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COVID-19 additional information sheet

TB043 – Adaptive measures taken due to the COVID-19 pandemic

Dear volunteer,

This information sheet is designed to accompany the volunteer information sheet entitled “*Studies of TB vaccines in healthy adults*” to explain the adaptations we have undertaken due to the COVID-19 pandemic, to ensure the safety and well-being of both volunteers and staff. It is important that you take the time to read and understand the information in this sheet carefully and discuss it with friends, relatives and your GP (General Practitioner), if you wish.

Ask us if you would like more information, or if anything is not clear. Take time to decide whether you wish to take part.

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Why are we continuing the trial at present?

Tuberculosis (also known as TB) is a disease caused by a bacterium (*Mycobacterium tuberculosis*) that is responsible for more deaths worldwide than any other infectious disease. The World Health Organisation has reported that in 2018, 10 million people worldwide became infected with TB and 1.5 million died. With this in mind, we believe it is important to continue our research, as long as the situation allows us to do so in a manner that ensures the safety of both volunteers and staff.

During the height of the COVID-19 pandemic in the UK, we paused all non-essential research activity – only continuing necessary safety checks for volunteers who had already been enrolled into the study. Now the UK has been able to start lifting lockdown restrictions, and with all necessary measures in place to ensure the safety of staff and participants, we believe strongly that now is the time to resume our work.

Throughout the study we will continue to monitor the evolving situation and will act in line with the most up to date guidance.

How will the clinic visits be conducted safely?

You will be required to wear a face covering during study visits, to both the Centre for Clinical Vaccinology & Tropical Medicine (CCVTM) and visits to the John Radcliffe or Churchill hospital sites. We can provide a disposable facemask on arrival if required.

Government social distancing guidelines will be adhered to throughout all sites. We have rearranged our facilities at the CCVTM to ensure adequate spacing in our waiting rooms, and a one-way flow system around the building. We request that you arrive as near to your appointment time as possible. If you arrive early for your scheduled appointment, we would ask that you wait in your car or outside (weather permitting) to allow us to plan for the appropriate numbers of participants in our waiting room.

We have alcohol hand gel available for staff and volunteers throughout the building, and will encourage regular use of this. We have also increased the frequency of cleaning at the CCVTM.

Staff members will wear appropriate personal protective equipment during study visits, as necessitated by current Public Health England policy.

We will check your temperature at the start of all study visits; if you record a high temperature (37.8°C or higher) the visit will be postponed. You will be advised to self-isolate and obtain a test to look for evidence of COVID-19 infection via the NHS test & trace system.

Staff members at both the CCVTM and hospital sites are adhering to government policy on self-isolation, should they or their household contacts develop symptoms consistent with COVID-19 infection.

Are there any special precautions needed for this study?

We have needed to carefully amend aspects of the way in which we carry out our study due to the COVID-19 pandemic. We will postpone enrolment of volunteers who have had confirmed COVID-19 infection, or symptoms that we deem highly suspicious for COVID-19 infection in the 3 months preceding their screening visit.

Furthermore, whilst levels of COVID-19 disease remain high in the general population it will be necessary to test for active COVID-19 infection prior to the Day 0 challenge visit (receipt of either inhaled or intradermal BCG and/or inhaled saline) and again prior to the bronchoscopy procedure.

As detailed in our volunteer information sheet "*Studies of TB vaccines in healthy adults*", both injection or inhalation of BCG and the bronchoscopy procedure have short-lived and commonly expected side effects – that may be confused with mild COVID-19 infection. We have therefore produced individualised self-isolation advice for you after these procedures (please refer to "**What is the study specific self-isolation advice?**" below).

Both lung function testing and induced sputum procedures are considered to result in increased production of respiratory droplets (also known as aerosol generating procedures). This increases the risk of spreading COVID-19 infection if undertaken in individuals with active infection. We have therefore reduced the amount of these procedures in our study, continuing them only if deemed necessary for safety checks. Additionally, we have adapted the way we perform these procedures to ensure ongoing safety of staff and volunteers.

What should I do if I have a scheduled visit but I am self-isolating?

The most up to date national guidance on when you and your household contacts should be self-isolating can be found here:

<https://www.gov.uk/government/publications/covid-19-stay-at-home-guidance>

At the time of writing, suspected COVID-19 symptoms are defined by Public Health England as:

- **a new continuous cough;**
- **a high temperature** (37.8°C or higher or you feel hot to touch on your chest or back if unable to check your temperature)
- **a loss of, or change in, your normal sense of taste or smell** (anosmia)

If at any point you develop any of these key symptoms then please ensure you and your household contacts self-isolate and arrange a test for COVID-19 using the NHS test and trace system:

<https://www.nhs.uk/conditions/coronavirus-covid-19/testing-and-tracing/get-a-test-to-check-if-you-have-coronavirus/>

If you have to self-isolate then **do not attend** any scheduled visits during the isolation period and **please inform the study team**. If you cannot attend a visit due to isolation requirements, we will either reschedule the visit or perform the visit by telephone. If you have a COVID-19 test outside the study (e.g. via NHS test & trace scheme or via your workplace) then **please inform the study team of any results**.

