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

1. An update on the Com-COV3 study

Thank you very much for your participation in the Com-COV3 study.

We are writing to inform you of recent developments.

(a) A new part to the study

We plan to add a new part (or "cohort") to the study. The existing part of the study, in which you are participating, will be referred to as Cohort A. The new part will be referred to as Cohort B.

The aim of this new part of the study will be to explore the options for a third dose of COVID-19 vaccine in young people. We aim to recruit 380 participants aged 12 to 15½ years, who have already received two standard doses of Pfizer vaccine in the community. They will be randomised to 5 groups, each of which will be given a different vaccine schedule. The options for the third dose of COVID-19 vaccine we will investigate are:

- A full dose of adult Pfizer vaccine
- A one-third dose of adult Pfizer vaccine
- A full dose of children's Pfizer Vaccine
- A full dose of Novavax vaccine

The fifth group in the study will be given their third dose of COVID-19 vaccine later in the study than the other groups. This "control group" will improve our understanding of the immune responses in the other groups.

We hope to start enrolling participants to Cohort B in May or June 2022.

Please note that participants who are currently in Cohort A will not be able to enrol in Cohort B.

(b) Recruitment to the first part of the study (Cohort A)

Following the advice of the Trial Steering Committee, it has been decided not to recruit any further participants to the original part of study. Those who have already enrolled may continue with their remaining visits, as planned.

This decision was influenced by the announcement of the Joint Committee on Vaccination and immunisation (JCVI) on 29th November 2021 that all 12 to 15 year-olds would be offered a second dose of Pfizer vaccine.

(c) Results of the first part of the study (Cohort A)

We are analysing information from blood tests and study diaries from participants in the first part of the study, and the results are being prepared for publication.

Summary for Cohort A

- **Young people aged 12 – 16 years are invited to receive a COVID-19 vaccine**
- **We would give the first and second dose, or the second dose only**
- **5 or 6 visits over the next 10 months**
- **5 or 6 blood tests in total, taking place in Children and Young Adults' Research Unit, Cardiff**
- **Complete an online diary for 4 weeks after vaccination**

The information in the Appendix, about travel, has been updated. The remainder of this information sheet is unchanged since the previous version.

2. 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.

3. 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 has provided vaccines for the study. Neither your GP nor the researchers are paid for recruiting you into this study.

4. What is the purpose of this research study?

The purpose of this study is to investigate different options for immunising 12 to 16-year olds against COVID-19 in the UK. Following an initial dose of the Pfizer COVID-19 vaccine (whether

received in the study or through the NHS) participants are randomly allocated to different options for their second dose, to be given at least 8 weeks later.

Prior to the 29th November participants were receiving one of three different options for the second dose, including a COVID vaccine produced by Novavax. However following the JCVI recommendation on 29th November 2021 that all 12 to 15 year olds should be offered a second dose of the Pfizer vaccine, the study design has been amended to focus on two different options for the Pfizer vaccine. This does not reflect any concern regarding the safety or immunogenicity of the Novavax vaccine in this or other studies.

Accordingly, the study will now investigate how well 12-16 year olds respond to two standard doses of the Pfizer COVID-19 vaccine, compared to a standard dose followed by a lower (one-third) dose. Participants will have an equal chance of receiving either full or one-third Pfizer vaccine for their second vaccination.

We are looking at whether giving a different or lower dose of vaccine (one third of the standard adult dose) for the second vaccination produces an immune response similar to that seen after two doses of the Pfizer vaccine, and whether the lower dose results in fewer vaccine side effects.

If lower doses of vaccine can be used, this should help to minimise the adverse effects of vaccination, and more people could be vaccinated with the available vaccine.

We will also investigate how previous infection with COVID-19 affects the immune response to vaccination.

The results of this study will be presented to the JCVI and may be used to guide national vaccination policy.

5. Background information

Since early 2020, COVID-19 has spread around the world. It has killed over 140,000 people in the UK and over 5 million people worldwide (by 10th November 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 10th November 2021, 87.5% of the population aged 12 years or over in the UK had received at least one dose of vaccine.

The vaccination programme in the UK initially mainly 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.

