

## INVESTIGATOR SITE HEADED PAPER

## Sepsis Trials in Critical Care - SepTiC Patient Information Sheet

We are inviting adults who have been admitted to the Intensive Care Unit (ICU) with sepsis to participate in our research study. Sepsis is when the body overreacts to an infection and starts to damage itself. This study is trying to find the best treatments for sepsis. This form provides information on the study, the treatments we are using, and risks and benefits of taking part.

Please take time to read the following information carefully and do talk about it with other people if you would like to. Ask us if there is anything that you do not understand or if you would like more information. You can take time to think about your participation.

Thank you for reading this.

### **What is the purpose of the SepTiC study?**

SepTiC is the name of a research trial which is looking at treatments for sepsis. A research trial is a study that focuses on finding a treatment for a specific condition or disease. The trial aims to find out what are the best treatments for sepsis.

Sepsis happens when your body is reacting to an overwhelming infection. This can cause damage to the tissue and organs in your body. Sepsis is a medical emergency that requires urgent treatment with antibiotics, fluids, and other drugs to help oxygen flow to important organs and help the heart. There are different treatments available for sepsis and in this trial, we want to know which treatments are best.

### **What are we testing in this research?**

We are testing three different things in this study: -

#### **1. Diagnostic Trial**

Patients who have sepsis due to a serious infection need treatment as soon as possible. The treatment usually starts with drugs such as antibiotics to help fight the infection. Sometimes these drugs are used for longer than needed, which can cause side effects that can be harmful to patients. This might also make infections more difficult to treat in the future as it risks bugs (bacteria and other microorganisms) becoming used to and not being killed by antibiotics. Also, not all patients who are at first thought to have sepsis (and receive antibiotics) have an infection, so they may not have required antibiotic treatment at all. So, it is really important that we find out which patient needs antibiotics for an infection, who does not need them and if we can stop them, as soon as possible.

Patients in this group will have a Rapid-PCR test. A blood sample will be taken either using a needle or via a line if already in place. It will be sent to a laboratory for testing using a technique called PCR (polymerase chain reaction), which can quickly identify bacteria.

If the PCR test is positive for a microorganism, the patient's medical team will be told, so that the antibiotics are urgently looked at to check that they will kill the microorganism found by the PCR test, and that the patient has them for long enough to treat their infection. If the test is negative (no microorganisms are found) the patient's medical team will use this information, as well as with other routine tests, to see if antibiotic treatment may be stopped.

#### **2. Fluid Trial**

Giving fluids, through tubing in the arm known as a 'drip', is standard practice in treating sepsis, but there is no clear guide on how much fluid is enough or too much, and so a build-up of fluid in the body can occur which may be harmful. We will test how much fluid should be given and whether to remove any build-up of extra fluid.

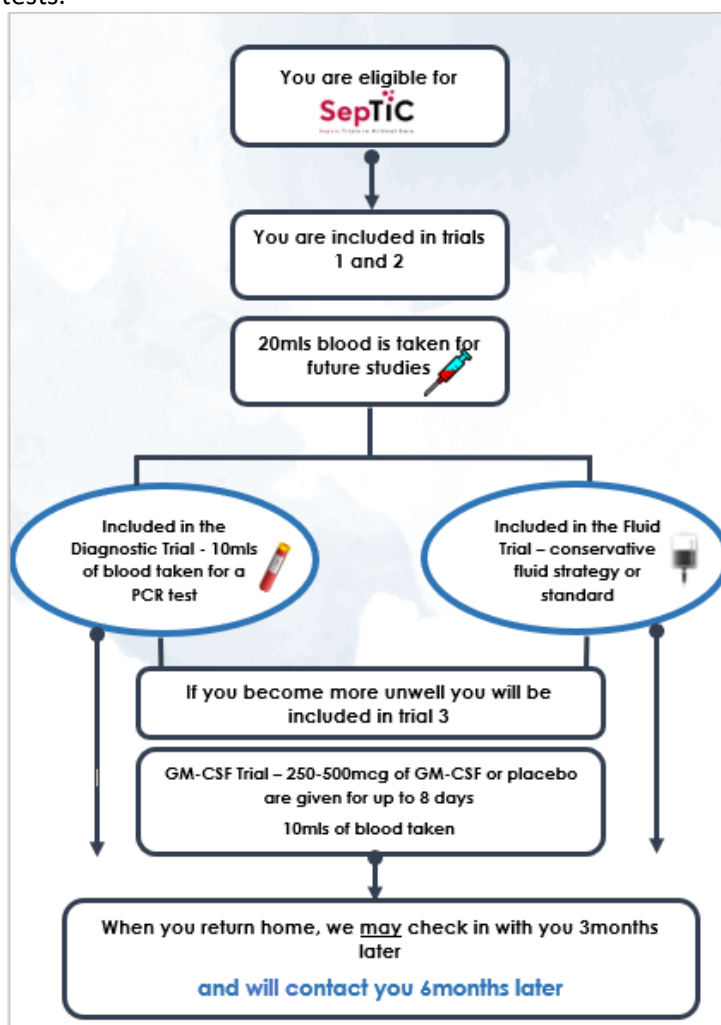
For patients in this group, depending on their condition, we will give as little fluid as possible and, when safe, will treat any build-up of fluid which has occurred using medications called diuretics. If the patient is already receiving kidney dialysis, we will use this to remove excess fluid instead of diuretic medications.

