

# PARTICIPANT INFORMATION SHEET

A Phase I open-label study to assess the safety, tolerability and potential efficacy of a novel tracheal replacement consisting of a tissue engineered de cellularised tracheal scaffold with seeded autologous mesenchymal cells in subjects with severe tracheal stenosis or malacia

**Title of Trial:** A Phase I open-label study to assess the safety, tolerability and potential efficacy of a novel tracheal replacement consisting of a tissue-engineered de-cellularised tracheal scaffold with seeded autologous mesenchymal cells in subjects with severe tracheal stenosis or malacia

**Trial Number:** D-00173-CT2013002

**Trial Sponsor:** Cell Therapy Catapult

**Site Name:** Royal National Throat, Nose and Ear Hospital, UCLH

**Tel:** 020 3456 7890

**Principal Site Investigator:** Prof. Martin Birchall

This information sheet describes a clinical trial that will look at the safety and potential efficacy of a novel treatment for tracheal stenosis and malacia. One of our trial team will go through the information sheet with you to explain the trial and answer any questions you have. You do not need to make a decision on this day and we encourage you to go away, read through this document thoroughly and then come back to ask any questions you may have to your treating doctor. The trial only includes people who choose to take part.

Some of the information in this sheet is required by law. This information sheet has been reviewed and approved by South Central – Oxford A Ethics Committee. This committee reviews research trials to protect the rights and well-being of the people taking part.

We would like to invite you to take part in our research trial. Before you can decide, we would like you to understand why the research is being done and what it would involve for you.

You should only make your decision after:

1. A trial staff person has explained the trial to you;
2. All your questions have been answered
3. You know what the purpose of the trial is and what the risks are to you;
4. You are willing and able to do what is asked of you in the trial

Please talk to your family, friends and your doctor about the trial if you wish, to help you make your decision. You can take as much time as you like to decide to take part.

If you do decide to take part, you must sign the page(s) at the end of this sheet [Appendix 2] to show that you agree. This is called “giving consent”.

After you give consent, you can change your mind at any time during the trial. You can leave the trial, even after you have signed this form. You do not need to give a reason.

### **1. WHY IS THE TRIAL BEING DONE?**

You are being offered participation in this study as you have been diagnosed with a breathing disorder known as tracheal stenosis or tracheal malacia. Tracheal stenosis is a narrowing of the windpipe whilst tracheal malacia is having floppiness of the trachea.

There is a need for better treatments of tracheal stenosis/malacia to increase the survival rate and quality of life in patients with these conditions.

The company running this trial are investigating whether using a new technique of replacing your damaged trachea with a tracheal scaffold and your own cells will potentially cure and/or ease symptoms of your disease. If you choose to take part, you will be one of 4 patients who will be enrolled into this research study.

This is a first in human study, being done to investigate the safety and potential benefit of this novel type of tracheal replacement in patients with tracheal stenosis or malacia.

### **2. WHAT IS THE EXPERIMENTAL TREATMENT BEING TESTED?**

This trial involves a new experimental technique which uses a combination of a human trachea donated after death that has been stripped of any cells from the original donor (known as the trachea scaffold) and to which your own cells will be added. To make this new treatment, we will take cells from your bone marrow and grow and multiply them in a special laboratory. These cells will then be transferred onto the donor trachea scaffold. During a surgical procedure your own damaged trachea will be removed and the new trachea scaffold (that has been seeded with your own cells previously harvested and grown in the laboratory) will act as the replacement. As this new trachea has your own cells seeded within it, it is thought this new section will become part of your tissue.

### **3. ARE THERE OTHER TREATMENTS I CAN HAVE?**

There is no real cure available for a patient who has been diagnosed with severe tracheal stenosis or malacia. Whilst on the trial, you can continue to receive regular care from your doctor. Under normal situations, patients would normally receive treatments such as laser and stenting (using a small expandable tube to prop open the narrowed trachea) procedures which are designed to help relieve symptoms. Patient with tracheal stenosis/malacia often become dependent upon these treatments which they will need repetitively. However, these treatments often lead to poor outcomes resulting in further medical complications and reduced quality of life.

If you have any questions on alternative treatments, you should discuss this with your doctor when discussing this trial with them.

