**PATIENT INFORMATION SHEET**

(Patient Consent at Commencement)

Rec Ref: 19/WA/0310  **IRAS ID:** 271269

**Version** 1.2**,** Date 31/10/19

**Study Title: AspiFlu**

**Asp**ergillosis **i**n patients with severe in**flu**enza

Name of Researcher:

**Invitation to participate in this study:**

We would like to invite you to take part in a research study which we are conducting to look at how common a certain type of fungal infection is in patients on intensive care units (ICU) with influenza. **It is an observational study which means that the care and treatments you receive will not be any different whether you decide to take part or not.**

It is important for you to understand why the research is being done and what it involves. Please read the following information carefully and, if you wish, discuss it with your relatives or friends. Ask your nurse or doctor if there is anything that is unclear or if you would like any more information. Thank you for reading this.

*REPLACE THIS PAGE WITH RELEVANT ‘FRONT SHEET’*

**Quick summary**

Patients on intensive care units (ICU) with severe influenza (‘flu) may be susceptible to a second infection with a type of fungus, a mould, called *Aspergillus*.

This can be serious but antifungal treatments are available. The trouble is that it can be difficult to diagnose *Aspergillus.*

The aims of this study are:

1. Find out how common *Aspergillus* infection is for people with severe ‘flu on ICU and whether there are any ways to predict who is most at risk
2. Validate a new test called the ‘*Aspergillus* lateral-flow device’ (AspLFD) for use in ‘flu patients - this could make it much easier to diagnose *Aspergillus* in future
3. Look at how ‘flu affects the immune system and whether certain immune responses and immune genes place people at greater risk of *Aspergillus* infection.

If you decide to take part:

1. Your stay in hospital will continue as normal – **the care and treatments you receive will not be any different** whether you decide to take part or not.
2. A single set of research blood tests will be taken on the day you are enrolled into the study. **This can be taken via a venous/arterial line if you have one, or at the same time as your other blood tests.**
3. If your doctors feel a bronchoscopy is indicated as part of your care the study team will take a sample of surplus bronchoalveolar lavage (BAL) fluid. **A bronchoscopy will not be performed, or delayed, for the purpose of this study.**
4. Any testing we perform on your sampleswill be done after the ‘flu season is over. This means **the results will not influence your treatment.** Your doctors will request any tests for *Aspergillus* they think are needed in the normal way.
5. We will collect relevant information from your medical notes which will be stored securely in a confidential way.

**Part 1**

**Why do we need this study?**

Some people with seasonal influenza (‘flu’) develop severe infection requiring admission to an intensive care unit (ICU) to support their breathing. Recent research has suggested that when patients have such severe influenza they may be susceptible to a second infection with a type of fungus called *Aspergillus*. The main purpose of this study is to find out how common invasive *Aspergillus* infections are for people with severe ‘flu on intensive care and whether there are any ways to predict who is most at-risk.

*Aspergillus* is a mould that is all around us in the environment. It is common in soil, compost and also air conditioning units. We all regularly breathe in spores of *Aspergillus*, and this is usually harmless for those with a healthy immune system. In those whose immune system is impaired, however, *Aspergillus* can cause invasive infection. This can be very serious but antifungal treatments are available. The trouble is that it can often be difficult to diagnose *Aspergillus.*

Invasive *Aspergillus* infections have until recently only been recognised in patients with extremely weak immune systems – such as occurs following certain treatments for blood cancer. But a recent research study from The Netherlands and Belgium found that people on ICU with ‘flu may also be at risk. We need to establish if this is the case for patients with severe ‘flu in the UK. This is so that our intensive care doctors can be on the lookout for *Aspergillus* allowing the diagnosis to be made early and antifungal treatment started promptly.

**Biomarkers & Bronchoalveolar lavage (BAL)**

Invasive *Aspergillus* infection does not produce distinctive symptoms or changes on imaging (such as a chest x-ray) in people with ‘flu and there is no quick reliable diagnostic test. This means that invasive *Aspergillus* infection can bemissed.

Often when people are on intensive care with a chest infection they have a procedure called a ‘bronchoscopy’. This is where small flexible tube with a tiny camera on the end (a bronchoscope) is used to examine the insides of the trachea (windpipe), bronchi (airways) and some areas of the lungs. Fluid can then be squirted into areas of the lung that look infected and re-collected. This is called a bronchoalveolar lavage or ‘BAL’ for short. Tests can be performed on this BAL fluid to help diagnose the cause of the infection. The picture below is borrowed from the British Thoracic Society (BTS) Bronchoscopy Patient Information Sheet illustrates the procedure:



As it invades the lungs and grows, *Aspergillus* sheds a substance called Galactomannan. We can measure Galactomannan levels in either blood or BAL fluid to try and diagnose the infection, but measuring it in BAL is best because it is more sensitive. Galactomannan testing is not available in all hospitals so samples have to be sent off-site for testing. This can often delay diagnosis by days to weeks.