### 3. GM-CSF Trial

GM-CSF is the short name for granulocyte-macrophage colony-stimulating factor. This is approved in the USA by the FDA as type of protein that helps to make more white blood cells to help the immune system fight infection. The GM-CSF used in this trial is called Sargramostim.

This treatment will only be given to patients who need support for their breathing or other important organs. For patients in this group, an injection under the skin of 250-500mcg Sargramostim is given once a day for up to 8 days. To help test if this does help patients, they will be compared with other patients who will have a sugar solution made to look the same as the drug. This is also given once a day for 8 days. This is known as a 'placebo'.

To test if these different things help patients with sepsis, patients will be compared with other patients who are having standard care. Standard care means having the treatment you would normally get for sepsis without the PCR test, or changes to fluid, or having GM-CSF. This means that even if you are in the SepTiC trial, you may not have any of these treatments or PCR tests.



### Why have I been chosen?

You have been asked to take part in this study because you are being treated for suspected sepsis in an intensive care unit. We know that treating patients with sepsis early provides the best chance for treatments to work and so we need to include patients as soon as possible once they develop the condition, and so some of the treatments may

already have started before you were given this consent form. Over a 3-year period we are planning to study up to 3800 patients like you, in hospitals in the UK.

### **Do I have to take part?**

You do not have to take part and you can decide if you want to take part or not. It will not make a difference to the standard healthcare you receive if you do or do not take part.

If you do want to take part, you will be given this information sheet to keep and be asked to sign a consent form. If you change your mind later, you can stop being part of the trial at any time without giving a reason.

### **Which treatments will I receive?**

Your doctor will decide whether you are suitable to participate in 1, 2 or all three parts of the trial in this research. You will be allocated treatments in these trials by a 'randomisation' process. Randomisation is a process that is like tossing a coin and means people are put into groups by chance rather than chosen for each group. This helps us compare very similar groups of patients to see which way of treating patients is the best. The groups are selected by a computer which has no information about the individual.

### **What else will I need to do?**

If you are in the PCR test group, we take a blood sample needed for the PCR test to be done.

If you are in the fluid trial, you will either receive less fluid and have any build-up of fluid treated or have the standard amount used in your hospital.

If you are in the GM-CSF part of the trial, you will have the treatment or placebo (a solution which looks like the treatment) every day for up to 8 days.

Once your treatment is finished, we may contact you 3 months later to see how you are. We will contact you 6 months after you started in the trial with a short telephone call to ask about your quality of life and wellbeing using questionnaires to check how you are doing. This helps us to see the longer-term effects of treatment for sepsis.

### **Blood Samples**

So that we can understand more about how the treatments in this study work, we will also collect a small amount of blood. We will collect 20mls, about one tablespoon, of blood, which will be sent to a central laboratory for storage. We will use this blood to look for elements of the genetic code (DNA), the way it is turned on and off (RNA) and proteins that are involved in inflammation to understand if these can tell us how future patients will respond to the treatments being tested. For patients in the GM-CSF trial half a tablespoon of additional blood will be collected on the third and fifth day of treatment. These blood samples will be stored and may be used in other, ethically approved research projects. The blood will be stored pseudonymously (without your name included on it, only a code), will be held securely, and no attempts will be made to identify you from it.

### **Do I have to answer questions while I am in intensive care for this research?**

You do not need to do anything for the study while you are in hospital. A researcher will collect data about you for the study, and you will not be asked anything extra for this research. The data collected for the study are already collected as part of your daily and ongoing medical care. With your permission, we will also use routinely collected data held by either the Case Mix Programme, the national clinical audit of UK intensive care units, run by the Intensive Care National Audit & Research Centre (ICNARC), NHS Digital or by The Scottish Intensive Care Society Group (SICSAG). These data will include your NHS number and information regarding your health that will be important to answer the objectives of the study and will include, data from this, future hospital stays and survival data. We would also like to contact you after your inclusion. We may contact you 3 months later to see how you are and would like to contact you 6 months later with a short telephone call to ask about your quality of life, wellbeing and how well you are able to understand and remember things.