#### **4. WHAT WILL HAPPEN TO ME IF I TAKE PART?**

If you agree to take part in this trial and you sign the consent form found at the back of this document, you will first need to do a number of examinations and tests called “Screening tests” to be sure that you can take part in the trial. Once the results of these tests are known, the trial doctor will tell you whether you can continue in the trial or not. You may not be eligible to move into the trial due to a strict number of criteria which each patient is required to meet to enter the study. If you do meet these criteria and you continue, you will be involved in this research trial for up to 5 years. However, after the first year you will only need to be seen once per year for the purposes of this trial.

During this initial screening period, you will be required to attend on 3 occasions to see if you are eligible to take part in this trial. On the first screening visit, you will have a physical examination, some blood drawn, a heart trace (electrocardiogram or ECG), blood pressure and heart rate measurements, a CT scan which will enable doctors to have clear pictures of the throat and windpipe, a lung function test which will measure how well your trachea allows your lungs to take in and release air and then a rigid bronchoscopy which involves passage of a small camera to allow the doctors to see within your windpipe. For the rigid bronchoscopy you will need to be sedated (under general anaesthetic) to have this performed. It is anticipated that these tests can be performed in one day. However, if required these can be performed over a number of days.

Once the results of these initial screening tests are available and it is confirmed that you can move forward into the trial, a date for the second screening visit will be scheduled for you to undergo the collection of the required cells. This will be via a bone marrow aspirate procedure. This involves taking a sample of your bone marrow (the soft tissue inside your bones) usually from the back of the hip bone. This will require local or general anaesthetic which will be decided after a discussion with your doctor. It would be worth discussing with your doctor any requirement to rest at home after this procedure. Whatever is collected from the bone marrow aspirate will be sent off to a special laboratory where your bone marrow cells will be multiplied. During this process there will be no need for you to visit the hospital for approximately another 4 weeks.

At the third screening visit, you will have a physical examination, some blood drawn, a heart trace (ECG), blood pressure and heart rate measurements and a lung function test. These will confirm your eligibility to have the surgery to remove your damaged trachea and replace it with the tracheal scaffold seeded with your own cells from the bone marrow aspirate.

Once the replacement trachea is ready, you will be brought back to the hospital to undergo the replacement surgery. Before your surgery you will need to be admitted into hospital. The doctor will do their final checks and talk you through what is going to happen. During this process you will have some blood drawn and have another ECG and exam to check your blood pressure and heart rate. Your surgery will take place under general anaesthetic. The section of damaged or diseased trachea will be removed using the rigid bronchoscopy technique you

would have had at the first screening visit and the new trachea will be grafted in place. During the same operation, the trial doctor will do a surgical technique called a laparoscopy which is a surgical procedure that allows a surgeon to access the inside of the abdomen (tummy) without having to make large incisions in the skin. The trial doctor will perform a laparoscopy to take some omentum (which is fatty tissue around your intestines) and then use this to wrap the tracheal implant with what is known as an omentum wrap; this will act to support the tracheal implant. If however, you do not have enough omentum then the doctor may use as an alternative, a local muscle to wrap and support the new graft. To further support the tracheal implant a removable stent (small tube to prop open the trachea) will also be added. You will be in hospital until you are fit enough to go back but on average this could be around 3 weeks.

After your surgery, you will be followed up closely by your doctor who will be required to take a number of blood draws and a look down the grafted trachea using a flexible bronchoscopy technique, which uses a flexible camera. These examinations will occur on a number of days during your 4 week stay. However, after the first week these become less frequent.

Discharge after your surgery will occur once your care team and you feel you are well and strong enough to go home. Once you are well enough to be discharged (which is thought to be around 3 weeks after your surgery), you will need to keep in contact with your doctor and/or care team who will either call or visit you once per week to ensure things are ok. During these calls/visits you will need to be able to report if anything has been wrong with you. Your doctor should prompt you for this information during these contacts. Further blood draws will be required at 4 and 6 weeks after initial surgery. There will be a need to visit the hospital at 6 weeks post-surgery to perform a FEES/Stroboscopy test to assess swallowing with a small camera and also to assess your voice box.

