Participant Information Sheet (12-15 years): Com-COV3 Cohort B

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

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

We would like to invite you to take part in our COVID-19 vaccine study. Whether or not you take part is **your** decision. Remember, if you don't want to take part, you should say so (even if your parents want you to be in the study).

If you think you might like to take part, please read this leaflet which explains what the study involves. We will provide another information sheet to your parent/legal guardian, which gives a full description of the study, so that you will be able to discuss it with them. Before making up your mind, ask any questions you want.

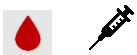
SUMMARY

- **Com-COV3 is a study looking at multiple options for immunising adolescents against COVID-19**
- **In this part of the study (Cohort B) we are looking at the immune response after a third dose COVID-19 vaccine**
- **To do this we are inviting young people aged 12 to 15½ years who have already received two doses of COVID-19 vaccine to take part**
- **For participants, the first study visit will take place 3 months or more after their second dose of COVID-19 vaccine**
- **We will give a third dose of a COVID-19 vaccine**
- **Participants will be allocated to one of five groups**
- **Participants in one of these groups will be given two separate doses of a meningitis B vaccine; they will be given their third dose of COVID-19 vaccine later**
- **There are either 4 or 5 visits over a period of 6 or 7 months at Leeds General Infirmary**
- **A blood sample will be taken at each visit**
- **Participants will complete an online diary for 4 weeks after their vaccination(s)**

Why have I been asked to take part?

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

The study design is summarised below:

	Study Visit				
	Visit1 Day0	**Visit 2 Day28**	**Visit 3 Day84**	**Visit 4 Day182**	**Visit 5 Day210 (Group 5 only)***
Groups 1-4					
Group 5					

*Only participants in Group 5 who receive the Pfizer bivalent COVID-19 vaccine will attend this visit and will have a blood sample taken.

 Blood test

 Vaccine

The group you are in determines which vaccination(s) you are given in the study:

Study Group	Visit 1	Visit 3	Visit 4
1	Full dose of adult Pfizer COVID-19 vaccine (=30 micrograms)		
2	One-third dose of adult Pfizer COVID-19 vaccine (=10 micrograms)		
3	Full dose of paediatric Pfizer COVID-19 vaccine (=10 micrograms)		
4	Full dose of Novavax COVID-19 vaccine		
5	MenB vaccine (Bexsero)	MenB vaccine (Bexsero)	Full dose of Pfizer bivalent COVID-19 vaccine (Original/Omicron BA.1)

			(= 15 micrograms/15 micrograms)

Some background information

1. **What are vaccines?**

Vaccines are medicines which are injected to prevent you from becoming unwell from certain diseases. They also help to stop you spreading disease to your friends and family. They protect you and those around you.

2. **What is COVID-19?**

COVID-19 is a new disease, which since early 2020 has spread around the world. It has caused many deaths and has made many more people seriously ill.

COVID-19 vaccines that have been shown to work are now being used. They are helping to prevent people from becoming seriously ill or dying from the disease. In this country, most adults have now been vaccinated against COVID-19. Older people are much more likely to be seriously ill from COVID-19 than young people. However, children and teenagers do occasionally become very unwell if they catch the disease.

At present, all 12 to 15 year-olds in this country are offered two doses of a COVID-19 vaccine. Vaccination of children and teenagers against COVID-19 is also occurring in many other countries around the world.

What is the purpose of this study?

The Com-COV3 study is divided into two different parts (or 'cohorts'). The first part (Cohort A) is investigating how well young people respond to a second dose of COVID-19 vaccine (when given in different combinations, or using a lower than standard dose for the second vaccination). This part of the study has completed recruitment.

The second part, Cohort B, is looking at different options for a third dose of COVID-19 vaccine in young people. You are being invited to take part in Cohort B, and this part of the study is described in more detail below.