A new test called the *Aspergillus* lateral-flow device (AspLFD) is also used on BAL, and it also detects a substance shed by the fungus. Unlike Galactomannan, it is a rapid point-of-care test, which means unprocessed BAL sample can be added to the cartridge directly and 30 minutes later a result is read visually, in a manner similar to a pregnancy test. The AspLFD would be easy to implement at any hospital, which could make diagnosing invasive *Aspergillus* easier, but its use in patients with ‘flu has not been validated. Below is a picture to give you an idea of what results of this look like:



After the ‘flu season is over, this study will use stored blood and leftover BAL samples taken from participants for some further research. Firstly, to evaluate the performance of the new AspLFD test on BAL fluid. Secondly, to look at how ‘flu affects the immune system and whether certain immune responses and immune genes place people at greater risk of invasive *Aspergillus* infection.

**Why have I been invited?**

You have been chosen because you are on ICU being treated for infection with likely or proven ‘flu. This winter we are looking to enroll as many ICU patients with influenza as we can. We expect around 70-85 patients will be enrolled into the study in total.

**Do I have to take part in this study?**

No, but we are inviting patients being treated for ‘flu on ICU to have the opportunity to take part. You do not have to take part, or give a reason why taking part is not for you. The standard of care that you receive will not be different whether you decide to take part or not. In fact, if you do decide to take part **your care will not be affected in any way whatsoever**. Your Doctors, not the research team, will still make all the decisions as they normally would if you weren’t in the study. The decision to take part in research is a personal one, we just ask that you consider the information.

If you do take part, you will be given this information sheet to keep and asked to sign a consent form. You are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time or not take part will not affect the standard of care you receive.

**What will happen if I take part?**

Your stay in hospital will continue as normal – **this is an observational study which means that the care and treatments you receive will not be any different whether you decide to take part or not.**

If you take part, a **single set** of research blood tests will be taken on the day you are enrolled into the study. These additional blood tests are approximately equal to 2 tablespoons of blood (30-40mls). In most cases the additional research blood sampling can be taken from an arterial or venous tube (cannula) which is already in place as part of standard care. In exceptional cases, blood sampling for both routine clinical care and the blood for research will be from a vein using a needle at the same time. There may be a sharp scratch when the needle is inserted and possible bruising from the area from which the blood was taken. **The research blood sample will not be taken if your clinicians feel that it is not safe to do so.**

If your doctors feel a bronchoscopy is indicated as part of your care the study group will take a sample of surplus bronchoalveolar lavage fluid and/or store any leftover samples. **A bronchoscopy will not be performed, or delayed, for the purpose of this study**. We do not expect that taking of surplus BAL sample at the time of a bronchoscopy already being performed will increase the risk associated with the procedure.

After the ‘flu season is over these stored blood and BAL samples will be tested using both galactomannan and the AspLFD to compare how well both tests perform in diagnosing invasive aspergillosis. Since this will occur after the ‘flu season **the results of this testing will not influence your treatment** - its sole purpose is to assess how well the AspLFD performs, helping us decide whether to use it *in the future*.

At a later date we will perform some basic scientific research profiling and measuring levels of immune system cells and immune parameters known as cytokines to look at how ‘flu affects the immune system to make people at risk of invasive *Aspergillus* infection. We will also use stored DNA to look at whether specific immune genes also play a role.

In addition to the samples that will be taken and stored, we would like to collect some clinical information from your medical notes until your discharge from hospital or 90 days, whichever is the latest. We, the site research team, will do this in a standardised way during this hospital admission. This will be done centrally through electronic medical records.

**What do I have to do?**

You will not have to do anything as a participant in this study. We will collect the leftover samples and information for the study without your direct involvement. You will not need to attend any appointments with us.

**What are the possible disadvantages or risks to me taking part?**

The only way participants will be directly affected by this research study is the extra blood and BAL sample we will take. It is therefore not expected that any patients will come to harm.

**What are the possible benefits to me in taking part?**

You are unlikely to directly benefit from taking part in this research. It is important to realize that any extra testing we perform on your samples (such as with the AspLFD) will be done at a much later date in the Spring/Summer. The results will therefore not be relevant to your current stay in hospital and will not be communicated back to you or your doctors. Your doctors will request any tests for *Aspergillus* they think are needed in the normal way.

Your participation is likely to help future patients with severe influenza. By taking part you are helping to increase awareness and understanding of the link between influenza and invasive *Aspergillus*. Your participation could help us to understand who is at risk of this condition, why it happens and what we can do to prevent and diagnose it. You will not be paid or reimbursed for participation in this study.

**What if there is a problem or I have a complaint?**

Please find more information regarding this in part 2

**Will my taking part be kept confidential?**

Yes. Any information collected during the study will be kept strictly confidential, anonymised where possible and will only be used for research purposes. If you agree to take part, you will be allocated a unique, personal study number. Information about you will be stored under this number to protect your identity. This system (sometimes called ‘pseudonymised’ data) ensures that confidentiality is protected during routine collection of your data. People who do not need to know who you are will not be able to see your name or contact details. We will write our reports in a way that no-one can work out that you took part in the study. We would like to inform your General Practitioner (GP) of your involvement in the study, but you can opt out of this if you wish.

