Participant Information Sheet (Parent/Guardian): 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 child's 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 your child is 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 adolescents. 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 paediatric 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 your local study site**
- **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 YOUR CHILD IS 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. Why has my child been asked to take part?

We are asking your child to take part because they are the right age and live in an area where we are doing the study.

4. 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 your child into this study.

5. 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 as these are more likely to be policy relevant. 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 standard 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.

6. 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 vaccination.

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.

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 lower dose of the Pfizer 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.

7. What happens in the study?

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

The study had been designed to enrol up to 270 participants aged 12 to 16 years to 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 options for the second dose were full or one third Pfizer or a standard dose of Novavax. However, in line with the change in national vaccination guidance, we have amended the study design to focus on the immune response to the Pfizer BioNTech vaccine and have removed the option of Novavax as a second dose from the study.

The following information applies to children who have not yet had the second dose of COVID-19 vaccine:

They will be given a second dose of COVID-19 vaccine eight weeks after the first. 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).

The following information applies if your child has already had the second dose of COVID-19 vaccine:

The second dose of COVID-19 vaccine is given eight weeks after the first. 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
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 local study site.

8. What vaccine are we testing?

This study is testing the Pfizer-BioNTech vaccine 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 5).

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).

9. Does my child have to take part?

No. It is up to you and your child to decide whether or not to take part. They will not be penalised in any way if they decide not to participate. Their decision will not affect their standard medical care. If they do decide to take part, they will be given an information sheet to keep (or be sent it electronically). If your child is 16 years old or above, they will be asked to sign a consent form. If they are younger, a parent or guardian must sign the consent form, but your child must show that they assent to taking part. Your child is free to withdraw from the study at any time, without giving a reason (although we may request a follow up appointment for safety reasons).

10. Can my child take part?

To take part in this study your child must:

- Be aged between 12 and 16 years (i.e. up until their 17th birthday).
- Be able and willing (in the investigator's opinion) to comply with all study requirements.
- Allow the investigators to discuss their medical history with their GP and access all medical records.
- Provide written informed consent. Those 16 years or older, can provide consent for themselves. However, parents/guardians should also be involved in the decision to

take part. Children under 16 years old must have the written consent of their parent or guardian.

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

- They have received any vaccine (licensed or investigational) less than 7 days before enrolment (or intend to receive any vaccine less than 7 days after receiving the study COVID-19 vaccines).
- They have previously received two doses of COVID-19 vaccine, or one dose of a COVID-19 vaccine other than Pfizer BioNTech.
- They are a close family member of someone working at the study sites.
- They belong to 'a high risk group' (at increased risk of severe COVID-19 infection) already advised by the JCVI to receive two doses of Pfizer-BioNTech vaccine, e.g. if they have specific underlying health problems (such as Down's syndrome, severe neurodisability or immunosuppression), or if they live with an immunosuppressed person. (The full details can be found in the "Green Book").
- They have received immunoglobulins or blood products within 3 months of enrolment.
- They have any confirmed or suspected immunodeficiency (significant problems with their immune system).
- Their spleen has been removed or is not functional.
- They have recurrent severe infections.
- They have used immunosuppressant medication within the past 6 months (except topical steroids or short-term oral steroids for less than 14 days).
- They have a history of anaphylaxis, allergic disease or reactions likely to be worsened by any component of study vaccines, or if they are allergic to latex or polyethylene glycol/macrogol (PEG).
- They are pregnant or breast feeding, or intending to become pregnant within three months of the second dose of vaccine.
- They have had a malignant disease requiring chemotherapy or radiotherapy for malignancy within the past 6 months.
- They have a bleeding disorder, or prior history of significant bleeding or bruising following IM injections or blood tests.
- They are prescribed anticoagulants (such as warfarin, apixaban, rivaroxaban, dabigatran and edoxaban).
- They have any serious chronic illness requiring hospital specialist supervision.
- They have congenital heart disease.
- They have severe and/or uncontrolled respiratory disease, gastrointestinal disease, liver disease, renal disease, rheumatological disease, endocrine disorder or neurological illness. (If they have mild to moderate, well controlled conditions, they may participate in the study.)
- They have a history of active or previous auto-immune neurological disorders (e.g. multiple sclerosis, Guillain-Barre syndrome, transverse myelitis).
- They have significant kidney or liver impairment.
- They have elective surgery requiring overnight admission and/or general anaesthetic planned for during the study.

- They have participated in another research study involving an investigational product in the past 12 weeks.
- Their 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 them from participating. If you are unclear whether they are eligible to be involved in the study, you can contact the study team who will be able to advise you.

If your child has previously had confirmed or suspected COVID-19 infection, they may still take part in the study. However, their vaccination must be delayed by a minimum of 4 weeks from the date of their positive COVID-19 test.

11. What will happen if your child decides to take part?

If your child decides to take part in the study, you should complete the short online questionnaire to check that they 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 their current health and discuss details of their medical history, if required. You will also be asked to agree to allow us to contact their GP for further information, if necessary. If they are eligible, they will be invited to a face-to-face visit.