After vaccination, immunity may gradually decline. Giving a further dose of vaccine helps to boost immunity. A third (or "booster") dose of COVID-19 vaccine is now recommended in the UK for people aged 16 years or above.

We want to study the immune responses in young people after using different vaccines for the third dose.

One option is to give a third dose using the same vaccine as for the first two vaccinations (Pfizer vaccine).

Another possibility is to give the same vaccine but at a smaller dose. This might reduce the risk of unwanted effects from the vaccine, and would also enable the available supply of vaccine to be used for more people. It is known that using a smaller dose (one-third standard dose) produces a good immune response in children (aged 5 to 11 years). It is also known that younger people tend to produce a better immune response to COVID-19 vaccines than older people. We hope a smaller dose could work well in young people.

The smaller dose of Pfizer vaccine could be given in one of two ways. It could be given as a one-third dose of the adult vaccine. Alternatively, it could be given as a full dose of a paediatric (children's) version of the vaccine. We want to know if these two methods produce the same immune response. This is important because the adult vaccine is likely to be more widely available around the world and be cheaper to use than the children's version.

Another option is to use a different type of vaccine (Novavax) for the third dose. We know that giving a dose of Novavax after one or two doses of Pfizer produces a good immune response.

Some participants in our study will be allocated to receive two doses of a meningitis (Bexsero) vaccine before their third dose of COVID-19 vaccine. This "control group" is really important to help us properly understand the effects of COVID-19 vaccination in the other groups. This group will receive the Pfizer bivalent COVID-19 vaccine for their third dose. In each dose of this vaccine, half of the vaccine targets the original virus strain, and the other half targets the Omicron (BA.1) variant.

We are also interested in finding out the effect of previous COVID-19 infection on response to COVID-19 vaccination. Young people are welcome to participate in the study whether or not they have previously had COVID-19. The results of this study may be used to guide future vaccination policy.

Who can take part in the study (Cohort B)?

To take part in Cohort B of the study, you must be aged 12 to 15½ years on the day you enrol, and you must already have had your second dose of Pfizer vaccine (at least 3 months before you enrol).

Not everyone can take part. For example, if you have certain health conditions you are not able to participate. This is for safety, and also to make sure that the results we obtain are reliable. Your parent/ legal guardian can fill in a short online questionnaire to see if you would be suitable for this study.

What happens in Com-COV3 Cohort B?

If you take part in our study, we will look at how your body responds to vaccination. One way in which we do this is to ask you to fill in a diary, where you record any symptoms you may have after the vaccine. For example, if you have a sore arm, a temperature or a headache, you will record these symptoms in the diary. Another way to find out how you have responded to the vaccine is to test your blood. Your blood contains antibodies and white blood cells, which help your body to resist infections. We will take a blood test each time you visit us. The blood will be sent to a laboratory for special tests which show how well your body can resist COVID-19 infection.

If you decide to take part, we will ask you to visit us four or five times over a period of about six or seven months. The visits will be arranged to take place outside of school hours. The visits will take place at Leeds General Infirmary.

The first visit will be arranged to be 3 months or more after you received your second COVID-19 vaccination.

What happens at each study visit is summarised in the table below:

Visit	**First**	**Second**	**Third**	**Fourth**	**(Fifth)** Group 5 only*
Week	0	4	12	26	30
Eligibility	✓				
Consent	✓				
Lateral flow test	✓			(✓) Group 5 only **	
Blood test	✓	✓	✓	✓	(✓) Group 5 only
Vaccine	✓		(✓) Group 5 only	(✓) Group 5 only**	
Diary	✓			(✓)	

				Group 5 only**	

* Only participants in Group 5 who receive the Pfizer bivalent vaccine will be required to attend this visit and will have a blood sample taken at this visit.

**Participants in Group 5 who consent to receive the Pfizer bivalent vaccine will have a lateral flow test and receive a vaccine at the fourth visit.

