Your participation in this study may also be stopped at any time by the study doctor or the Sponsor for other reasons.

What will happen if I don't want to carry on with the study?

If, at any time after agreeing to participate, you change your mind about being involved with this study, you are free to withdraw without giving a reason. If you withdraw, we would not usually perform any more research procedures, although occasionally we might need to offer a follow up visit for safety purposes (for example, to check the injection site or a blood

result). You would not be penalised in any way for your decision. Unless you state otherwise, any samples taken whilst you have been in the study will continue to be stored and used for the research detailed above. You are free to request that the samples are destroyed at any time during or after the study. If you choose to withdraw from the trial, your standard medical care will not be affected.

What if something goes wrong?

The investigators recognise the important contribution that volunteers make to medical research and make every effort to ensure your safety and well-being. The University of Oxford, as the research Sponsor, has arrangements in place in the unlikely event that you suffer any harm as a direct consequence of participation in this trial.

In the event of harm being suffered, while the Sponsor will cooperate with any claim, you may wish to seek independent legal advice to ensure that you are properly represented in pursuing any complaint. The study doctor can advise you of further action and refer you to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment which may be provided if you need to be admitted to hospital.

What if I wish to complain?

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 research investigators who will do their best to address your concerns. You can contact us by e-mail at COMCOV3.HCRW@wales.nhs.uk. Alternatively, you may contact the University of Oxford Research Governance, Ethics and Assurance team (RGEA) office on 01865 616480, or the head of RGEA at ctrg@admin.ox.ac.uk.

Would my taking part in this trial be kept confidential?

All information collected about you during the course of the research will be coded with a study number and kept confidential. The information is available to the study team, authorised collaborators, ethical review committees, Cardiff and Vale University Health Board, government regulatory agencies and the Sponsor (University of Oxford), who can ask to access the trial data. Responsible independent monitors may be given access to data for monitoring and/or audit of the trial to ensure we are complying with regulations. They are bound by the same confidentiality rules.

Every effort will be taken to maintain confidentiality. Information about you may be stored electronically on a secure server, and paper notes will be kept in a key-locked filing cabinet at Children and Young Adults' Research Unit. Study results may be published in scientific journals, but nothing that could identify you will be included in any report or publication.

What will happen to my data?

UK Data protection regulation requires that we state the legal basis for processing information about you. In the case of research, this is 'a task in the public interest.' The University of Oxford is the sponsor for this study, based in the United Kingdom. The University

is the data controller and is responsible for looking after your information and using it properly.

We will be using information from your medical records in order to undertake this study and will use the minimum personally-identifiable information possible. We will keep identifiable information about you such as contact details for a minimum of 5 years and until the youngest participant turns 21 years as per the university requirements for studies that involve paediatric participants. The need to store this information for longer in relation to licensing of vaccines will be subject to ongoing review. De-identified research data will be stored indefinitely. If you have agreed that samples can be retained for future research, then your personally identifiable information will be kept with restricted access solely for the purposes of sample management for a minimum of five years after the last sample has been either used or disposed of in order to meet regulatory requirements. We will also store your consent form. Samples will be provided for future research only in a form that does not identify you. We store research data securely at the University of Oxford indefinitely following removal of identifiable information. If you agree to your contact details being held so you can be contacted regarding future research, we will retain a copy of the consent form until such time as your details are removed from our database; we will keep the consent form and your contact details separately.

The study team will use your name and contact details to contact you about the research study; to make sure that relevant information about the study is recorded; for your health care health during the study; and to oversee the quality of the study. At the completion of the study, unless you consent otherwise (e.g. if you request to be informed of other studies), your personal details will not be used to contact you other than in exceptional circumstances. If you consent to take part in another study carried out by the Cardiff and Vale University Health Board, personal information and medical information, including blood test results, may be accessed to avoid unnecessary repetition.

Data protection regulation provides you with control over your personal data and how it is used. When you agree to your information being used in research, however, some of those rights may be limited in order for the research to be reliable and accurate. Further information about your rights with respect to your personal data is available at: https://compliance.web.ox.ac.uk/individual-rights

Involvement of your General Practitioner (GP)

In order to enrol into this study, you will need to tick a box on an online form to say that you consent for us to contact your GP. Your GP may be asked to share information about your medical history and give access to any other medical records as required. We will write to your GP to let them know when you enrol and when you complete the study, so they can update your medical records accordingly.

What will happen to any samples I give?

If you consent, any of your leftover samples can be stored and used for future research on vaccines or infectious diseases. This is optional; your participation in this study will not be

affected by whether or not you decide to allow storage and future use of leftover samples. You may request at any time for your remaining samples to be destroyed.