**Part 2**

**What will happen if I decide that I no longer wish to take part in the study?**

You are free to withdraw from the study at any time without giving reasons, your decision will be respected and your usual standard care will not be affected. No further clinical data beyond this time-point or new samples will be collected, the data and samples already gathered will be retained and used for the study unless you request us not to do this.

**What if there is a problem?**

Given that this study does not involve alterations to the treatment you receive we feel this is very unlikely. However, St Georges, University of London has agreed that if you are harmed as a result of your participation in the study, you will be compensated, provided that, on the balance of probabilities, an injury was caused as a direct result of the intervention or procedures you received during the course of the study. These special compensation arrangements apply where an injury is caused to you that would not have occurred if you were not in the study. We would not be bound to pay compensation where: -The injury resulted from a drug or procedure outside the trial protocol and/or -The protocol was not followed. These arrangements do not affect your right to pursue a claim through legal action.

If you have a concern about any aspect of this study, you should ask to speak to your doctors or a member of the research team who will do their best to answer your questions.

The normal National Health Service complaints mechanisms are also available to you. You can ask any of your care team for further details about how to contact the hospital Patient Advice and Liaison Service (PALS) on (insert local details).

**What will happen to the results of the research study?**

Results from the first part of the study (analyzing the incidence of invasive aspergillosis in patients with severe ‘flu) are expected to be published in 2021. The publications will include anonymised data only. If you decide to take part, we would be happy to post or email you a summary of the findings (written for a non-medical audience) as well as a link to the published paper – there is a space to write your email address at the bottom of the Consent form (below). Results from the later parts of the study (looking at how the immune system and genes make people with flu at risk of *Aspergillus*)are not expected to be published until 2022/23.

**How will we use information about you?**

We will need to use information from your medical records for this research project. This information will include your name, date of birth, NHS number and contact details alongside information about your medical problems, investigations and treatment. People will use this information to do the research or to check your records to make sure that the research is being done properly.

People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

**What are your choices about how your information is used?**

•You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have.

• If you choose to stop taking part in the study, we would like to continue collecting information about your health from your hospital. If you do not want this to happen, tell us and we will stop.

•We need to manage your records in specific ways for the research to be reliable. This means that we won’t be able to let you see or change the data we hold about you.

• If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

**Where can you find out more about how your information is used?**

You can find out more about how we use your information:

SGUL Privacy link: https://www.sgul.ac.uk/privacy

For general information on how the NHS uses research data please visit <https://www.hra.nhs.uk/information-about-patients/>

**Will the data about me be kept securely?**

We will keep all information about you safe and secure. We will store all electronic information on secure (password-protected) confidential computer systems which can only be accessed by members of the research team. All documentation will be stored in areas where there is restricted access including only people involved in research. Once we have finished the study, we will keep some of the data so we can check the results.

**What will happen to any samples I give?**

The blood and BAL samples taken as part of the study will be stored in a secure freezer in the hospital laboratory. Samples will be transferred to a secure research laboratory freezer in St. George’s University of London at a later date. Samples will be stored with your anonymised unique personal study number only. Only members of the research team and laboratory staff will have access to the samples.

The samples will only be analysed within the scope described in this information sheet. If there is a desire to use the stored samples for a subsequent research project a new ethics application will be made. You can decide to opt-out of the possibility of your samples being used in a future research project in which case samples will be destroyed once the research project is complete. There is an option for this on the Consent Form, or you can speak to a member of the research team at any time if you change your mind.

**Will any genetic tests be done?**

We would like to use one of the blood samples to look for certain genes that are thought to make certain people more at risk of invasive *Aspergillus* infection. It is not yet known whether genes play a role in *Aspergillus* infection related to severe influenza.

You can decide to opt out of this part of the study by not ticking the relevant part of the consent form.

**What will happen after the study?**

You will continue to be receive routine clinical care from your NHS doctors. The electronic information we keep about you will be kept securely on computer servers at St George’s and paper information will be achieved securely at your local study site. The chief investigator, statistician and clinical research fellow will analyse and present the study findings at national and international conferences and write it up for publication in scientific and journals. Your samples will be handled as outlined in the section ‘What will happen to any samples I give?’ above. We will not contact you again unless you have asked us to provide you with the results of the study (see above).

**Who is organising and funding this study?**

The study is funded through a Gilead UK & Ireland invasive fungal disease fellowship, but the finder plays no role in study design or conduct. The Chief Investigator who is overseeing the study is Dr Tihana Bicanic, Reader and Consultant in Infectious Diseases at St George’s NHS Foundation Trust and University of London. The Principal Investigators for each hospital site are named below.

**Who has reviewed the Study?**

All research in the NHS is looked at by an independent group, called a Research Ethics Committee. This is to make sure that your interests are protected. This study has been reviewed and given favourable opinion by Wales Research Ethics Committee 5.

**Contact for further information:-**

Thank you for reading this information, if you have any questions please ask either the person who provided you with this information or your local research contacts who are:-

(Insert Local Research Team Details here)

Independent Research Patient Liaison – xxxxx

**What Next?**

If you would like to take part the researchers will go through this information with you and answer any questions you may have. They will ask you to complete and sign a consent form, giving them permission to complete the procedures explained in this information sheet.