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

IF YOUR CHILD HAS NOT ALREADY RECEIVED A COVID-19 VACCINE IN THE COMMUNITY:
They 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	**First vaccination**	**Booster vaccination**	**D14 post boost**	**D28 post boost**	**D132 post boost**	**D236 post boost**
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 your child is eligible to take part. Their temperature will be recorded. If it is above 37.8°C, or if they have symptoms of a respiratory tract infection,

the visit will be rescheduled. Their heart rate, and height and weight will be checked. A doctor may need to do a physical examination. 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). 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 and your child may be shown a video describing the study. You and your child will have the opportunity to ask any questions you want before being asked to sign the consent form for the study. Participants aged 16 years sign the consent form for themselves. For those under 16 years, a parent or guardian must sign the consent form.

Your child will have a blood test. If they want the skin numbed with local anaesthetic cream, this can be provided. Their 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 your child had them at the first visit. Your child can say no to these tests and still take part in this study.

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

Your child will be given a link to an e-diary to record any symptoms they experience after the vaccination. A back up paper version can be provided instead if you are unable to access the internet; to allow the study team to view the entries on a regular basis we would prefer you to complete the diary online. They will also be given a thermometer and tape measure. They 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 vaccination. Similarly, they will be asked to record general symptoms (fever, chills, joint pains, muscle pains, fatigue, headache, malaise, nausea, vomiting, diarrhoea) each day for seven days. They will also be asked to record any other symptoms they experience in the 28 days after vaccination. They may need help from an adult to complete the diary.

The 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, we will take a second blood test (and saliva/nasal fluid sample if this was taken at the first visit). For girls, we will check a urine pregnancy test.

For those who were randomised before 29th November, your child was “randomised” to decide which vaccine they received for the second dose (Pfizer BioNTech or Novavax). For those receiving their second vaccine after 29th November, your child will be “randomised” to decide which dose of the Pfizer vaccine they will receive for the second dose (whether they will receive a full or a third of a standard dose). You and your child will not be told which it will be until later in the study.

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

We will look at what they have recorded in their symptom diary and ask them to record their symptoms after the second vaccination. We will ask for the same information as the after the first vaccination. This visit will take up to an hour.

At the third, fourth, fifth and sixth visits (D14, D28, D132 and D236 post boost vaccine), your child will only have a brief health check and a blood test (and a saliva/nasal fluid sample at the third visit, if this was taken at previous visits). These will be scheduled at about 10, 12, 27 and 42 weeks after your first visit and will take about 30 minutes.

IF YOUR CHILD HAS ALREADY RECEIVED A COVID-19 VACCINE IN THE COMMUNITY:

Your child 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	Screening	Booster vaccination	D14 post boost	D28 post boost	D132 post boost	D236 post boost
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 your child is eligible to take part. You and your child may be shown a video, describing the study. You will both 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 child's first vaccination, they will have a brief health check. Your child's temperature will be recorded. If it is above 37.8°C, or if your child has symptoms of a respiratory tract infection, the visit will be rescheduled. Your child's heart rate b and height and weight will be checked. 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.

Your child will have a blood test. If they want their skin numbed with local anaesthetic cream, this can be provided. Your child's 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 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 the D14 post boost vaccine visit if your child had them at the boost vaccine visit. Your child can say no to these tests and still take part in this study.

For those receiving their second vaccine before 29th November, your child was "randomised" to decide which vaccine they received for the second dose (Pfizer BioNTech or Novavax). For those receiving their second vaccine after 29th November, your child will then be "randomised" to decide which dose of the Pfizer vaccine they will receive for the second dose (whether they will receive a full or half or a third of a standard dose). You and your child will not be told which it will be.

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

You will be given a link to an e-diary to record any symptoms your child experiences after the vaccination. A back up paper version can be given instead, if you are unable to access the internet; to allow the study team to view the entries on a regular basis we would prefer you to complete the diary online. Your child will also be given a thermometer and tape measure. Your child 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, your child will be asked to record general symptoms (fever, chills, joint pains, muscle pains, fatigue, headache, malaise, nausea, vomiting, diarrhoea) each day for seven days. Your child will also be asked to record any other symptoms they 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 your child to have a brief health check, and blood test (and a further saliva/nasal fluid sample will be taken at the D14 post boost visit, if this was taken previously). These will be scheduled at about 2, 4, 19 and 34 weeks after your boost vaccine visit. These visits will last about half an hour.

12. What should my child avoid during the study?

Your child should not take part in other studies that involve the administration of drugs or vaccines, or studies testing other interventions for COVID-19. If your child needs 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).

Your child should not give blood whilst 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.)