At the **first visit**, we will make sure you are happy to be in the study. We may show you a video about the study. We will answer any questions you want to ask about it. We will ask your parent/legal guardian to sign a consent form and will ask you to sign an assent form.

We will ask you to do a COVID-19 lateral flow test (which involves using a cotton bud to gently scrape the inside of your nose and back of your throat). If this is positive, the rest of this visit (including vaccination) will have to be put off for at least 4 weeks.

We will take a blood test. This can sometimes be uncomfortable, but we can give you some cream or spray to help numb your skin first, if you want. Having a blood test can make some people nervous, but it can help to do something fun as a distraction, such as listening to music or reading.

We will check your temperature, height and weight.

Participants in this part of the study are allocated to one of five groups. Which of the groups you are in is decided at your first visit by a process known as "randomisation". This is a bit like throwing dice. The decision is made by chance. However, there is a greater chance (33%) that you will be allocated to either the one-third dose of the adult Pfizer vaccine group or the one-third dose of the paediatric Pfizer vaccine (i.e., the children's version of the vaccine) group. There is a lower chance (11%) that you will be allocated to one of the other three groups. Neither you nor your parents decide which group you will be in. You will not be told which group you are in until a little before your third visit (and no earlier than 8 weeks after your first visit).

The Pfizer and Novavax vaccines help to protect against COVID-19. The Bexsero vaccine helps to protect against Group B meningococcal disease. There are more details about these vaccines in your parent/guardian's information sheet.

We will check that you are well enough to be vaccinated and then give you a dose of vaccine (into your arm). Like the blood test, this can also be a bit uncomfortable for a short while. After your vaccination, you will need to stay in the clinic for 15 minutes.

We will give you access to an online diary (or a paper diary) to record your symptoms and explain how to use it. We will also give you a thermometer and tape measure. We will want

you to record symptoms such as pain, redness or swelling where you had the injection, and also more general symptoms, such as fever, headache or diarrhoea. Not everyone has symptoms after a vaccination. Even if you have no symptoms, this information should be recorded in your diary.

We will give you a pack of lateral flow tests to take home, with instructions. You will be asked to do a lateral flow test every week between the first and second visits (including a test just before your second visit) and to record the results in your diary. You will also be asked to do a test if you have symptoms of COVID-19 (such as fever, cough, sore throat or loss of taste or smell) at any time while you are in the study, and then to repeat it 3 or 4 days later. These results are also to be recorded in your diary.

The **second visit** will be arranged at about 4 weeks after your first. You will have a blood test and brief health check. We will also check what you have recorded in your diary.

The **third visit** will be arranged at about 12 weeks after your first visit. You will be told which study group you are in ahead of this visit. You will have a blood test and brief health check. We will ask if you have had any medical problems since your last visit.

For participants in Group 5 (control group) only, we will check that you are fit to be vaccinated and then give your second dose of meningitis (Bexsero) vaccine. After your vaccination, you will need to stay in the clinic for 15 minutes. You do not need to fill in a symptom diary after this vaccination.

The **fourth visit** will be arranged at about 6 months after your first visit. If you are in Group 5, we will do a lateral flow test (if you are vaccinated at this visit). If this is positive, the rest of this visit (including vaccination) will have to be delayed for at least 4 weeks. You will have a blood test and brief health check. We will ask if you have had any medical problems since your last visit.

For participants in Group 5 (control group) only, we will check that you are fit to be vaccinated and then give your dose of COVID-19 vaccine (Pfizer bivalent vaccine). This vaccine targets two strains of the virus: the original strain and an Omicron variant. After your vaccination, you will need to stay in the clinic for 15 minutes. You will be asked to fill in a symptom diary after this vaccination. We will give you a pack of lateral flow tests to take home, with instructions. You will be asked to do a lateral flow test every week between this visit and the next (including a test just before your next visit) and to record the results in your diary.