How will I be tested for active COVID-19 infection by the study team?

Current UK guidelines recommend that COVID-19 infection is diagnosed by taking a swab from the back of the throat and nose. A trained member of the study team will perform this procedure. They will first wipe the soft tip of a swab (like a long cotton bud) across the back of the throat. They will then insert the swab deeply into the nasal passages (approximately 2 inches), and gently rotate it for a few seconds. These are known as oropharyngeal (meaning back of the throat) and nasopharyngeal (deep nasal) swabs, and can then be tested for genetic material of the virus.

Other methods may be used in the future including saliva testing or fingerprick blood testing, but these are not yet accurate enough or routinely available. COVID-19 testing may be performed as part of the study at the specified time points (pre-challenge and pre-bronchoscopy). If testing is indicated at other times, this will preferentially be via the NHS test and trace system but may be conducted by the study team if needed.

Is the swabbing procedure safe?

The combined oropharyngeal and nasopharyngeal swab is considered a safe way of looking for COVID-19 infection, and has been performed across the world during the COVID-19 pandemic. It is not painful but can be uncomfortable. Swabbing the back of the throat can cause individuals to cough or gag. The deep nasal swab can make your eyes water or rarely cause nose bleeding.

What will be done with the results of my swab?

For positive swab results, we are required by law to share your result and personal data (including your name, contact details and postcode) with Public Health England for referral to the NHS Test and Trace system. This allows Public Health England to monitor the extent of coronavirus active in communities, and undertake measures to reduce the infection rate.

We will contact you with the results of your swab test as soon as they are available (usually between 24-72 hours after being tested).

Identification of a positive result prior to the challenge (BCG or saline) would make you ineligible to proceed with our study for a minimum of 3 months.

If you have a positive swab result at any point after your challenge visit, we will keep you in the trial and continue to see you for follow up visits once you have completed the necessary self-isolation period. We may conduct telephone check-ups if needed while you are self-isolating.

If you have a positive swab result prior to your bronchoscopy procedure, we would suspend the bronchoscopy procedure for a minimum of 28 days. We may discuss a later bronchoscopy with you once you have fully recovered from all symptoms, if this fits within our study protocol timelines.

What is the study specific self-isolation advice?

Both injection or inhalation of BCG and the bronchoscopy procedure have short-lived and commonly expected side effects that may be confused with mild COVID-19 infection. We have therefore detailed study specific exceptions to the self-isolation advice laid out by PHE for use *only after the challenge visit and bronchoscopy procedure.*

At all other time points in the study please follow the latest PHE guidance on self-isolation (see website above).

Any of the circumstances in which you have to self-isolate whilst awaiting a COVID-19 test would also require any of your household contacts to self-isolate.

1. After the challenge visit - Intradermal BCG injection group:

All potential expected side effects after the intradermal challenge visit are detailed in the volunteer information sheet, *"Studies of TB vaccines in healthy adults."*

A low-grade fever can be experienced in the 48 hours following the challenge visit.

We will be performing a COVID-19 test in the 48 hours preceding your challenge visit, which will reassure us that any expected symptoms experienced in the immediate post challenge period are likely to be a side effect of the challenge itself.

- If you develop a **fever** (37.8°C and above) within the 48 hour period after your challenge visit we would advise you to self-isolate, and to contact the study team to discuss whether or not it is likely to be related to the challenge.

- **Cough or loss of sense of smell or change in sense of taste** are not expected side effects after the intradermal challenge visit. Therefore, if you develop these symptoms at any point we would advise you to self-isolate and arrange a COVID-19 test. Please inform the study team.

2. After the challenge visit - Aerosol only groups (inhalation of aerosolised BCG or saline):

All potential expected side effects after the challenge visit are detailed in the attached volunteer information sheet, "*Studies of TB vaccines in healthy adults.*" Cough is a common side effect usually seen in the days immediately following the aerosol challenge but can occur within the first two weeks. A low-grade fever can also be experienced in the 48 hours following the aerosol challenge visit.

We will be performing a COVID-19 test in the 48 hours preceding your challenge visit, which will reassure us that any expected symptoms experienced in the immediate post challenge period are likely to be a side effect of the challenge itself.

We therefore advise:

- If you develop a **cough** after your challenge visit, there is **no** need to isolate if this is within the 5 days after the visit. If the cough starts after 5 days or is ongoing beyond the 5 day period, we would advise you to self-isolate and arrange a COVID-19 test.
- If you develop a **fever** (37.8°C and above) within the 48 hour period after your challenge visit we would advise you to self-isolate, and to contact the study team to discuss whether or not it is necessary to arrange a COVID-19 test.
- **Loss of sense of smell or change in sense of taste** are not expected side effects after the challenge visit. Therefore, if you develop these symptoms at any point we would advise you to self-isolate and arrange a COVID-19 test.

3. After your bronchoscopy procedure:

All potential expected side effects after a **bronchoscopy procedure** are detailed in the attached volunteer information sheet "*Studies of TB vaccines in healthy adults.*" Cough is an extremely common side effect after a bronchoscopy procedure. Approximately 10% of participants will experience a fever in the 48 hours post bronchoscopy.