If you do not wish to be part of this study, no further information will be collected about you for the trial and the doctors will continue to provide you with whatever medical treatment is needed.

### **What are the side effects of any treatment received when taking part in this research?**

All medical treatments can cause side effects. The risks from side effects are similar if you choose not to be in the study as you will be having many different treatments for sepsis as part of your standard healthcare. Your doctor will

be aware that you are taking part in the study, and so the doctors will be looking out for any side effects which may be because of the trial treatments.

### **Diagnostic Trial**

In most patients this blood test can be collected from a 'drip' already in place. If there isn't already the right type of drip in place, there is a chance you could have a bruise or it might feel sore from the blood test, as can happen with any blood test. These procedures will only be carried out by an experienced health professional to limit these risks.

### **Fluid Trial**

For this part of the trial, we are testing if it is better for patients to have as little fluid as possible and, when safe, will treat any build-up of fluid which has occurred using drugs called diuretics. This will be compared to having a usual amount of fluid. These two ways of giving fluids are both often used in intensive care units.

Side effects from fluid do not often happen but it can include a build-up of fluid causing swelling. The main potential complications of our intervention (giving less fluid and giving drugs to remove any build-up of fluid) include abnormal salt (potassium) levels and other chemicals in the blood. These two things can often happen in patients who are seriously ill, no matter how fluid and diuretics are used. Potassium and chemical levels in the blood are checked often several times a day, for patients in ICU. We will therefore be able to see if these things have happened very early, before they cause problems, which may mean stopping the diuretics if needed.

### **GM-CSF Trial**

All drugs have side effects. If you have the white blood cell growth factor (GM-CSF) as part of this trial, you might have redness at the site of injection; allergic reaction; keeping more fluid in your body than you need (fluid retention) and swelling; heartbeat which is too fast or too slow; an elevated blood count; back, chest, tummy or joint pain or blood clots.

However, most of these side effects are uncommon and you will be very closely looked at (monitored) by your healthcare team who will look out for any signs of these side effects. Some of these things can happen when you have sepsis as well, without having GM-CSF.

### **Are there any other risks of taking part?**

When our team contact you by phone at 6 months after you are included in the study some patients might find the information shared is sensitive in nature. The person from our team who will speak with you will be aware of this and will be tactful. They will aim to reassure you and put you at ease. You can stop answering the questions if you want to or take a break and come back to them another time.

The researcher will treat your information with respect and in line with the highest standards of confidentiality and security. The information we collect about you will be non-identifiable, you will be assigned a patient number.

### **Pregnancy**

If you are pregnant, you will not be included in the GM-CSF trial. It is possible that if the treatment is given to a pregnant woman, it will harm the unborn child. Pregnant women must not therefore take part in the GM-CSF trial, neither should women who plan to become pregnant during the study. Women who might be pregnant may be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy.

Women who are pregnant or breastfeeding may be included in the Diagnostic and Fluid Trials.

### **What are the possible benefits of taking part?**

You may not benefit directly from this study, but the results may help future patients and assist doctors in the future in treating people with sepsis more effectively and successfully. If, during the study your doctor becomes aware of a condition to which you were unaware, your doctor will discuss treatment options with you as per your usual standard of care.

### **Will I be paid for taking part?**

There is no payment for taking part in this research trial.

### **How will my information be looked after?**

All data (information about you from this trial) will be kept private by the study team in a correct, confidential, and secure manner. The study will follow UK and EU regulations to make sure your data is protected. The only people allowed to look at your information will be the doctors running the study and authorised staff at Imperial College London. A privacy notice on the study is available on the website: - [www.septictrial.co.uk](http://www.septictrial.co.uk)

### **What happens when the research study stops?**

Your involvement with this research stops once you have completed your 6 month follow up telephone conversation with a member of the clinical research team. You will continue to receive the standard care available from your hospital if you need more treatment.

### **What if something goes wrong?**

Imperial College London holds insurance policies which apply to this study. If you experience harm or injury as a result of taking part in this study, you will be eligible to claim compensation without having to prove that Imperial College is at fault. This does not affect your legal rights to seek compensation.

If you are harmed due to someone's negligence, then you may have grounds for a legal action. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator **(Insert name and contact details)**. The normal National Health Service mechanisms are also available to you. If you are still not satisfied with the response, you may contact the Imperial College, Research Governance, and Integrity Team.