8 weeks after surgery the doctor will need to ensure that the grafted trachea is healing well and to also replace the supporting stent that was used in the initial surgery; for this to be checked, a rigid bronchoscopy will need to be done (under general anaesthetic) for which an inpatient stay will be required. This will be repeated again at 16 weeks where the stent will be replaced once again, and then again 24 weeks after the initial surgery when the stent will be permanently removed if things look suitable to do so. During these inpatient stays, the doctor will do a blood draw, ECG to check your heart and a rigid bronchoscopy to view the inside of your graft. These inpatient stays for the week 8, 16 and 24 visits are expected to be for around 24 hrs but might be up to 2 weeks during which you will be closely monitored by the trial doctor and care team and will be discharged once they think that you are fit enough to return home.

In between the 8, 16 and 24 week stent removal/replacement procedures, again your doctor or care team will contact you (at weeks 11, 13 and 15) to ensure things are ok with you. At 12 and 14 weeks after the initial surgery, you will be required to visit the hospital to undergo blood draws, urine tests, a flexible bronchoscopy and a lung function test. Once the stent is

replaced at 16 week post initial surgery, the visits to your trial doctor will be required at week 24 and 32 weeks past initial surgery where additional blood draws, a CT scan, lung function test and rigid bronchoscopy will be required.

You will then be required to visit your trial doctor at 1 and 2 years post initial surgery where the doctor will complete blood draws and lung function tests. The final follow up visit will be required at 5 years after the initial surgery where you will have lung function tests done.

During the course of the trial, there will be a requirement for a number of CT scans which will be used initially to analyse the trachea and to assess the damaged or diseased section to be replaced and then to ensure that the graft is integrating and is functioning as required. The CT scans use X-ray radiation to generate images, which carry a very small long-term risk of inducing cancer. The amount of radiation used in each CT scan is about the same as you would be exposed to from background radiation in the UK in 9 months. There will be a total of 9 CT scans used during the course of the 5 years on trial.

The doctor may require you to perform additional tests and/or procedures which are not required as per the trial. This will be part of their standard follow up procedures and care for your new grafted trachea.

The list at the back of this sheet [Appendix 1] describes all the examinations and tests that you will do during the trial, including the Screening tests.

## **5. HOW WILL BEING IN THE TRIAL AFFECT MY LIFESTYLE?**

When deciding to take part in this trial, you need to consider how the tests and hospital visits will affect your work and family schedules. The number of required inpatient surgeries will mean that there will be extended period of times when you are unable to work or leave the hospital due to the care and follow up required. You should consider if you need transport to get to and from the trial hospital.

You may find the tests and visits are inconvenient and require special effort. In addition, some of the tests and procedures may be uncomfortable. If you decide to take part in the trial, you must attend all the trial visits and follow your trial doctor's instructions. There will be some restrictions on what you can eat and drink the day before each scheduled surgery however, this can be discussed with your doctor during the trial.

Due to the nature of the required surgeries and the stent application, replacements and removal, you will be placed on courses of antibiotics to reduce the risk of a bacterial infection. Due to this, it is advised that you do not drink alcohol during these periods on the trial. Also, due to the number of possible stent replacements and removal procedures there is a possibility of damage to your teeth. If this does occur, this should be discussed with the doctor responsible for your care, who will be able to refer you to the local dental institute Eastman Dental Hospital, UCLH for review and repair at no cost to yourself.

Some of the treatments given to you during the duration of the trial could cause harm to an unborn child or carry a risk to the baby if you are breast-feeding. Due to this, you will be unable to undergo surgeries if you are pregnant and you will be required to use highly effective methods of contraception during the trial and if you are a woman, to undergo pregnancy testing. The trial doctor will explain effective methods of contraception with you.

If you become pregnant during the trial period, you need to inform the trial staff. The pregnancy will need to be monitored and reported to the trial Sponsor.

Before participating you should consider if this will affect any insurance you have and seek advice if necessary.

## **6. EXPENSES AND PAYMENTS**

As part of the trial, you will receive the experimental treatment and all the tests and procedures at no cost to you. You and your insurance company or national health provider will continue to pay for your regular health care.

We will reimburse you for the cost of travelling to your trial visits, upon presentation of receipts. You may receive up to £50 per visit for travel.

However, you will not be paid to take part in the study.

## **7. WHAT ARE THE ADVERSE SIDE EFFECTS I COULD GET FROM THE RESEARCH TREATMENT?**

The process of using a donor trachea and using a patient's own special cells to replace a section of damaged or diseased trachea is a relatively new technique. We need to make you aware of the possible side effects of each of the procedures involved.