On 15th November 2021, the JCVI recommended that healthy young people aged 16 to 17 years should be offered a second dose of Pfizer-BioNTech vaccine, to be given 12 weeks or more after the first. On 29th November 2021, this was revised to also include 12 to 15 year olds. This is in addition to existing recommendations that those with specific underlying health problems (such as Down's syndrome, cerebral palsy or some conditions causing susceptibility to infections), who are at particular risk of serious COVID-19, are advised to have two doses of Pfizer-BioNTech vaccine, given 8 to 12 weeks apart, as are those living with a person with impaired immunity. Those with a weakened immune system may be offered a third dose.

There is very close surveillance of all vaccines to identify any rare, serious unwanted effects. The Pfizer-BioNTech vaccine has now been given to many millions of people across the world. It is 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). These have been observed more often after the second dose, especially in young men (12 to 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. In the USA, the two doses are usually given 3 weeks apart. There is now some evidence that in countries with a longer interval between the two doses there is a lower incidence of myocarditis after the second dose.

It is important to understand that our study will not be large enough to compare the risk of myocarditis in those receiving two full doses of Pfizer-BioNTech vaccine with the risk in those receiving alternative schedules, since myocarditis is such a rare event. However, the study will 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 values of these tests in adolescents, and whether the levels are affected by immunisation.

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 know from previous studies that using different COVID-19 vaccines for the first and second dose can produce very good immune responses in adults. We would like to find out if this is also the case in adolescents.

A recent study found that two doses of Pfizer-BioNTech vaccine, given to children aged between 5 and 11 years at one-third of the standard adult dose, stimulated as good an immune response as two full doses in people aged 16 to 25 years. The one-third dose has

recently been approved for use in children aged 5 to 11 years in the USA. We are interested in studying the effects of a one-third dose of this vaccine in adolescents.

We are therefore exploring different vaccine strategies in our study. We are aiming to find out whether a different or lower dose for the second vaccine will produce a similar immune response to two standard doses of Pfizer-BioNTech in adolescents. The study will provide valuable information on different vaccine dose combinations in adolescents, helping to identify the combinations that produce fewest common side effects and the best quality immune responses.

6. What happens in the study?

This study will enrol up to 270 young people aged 12 to 16 years from various sites in the UK.

Participants will receive a second dose of COVID-19 vaccine eight weeks after the first vaccine (a standard dose of Pfizer-BioNTech vaccine given in the community or in the study).

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

1. A full standard dose of Pfizer-BioNTec vaccine
2. A third of a standard dose of Pfizer-BioNTec vaccine

For each participant, this is decided by chance using the process of randomisation (which is similar to throwing dice: no-one can choose the result). The chance of being allocated to each of these is the same (one half).

For participants who have already received the second dose of vaccine before 29th November 2021, the second dose of vaccine will have been one of the following:

1. A full standard dose of Pfizer-BioNTec vaccine
2. A third of a standard dose of Pfizer-BioNTec vaccine
3. A standard dose of Novavax vaccine

For each participant, this is decided by chance using the process of randomisation (which is similar to throwing dice: no-one can choose the result). The chance of being allocated to each of these is the same (one third).

Participants will be required to make five or six visits to the study site. At each visit a blood sample will be taken. Participants will be asked to record symptoms for 28 days after each study vaccination (a paper version of the diary is available, if required). At some sites, participants will also be asked to provide saliva samples and have a sample of nasal fluid taken at some visits; this is completely optional. Visits will take place at the Children and Young Adults' Research Unit, Cardiff.

7. What vaccine are we testing?

This study uses two different vaccines: Pfizer-BioNTech and the Novavax vaccine.

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 Section 4).

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.

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 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).

8. 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.

9. 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 'high risk group' (at increased risk of severe COVID-19 infection) 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. However, your vaccination must be delayed by a minimum of 4 weeks from the date of any positive COVID-19 test.

10. 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 42 weeks. 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	First vaccination	Boost vaccine	D14 post boost vaccine	D28 post boost vaccine	D132 post boost vaccine	D236 post boost vaccine
Week	0	8	10	12	27	42
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 four 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 (boost vaccine visit)**, 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).

For participants who received their second vaccine before 29th November, you were "randomised" to decide which vaccine you received for the second dose (Pfizer BioNTech or Novavax). For participants receiving their second vaccine after 29th November, you will be "randomised" to decide which dose of the Pfizer vaccine you will receive for the second dose (whether you will receive a full or a third of a 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 (D14, D28, D132 and D236 post boost vaccine visit) 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, 27 and 42 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 34 weeks. 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	Screening	Boost vaccine	D14 post boost vaccine	D28 post boost vaccine	D132 post boost vaccine	D236 post boost vaccine
Eligibility	✓					
Consent	✓					
Blood test		✓	✓	✓	✓	✓
Saliva sample/nasal fluid sample (at some sites only, and optional)		✓	✓			
Vaccine		✓				
Diary		✓				

The screening and boost vaccine 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 boost vaccine 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 boost vaccine visit and D14 and D28 post boost vaccine 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.