We will be performing a COVID-19 test in the 48 hours preceding your bronchoscopy procedure, which will reassure us that any expected symptoms experienced in the immediate period after bronchoscopy are likely to be a side effect of the procedure.

We therefore advise:

- If you develop a **cough** after your bronchoscopy procedure then there is **no** need to self-isolate, if this is within the 5 days after the procedure. If the cough starts after 5 days or is ongoing beyond the 5 day period, then we would advise you to self-isolate and arrange a COVID-19 test.
- If you develop a **short-lived fever** (37.8°C and above) within the 48 hour period after your bronchoscopy procedure there is **no** need to self-isolate. If the fever lasts more than 24 hours in total or occurs over 48-hours after your bronchoscopy procedure then we would advise you to self-isolate and arrange a COVID-19 test.

- **Loss of sense of smell or change in sense of taste** are not expected side effects after the bronchoscopy procedure. Therefore, if you develop these symptoms at any point we would advise you to self-isolate and arrange a COVID-19 test.

After both the challenge visit and the bronchoscopy procedure, we will monitor your symptom diary and may contact you if we have any concerns. Please do not hesitate to call the study team on the 24-hour on-call number, should you have any concerns about your symptoms or questions about self-isolation.

07917 882967

How has the lung function procedure been adapted?

Lung function testing is an important safety check for those receiving the aerosol challenge that we perform in our study, to ensure you have healthy lungs prior to receiving any inhaled substances and after you have received the aerosol challenge. We will therefore continue this procedure at visits where necessary for safety purposes. As lung function testing is an aerosol generating procedure, the staff administering the tests will wear additional protective clothing for this visit. Rooms used for this procedure will also be thoroughly cleaned afterwards.

SUMMARY OF SELF-ISOLATION ADVICE *

Time point	Symptom	Advice for volunteer	Advice for Household contacts
After D0 challenge visit – All groups	New fever (37.8°C and above)	Self-isolate & contact the study team to discuss need for COVID-19 test.	Self-isolate whilst awaiting discussion & further advice from study team.
	Loss of sense of smell/ change in sense of taste	Self-isolate & arrange COVID-19 test.	Self-isolate whilst awaiting volunteer's COVID-19 test.
After D0 challenge visit – Aerosol group ONLY	New continuous cough	No need to isolate if resolves within 5 days after the visit. If lasts longer than 5 days please: Self-isolate & arrange a COVID-19 test	No need to isolate if resolves within 5 days after the visit. If lasts longer than 5 days please: Self-isolate whilst awaiting volunteer's COVID-19 result.
After D0 challenge visit – Injection group ONLY	New continuous cough	Self-isolate & arrange COVID-19 test.	Self-isolate whilst awaiting volunteer's COVID-19 test.
After bronchoscopy procedure	New continuous cough	No need to isolate if resolves within 5 days after the procedure. If lasts longer than 5 days please: Self-isolate & arrange a COVID-19 test	No need to isolate if cough resolves within 5 days after the visit. If lasts longer than 5 days please: Self-isolate whilst awaiting volunteer's COVID-19 result.
	New fever (37.8°C or higher)	No need to isolate if fever develops within the 48 hours post bronchoscopy and lasts less than 24 hours in total. If fever lasts more than 24 hours or occurs over 48 hours after procedure then self-isolate & arrange COVID-19 test.	No need to isolate if fever develops within the 48 hours post bronchoscopy and lasts less than 24 hours in total. If fever lasts more than 24 hours or occurs over 48 hours after procedure then self-isolate whilst awaiting volunteer's COVID-19 test result.
	Loss of sense of smell/ change in sense of taste	Self-isolate & arrange COVID-19 test.	Self-isolate whilst awaiting volunteer's COVID-19 test.
At ALL other time points during study (<i>except post challenge & bronchoscopy procedures</i>).	Volunteer develops key COVID-19 symptoms as per PHE guidance.	Follow latest PHE advice (see website below) Currently self-isolate & arrange COVID-19 test.	Follow latest PHE advice
At ANY time point in study	Household contact of volunteer develops key COVID-19 symptoms as per PHE guidance.	Follow latest PHE advice (see website below) Currently self-isolate whilst awaiting contacts COVID-19 test result.	Follow latest PHE advice

* Latest PHE guidance for symptoms requiring self-isolation and COVID-19 testing can be found online at

<https://www.gov.uk/government/publications/covid-19-stay-at-home-guidance>

**NHS test & trace system to arrange COVID-19 test can be found online at <https://www.nhs.uk/conditions/coronavirus-covid-19/testing-and-tracing/get-a-test-to-check-if-you-have-coronavirus/>

PLEASE INFORM THE STUDY TEAM OF ANY COVID-19 TEST RESULTS.

PLEASE INFORM THE STUDY TEAM AND DO NOT ATTEND ANY ROUTINE SCHEDULED VISITS IF YOU ARE SELF-ISOLATING.