Analysis of your samples, measuring the immune response of your body, will be done both at the University of Oxford and at other collaborating laboratories in the UK and overseas. Any samples or data sent to them would not include information that identifies you.

Will any genetic tests be done?

We may do genetic tests on your blood samples, for example to look at the patterns of genes that regulate your own individual immune response (these are called Human Leukocyte Antigen genes). This helps us to work out which aspects of the immune response to vaccines are due to genetic differences between individuals. We may also look at the expression of certain genes which relate specifically to the immune response to COVID-19. Any samples and information recorded will be marked only with a study number, so that we cannot directly identify you. However, your DNA is unique, and so will never be completely anonymous.

What will happen to the results of the research study?

The results of this research study will be presented to UK policy makers, and at scientific meetings or conferences and published in scientific medical journals. This may not happen until 1 or 2 years after the study is completed. A copy of the results will be made available to you after the study. You will not be identified in any report or publication.

The de-identified data from this study will be shared with the collaborating partners who are organising and funding this research work. Data from this study may be used to file patents, licence vaccines or make profits in other ways. You will not be paid for any part of this. Data from this study may be used as part of a student post-graduate degree, for example an MD or PhD.

Taking part in future vaccine-related research

With your consent, we would like to keep your contact details after your participation in this study is complete, so we may inform you of opportunities to participate in future vaccine related research. This is entirely optional and your participation in this study will not be affected by your decision to allow or not allow storage of your contact details at the end of this study. Being contacted does not oblige you to agree to take part in future research. Your details will be stored electronically on a secure server to which only authorised individuals at the Cardiff and Vale University Health Board will have access. You can ask us to remove your contact details from our database at any time.

We will not, under any circumstances, share your contact details with any third-party institutions without your permission.

Who has approved the study?

This study has been approved by the NHS Research Ethics Service (RES) – Berkshire Research Ethics Committee. 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 for use of an unlicensed vaccine in this clinical study.

Further information and contact details

We hope this information sheet has answered all of your questions. If you would like further information about participating in research, please visit the following website: http://www.nhs.uk/conditions/Clinical-trials/Pages/Introduction.aspx.

For independent advice about participating in this trial, you may wish to contact your GP.

If you would like to speak to one of our team members to discuss any aspect of this study, or **if you are interested in taking part, please contact us**:

COMCOV3.HCRW@wales.nhs.uk or 02921 847816

APPENDIX

HOW TAKING PART IN THE STUDY MAY AFFECT YOUR TRAVEL ARRANGEMENTS

At the vaccination visits you will be given a COVID-19 vaccination card or letter, which is the same as that used in the national vaccination program. However, unlike in the national program, for your second dose of vaccine this card or letter will not give the name and batch number of the vaccine you have received; it will simply say "COVID-19 vaccine". These cards or letters are not at present considered to be "vaccination passports" (this is true whether you receive them through the national immunisation programme or through a study).

In England and Wales, it has been agreed that adult participants in COVID-19 vaccine clinical studies will be eligible for an NHS COVID Pass (a 'green tick' on the NHS App). This is the case even if they have received a vaccine (or vaccine dose) that is not yet approved for use outside clinical studies, or if they do not know which vaccine they have received. However, this is not the case for under 16-year-olds, who may not be able to attend events in England and Wales where an NHS COVID Pass (green tick) is required.

For foreign travel, many countries require evidence of approved COVID-19 vaccination before allowing travellers into their country. Vaccination status can also make a difference to the requirements to quarantine in a foreign country on arrival. The vaccinations considered acceptable for these purposes vary between countries, as does the lower age limit applied. For example, some countries require adolescents to have received a COVID-19 vaccine, whereas others do not. People under the age of 18 travelling to France from the UK automatically have the same vaccination status as their accompanying adult. Current requirements may change in future.

At present, most foreign countries will not grant permission for entry based on participation in a clinical study if the participant has received a vaccine (or vaccine dose) that is not yet approved for use outside clinical trials, or if the participant does not know what vaccine they have received. As some participants in this study will be receiving half standard doses of vaccines, or a vaccine that is yet to be licensed (Novavax), it is possible that they may, in

future, have restrictions on travel to countries that require proof of immunisation for adolescents. At present participants would not be disadvantaged compared to others of their age.

At present, vaccination status does not affect whether people under 18 years old need to quarantine on return to England or Wales from abroad (although it may affect quarantine requirements for adults).

International travel requirements could change at very short notice, and this is outside of the control of the research team.