For participants who received their second vaccine before 29th November, you were "randomised" to decide which vaccine you received for the second dose (Pfizer BioNTech or Novavax). For participants receiving their second vaccine after 29th November, you will be "randomised" to decide which dose of the Pfizer vaccine you will receive for the second dose (whether you will receive a full or a third of a 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 (D14, D28, D132 and D236 post boost vaccine) 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 D14 post boost vaccine visit, if this was taken previously). They will be scheduled at about 2, 4, 19 and 34 weeks after your boost vaccine visit. These visits will last about half an hour.

11. 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.)

12. Are there any risks from taking part in the study?

a. 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 a vaccine are given above in Section 7.

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.

b. 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.

c. Potential for reduced protection against infection after vaccination

All 12 to 15 year olds in the UK are now recommended to have two standard doses of Pfizer-BioNTech vaccine. By taking part in this study, you may receive a dose of the vaccine at one-third of the standard dose as your second vaccine. It is possible that this will mean you are more susceptible to COVID-19 infection than if you received the recommended dose. However, it is known that two vaccinations with the one-third dose produce good immune responses in younger children (aged 5 to 11 years). If it were to be found that the immune response to this reduced dose schedule was substantially lower than the standard schedule, we would seek the advice of the study Data and Safety Monitoring Board and the Trial Steering Committee (who oversee this study) for their opinion on whether an offer of an additional dose would be appropriate.

d. 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.

e. 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.

13. What are the advantages of taking part?

16 year olds in the UK are now eligible to get two doses of Pfizer COVID-19 vaccine. However, you can still take part in this study. 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.

14. 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 02921847816.

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.

In this study, we will wait 4 weeks from the date of COVID-19 diagnosis before giving a study vaccine. The UKHSA recently recommended an interval between COVID-19 infection and vaccination of 12 weeks in healthy children aged 12 to 17. This recommendation was based on emerging evidence which may suggest that leaving a longer interval between infection and vaccination might reduce the very small risk of myocarditis; also, young people are likely to have high levels of protection for at least 3 months after COVID-19 infection. The advice adopts a highly precautionary approach. Children at "high risk" and all adults are advised to wait 4 weeks between infection and vaccination. If the study waited 12 weeks between infection and vaccination, some children would be excluded from participating, and the usefulness of the results of the study may be adversely affected.

15. Can I take part in the study given that I am eligible for routine immunisation against COVID-19?

16 year-olds, who are now eligible for <u>two doses</u> of COVID-19 vaccine may still take part in this study, unless they are at high risk of COVID-19 disease, or living with someone with a poorly functioning immune system. 16- to 17- year- olds in the UK are eligible to get two doses of the Pfizer COVID-19 vaccine. 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, the second vaccine received as part of the study may not be a standard dose of Pfizer. It is also important to note that participants in this study will not know which vaccine schedule they have received until after the D84 visit. This may have implications for you if you wish to travel abroad. Please read the Appendix at the bottom of this information sheet for further information

The Data Safety and Monitoring Committee and Trial Steering Committee will review the results of this study and advise of the need for further doses if any study group generates an immune response substantially below that of routine immunisation.

16. 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.

17. 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 will 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.

18. 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.

19. 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.

20. 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.

21. 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 the 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.

22. 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

23. 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.

24. 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.

25. 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.

26. 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.

27. 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.

28. 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.

29. 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

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. Current requirements may change in future.

Covid vaccinations given during the study will be recorded on a participant's NHS records once the participant is informed of the vaccination they have received, not at the time of vaccination. For participants 12 years old and over, the vaccination will appear on their NHS Covid Travel pass (often called the "vaccination passport") within a few days of being recorded on their NHS records. Prior to being informed of the vaccination they have received; a participant will not usually be able to use their trial vaccination as a qualifying vaccination for travel purposes.

International travel requirements, as specified by the UK and independently by foreign countries, can change at very short notice, and this is outside of the control of the research team.