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

The results of this study will be presented at medical meetings and published in scientific medical journals. Only anonymous group information and no personal information will be presented so you will not be identified as being involved with this research. If you are interested in the results, you will be able to look them up after the study has finished on our study website: - [www.septictrial.co.uk](http://www.septictrial.co.uk)

### **Who is organising and funding the research?**

This study is being organised and sponsored by Imperial College London and the Chief Investigator is Professor Anthony Gordon. It is funded by the National Institute for Health and Care Research (NIHR).

### **Who has reviewed the study?**

This study was allowed to go ahead after being approved by the Research Ethics Committee having given a favourable ethical opinion for conduct in the NHS by the Seasonal REC and the MHRA (Medicines and Healthcare products Regulatory Agency).

### **Who can I contact for independent research information?**

#### ***England/Wales sites only***

If you have any questions about being in a research study, you can contact the Trust's Patient Advice Liaison Service (PALS). They will give you advice about who you can talk to for independent advice.

<b>Local PALS office telephone number</b>	<b>Local PALS office address</b>

#### ***Northern Ireland sites only***

If you have any questions about being in a research study, you can contact the person listed below. They will give you advice about who you can talk to for independent advice.

<b>Local Contact</b>	<b>Local address</b>

### **Scotland sites only**

If you have any questions about being in a research study, you can contact **[insert full name]** (contact details below) who is not involved in the study and will be able to give you independent advice.

**[insert independent contact telephone number/email address/postal address]**

### **Site Contact Information**

Investigator name:-

Site Contact details:-

### **Study Contact Information**

Please contact The **SepTiC** Trial team using the following contact details:

Name: The **SepTiC** Trial Team

24hr Telephone: 0207 5949725

Email: [septic@imperial.ac.uk](mailto:septic@imperial.ac.uk)

Website: [www.septictrial.co.uk](http://www.septictrial.co.uk)

Thank you very much for taking part in this study!

A copy of the written information and signed Informed Consent form will be given to you to keep.

## Consent Form for Participants

**Full Title of Project:** Sepsis Trials in Critical Care - **SepTiC**

<b>Site number:</b>	
<b>Patient Number:</b>	
<b>Patient Name:</b>	
<b>Name of Principal Investigator:</b>	

**Please initial box**

1. I confirm that I have read and understand this document and have read/received a copy of the appropriate patient information sheet and privacy notice for <b>SepTiC</b> .	
2. I confirm I am happy to consent to participate in the following trials:  Diagnostic and Fluid Trial <input type="checkbox"/>  GM-CSF Trial. <input type="checkbox"/>	
3. I confirm that I understand the <b>SepTiC</b> study and I have had the opportunity to ask questions which have been answered fully.	
4. I understand that my participation is voluntary, and I am free to withdraw at any time, without giving any reason and without my legal rights nor treatment / healthcare being affected.	
5. I understand that sections of any of my medical notes may be looked at by responsible individuals from Imperial College London, from the NHS Trust or from regulatory authorities where it is relevant to my taking part in this research.	
6. I give consent for information collected about me to be used to support other research or in the development of a new test, medication, or treatment by an academic institution or commercial company in the future, including those outside of the United Kingdom (which Imperial has ensured will keep this information secure).	
7. I give consent for samples (human tissue) collected about me to be used to support other research or in the development of a new test, medication, or treatment by an academic institution or commercial company in the future, including those outside of the United Kingdom (which Imperial has ensured will keep this information secure).	
8. I understand that tissue samples and / or data collected from me are a gift donated to Imperial College and that I will not personally benefit financially if this research leads to an invention and/or the successful development of a new test, medication treatment, product or service.	

9. I give consent to being contacted about the possibility to take part in other research studies.	
10. I consent to allow the use of data already collected in the trial, as well as ongoing data collection and follow up information to be obtained from my medical records at 3, 6 months and 12 months after my inclusion	
11. I agree that my medical records and other personal data generated during the study may be examined by representatives of the sponsor (Imperial College London), by people working on behalf of the sponsor, and by representatives of Regulatory authorities, ICNARC, NHS Digital and SICSAG where it is relevant to my taking part in this research.	
12. I agree to my tissue samples being used to undertake genetic research which may have the potential to generate data that can be tracked back to me	
13. I consent to take part in <b>SepTiC</b>	

\_\_\_\_\_  
Name of patient

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name of staff member  
(Listed on delegation log)

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

1 copy for participant; 1 copy for Principal Investigator 1 copy for hospital notes

To ensure confidence in the process and minimise risk of loss, all consent forms must be printed, presented, and stored in double sided format