Note that if you are in the control group and decline a COVID-19 vaccine at this fourth visit, you will just have a final blood test and will not be required to attend a fifth visit. We ask that you let us know as soon as possible (and in advance of the fourth visit) if you decide that you do not want a dose of COVID-19 vaccine. You can discuss this with the study team at any time.

The **fifth visit** is for participants in Group 5 (control group) only (if you received a vaccine at the fourth visit). If you are in this group, you will have a blood test and brief health check. We will review your symptom diary and ask if you have had any medical problems since your last visit.

What if I change my mind?

Taking part in research is entirely **your** choice. You are free to change your mind at any time. You can decide to stop being in the study, even if your parent/legal guardian thinks you should continue.

What are the disadvantages of being in the study?

After the blood test and/or vaccine, your arm may be sore and you may have a bruise.

Vaccines, like all medicines, can sometimes cause unwanted side-effects. Usually these are a minor nuisance (like a sore arm) and they disappear within a few days. Very occasionally the side-effects can be more serious.

Common side-effects after vaccination include pain, redness and swelling where the injection has been given. Other common side effects include: tiredness; headache; aches in joints and muscles; feeling sick; vomiting.

We now know that the Pfizer and Novavax vaccines can, very rarely, cause a serious condition called myocarditis (inflammation of the heart muscle). It seems that this is more likely to occur in boys and young men shortly after their second dose of the vaccine (but, even then, it is very rare). Although myocarditis (inflammation of the heart muscle) is very rare following vaccination with either the Pfizer or Novavax vaccine, if you experience any symptoms such as chest pain, shortness of breath, or palpitations (the feeling of an abnormal heartbeat) you should let your parent (or guardian) know.

It is important to be aware that a routine third dose of COVID-19 vaccine may possibly be offered to 12 to 15 year-olds in the future. It is possible that a different COVID-19 vaccine or dose of vaccine from what you are given in the study may be recommended.

Taking part in the study might possibly affect how easy it is for you travel to some countries abroad in the future. There is more information about this in your parent/legal guardian's information sheet, which you can discuss with them.

What are the advantages of being in the study?

In this country, young people aged 12 to 15 years are currently advised to receive two doses of a COVID-19 vaccine, but are not offered a third dose of vaccine (unless they have underlying health problems, or live with someone who is at increased risk from COVID-19). By taking part

in this study, you would receive a third dose of COVID-19 vaccine. This may mean that you are better protected against the disease than if you had not received the third dose. However, you should remember that vaccination doesn't guarantee that you will be protected from COVID-19; you should continue to take care to protect yourself and others.

If you are in Group 5 (control group) of the study, you will also receive two doses of the Group B meningitis vaccine which could reduce your risk of serious illnesses (meningitis and sepsis) from this infection.

By taking part in this study, you would be helping us to learn more about which vaccine combinations and doses work best in young people. The results might help to guide future decisions about how best to use vaccines in children and young adults.

What happens when the study finishes?

Once all participants in the study have completed their visits, we will start the analysis and interpretation of the findings. Once complete, we will publish these results, and provide you with a link to the published paper on the Oxford Vaccine Group website. None of the reports will contain any information that might allow the readers to identify anyone who took part in the study. In addition to the published paper, we will also provide you with a summary of the key findings of the study.

What is happening in other parts of the study?

The study is divided into two different parts (or "cohorts").

The first part of the study (Cohort A) has completed recruitment. This part looked at three possibilities for the second vaccination. The standard dose of Pfizer vaccine was given for the first vaccination. The second vaccination, given 8 weeks after the first, was one of the following:

1. Standard dose of Pfizer vaccine
2. One-third standard dose of Pfizer vaccine
3. Novavax vaccine

The initial results of this part of the study are being analysed and submitted for publication.

I want to be part of Cohort B of this study, what should I do?

If you want to take part in this study, let your parent/legal guardian know and they will contact us.

Remember that taking part in the study is up to you. Even if your parents want you to take part, you should refuse if you don't want to be in the study.

Thank you for thinking about helping us.