13. 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 vaccine are given above, in Section 8

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 the reason we ask your child to stay for at least 15 minutes after your vaccination. The study staff are trained and equipped to recognise and treat anaphylaxis.

b. 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, your child may receive a dose of the Pfizer-BioNTech vaccine at one-third of the standard dose. It is possible that this will mean your child is more susceptible to COVID-19 infection than if they received the recommended dose, particularly before they have their second vaccination in the study. 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 these reduced dose schedules were to be substantially lower than standard schedules 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.

c. Blood tests

Having blood taken may cause some pain, although we will use anaesthetic cream to numb the skin if requested. Your child may feel light-headed or even faint. Your child 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 child permission for a second attempt.

d. 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 the nostril and leaving it in there, pressed up against the inside of your child's 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.

e. 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.

f. Implications for travel and attending events

If your child is planning to travel abroad, please read with them the Appendix at the bottom of this information sheet. This will help them to decide whether to take part.

14. What are the advantages of taking part?

All 12-to-15- year-olds in the UK are now going to be offered two doses of Pfizer-BioNTech vaccine. However, by taking part in this study, your child may receive a lower dose of the Pfizer COVID-19 vaccine as the second vaccine. It is possible that the one-third dose will have fewer unwanted effects than the full dose. It is expected that two doses of COVID-19 vaccine will provide better protection for young people against disease than a single 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, your child will have contributed to this.

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

The vaccinations your child 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 your child is unwell then contact the NHS 111 service or phone 999.

If your child has a positive swab performed in the community or is diagnosed as having COVID-19 disease while in the study, then you must contact the study team on the contact details provided to you.

If your child is admitted to hospital during the study (for any reason), then you should inform the medical or nursing staff that they 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 your child becomes seriously unwell and needs 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 your child is diagnosed with COVID-19, they should not come to any scheduled visit until they have fully recovered. Similarly, they should not attend during any period of self-isolation or quarantine. If your child is unable to attend for any of these reasons, please telephone us. No-one who has current symptoms of COVID-19 or a recent positive test should accompany your child to study visits.

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 still advised to wait only 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.

16. Can my child take part in this study, given that they are eligible for routine immunisation against COVID-19?

12 to 16 year-olds, who are now eligible for two doses of COVID-19 vaccine, may still take part in this study, unless they are at high risk of COVID-19 disease, or live with someone with a poorly functioning immune system. 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.

The second vaccine received as part of the study however, may not be a standard dose of Pfizer. This may have implications for participants if they wish to travel abroad. Please read the Appendix at the bottom of this information sheet for further information.
The Data Safety 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.

17. **Will we be compensated for taking part?**

Yes, we are able to reimburse you at a rate of £10 for each study visit, to help towards travel and other expenses. This may be given to your child as vouchers. Reimbursement 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.

18. **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 and your child about it. We would discuss whether your child wants to, or should, continue in the study. If your child decides 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 child's best interests to withdraw from the study. Your child's participation in this study may also be stopped at any time by the study doctor or the Sponsor for other reasons.

19. What will happen if your child does not want to carry on with the study?

If, at any time after agreeing to participate, your child changes their mind about being involved with this study, they are free to withdraw without giving a reason. If your child withdraws, 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). Your child would not be penalised in any way for their decision. Unless you request otherwise, any samples taken whilst your child has been in the study will continue to be stored and used for the research detailed above. You or your child can request that the samples are destroyed at any time during or after the study. If your child chooses to withdraw from the trial, your child's standard medical care will not be affected.

20. 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 your child suffers 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 your child is properly represented in pursuing any complaint. The study doctor can advise you of further action and refer your child to a doctor within the NHS for treatment, if necessary. NHS indemnity operates in respect of the clinical treatment which may be provided if your child needs to be admitted to hospital.

21. What if I wish to complain?

If you wish to complain about any aspect of the way in which you or your child 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 your local study site. Alternatively, you may contact the University of Oxford Research Governance, Ethics & Assurance team(RGEA) office on 01865 616480, or the head of RGEA at ctrg@admin.ox.ac.uk.

22. **Would my child's 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, 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 your child may be stored electronically on a secure server, and paper notes will be kept in a key-locked filing cabinet at the local study site. Study results may be published in scientific journals, but nothing that could identify your child will be included in any report or publication.

23. **What will happen to my child's data?**

UK Data protection regulation requires that we state the legal basis for processing personal information. 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 child's information and using it properly.

We will be using information from your child's medical records in order to undertake this study and will use the minimum personally-identifiable information possible. We will keep identifiable information about your child, 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 child's 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 your child. 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 local study site, 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

24. Involvement of your child's 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 child's GP. The GP may be asked to share information about your child's medical history and give access to any other medical records as required. We will write to your GP to let them know when your child enrols and when they complete the study, so their medical records can be updated accordingly.

25. What will happen to any samples my child gives?

If you consent, any of your child's leftover samples can be stored and used for future research on vaccines or infectious diseases. This is optional; your child's 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 child's 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 your child.

26. Will any genetic tests be done?

We may do genetic tests on your child's blood samples, for example to look at the patterns of genes that regulate your child's 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 ID so that we cannot directly identify your child. However, your child's DNA is unique, and so will never be completely anonymous.

27. 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.

28. Taking part in future vaccine-related research

With your consent, we would like to keep your contact details after your child's 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 Oxford Vaccine Group 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.

29. 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.

30. 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**:

APPENDIX

HOW TAKING PART IN THE STUDY MAY AFFECT YOUR CHILD'S 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.