The risks associated with the administration of your own cells (used to plant onto the donor trachea scaffold) are considered to be very small on the basis that these will be your own cells that have undergone a limited process in a special laboratory facility before they are re-administered into you. Due to using your own cells in this treatment, you will not need to use any long term immunosuppressant drugs.

The risks associated with implanting the trachea scaffold are as follows:

- Potential for contamination of the scaffold or ability for it to develop a harmful immune response in your body. However, the donor trachea is supplied by the NHS Blood & Transplant service who provide robust compliant tissue sourcing and processing capability and it undergoes sterilisation by irradiation to make sure it is free from any germs. The donor trachea goes through a process known as "decellularisation" which means to remove all the cells from the donor trachea so

that afterwards only the scaffold remains which has a low risk of developing an immune response in your body.

- The new tracheal scaffold graft will be supported by a stent that will keep the tracheal scaffold open. The stent is CE marked and suitable for this use although any stent has a risk of infection and tissue damage.
- Glyaderm will be used to help line the new graft protecting it and assisting in healing. Glyaderm is obtained from human donor skin from the Euro Tissue Bank. The donated skin undergoes viral testing to make sure it carries no viruses and is produced under germ-free conditions. There are no side effects associated with the use of Glyaderm but there is a risk of an allergic reaction in extremely allergic patients due to the potential of traces of some antibiotics such as penicillin used in the process to make it
- Whilst the tracheal scaffold graft integrates and fuses with the surrounding tissue, it will remain vulnerable to infection.
- During the time taken for the tracheal scaffold to integrate with the surrounding tissue, there is the possibility you may suffer from obstruction (blockage) of your airways and as a result develop difficulty in breathing.
- There is a risk of graft failure due to infection and breakdown of its tissue. Tracheal infections will be treated with antibiotics. If the trachea graft breaks down then some of it will have to be removed and a new stent put in place and a tracheostomy (artificial opening into the trachea so that air goes in and out through a tracheostomy tube) may be required. Please discuss this point with your doctor to better understand the potential complications.

There are side effects that you may have that are not listed here and we do not know about.

The trial doctor will ask you at every visit about any side effects that you have had during the period in between trial visits. If you have any new, unusual or worsening symptoms, you should let the trial doctor or their staff know immediately, including between trial visits even if you do not think it is relevant.

## **8. WHAT ARE THE ADVERSE EFFECTS I COULD GET FROM THE RESEARCH PROCEDURES?**

There are side effects which you could get from the procedures performed on you or other medicines you need to take during the trial as listed below:

- The requirement to perform the flexible and rigid bronchoscopies will require the use of a local or general anaesthetic. There is a small risk of a reaction to the anaesthetic which could include feeling sick or vomiting, shivering and feeling cold, confusion and dizziness. There is also a small risk of bleeding and teeth damage as the doctor inserts or retracts the small camera into your windpipe during the bronchoscopy procedure.
- During the bone marrow aspirate procedure to harvest the special cells for the new trachea replacement, there is a risk of excessive bruising where the needle was inserted



and associated pain after the anaesthetic wears off. This pain can be managed with painkillers which can be prescribed by your trial doctor if required.

- The surgical implant of the donated trachea scaffold seeded with your cells will require a general anaesthetic which will put you to sleep during the surgery. After you wake up from your surgery, you could feel a number of side effects which could include feeling sick or vomiting, shivering and feeling cold, confusion and dizziness. There is a small risk that you could experience a serious allergic reaction to the anaesthetic which could lead to anaphylactic shock (this is a severe, potentially life-threatening allergic reaction that can develop rapidly). Your trial doctor and surgery team will know how to treat you if this was to occur. Discuss this with your doctor before consenting into this study. The surgery could also lead to blood clots or other airway obstructions (secretions) in and around the trachea. Drainage will be required to help prevent this.
- Due to the surgery you will be given antibiotics to help combat against possible infections. There is a chance that these infections can still occur which could lead to damage to your new graft and leading to a more aggressive course of antibiotics.

#### **9. WHAT IF NEW INFORMATION BECOMES AVAILABLE?**

During the course of your participation in this study, new information about the treatment being studied may be found. This new information may come about from other similar studies or research being performed. If new information does become available, your trial doctor will inform you of such and organise a visit to site to discuss these findings and whether you should continue in the trial. If you decide not to carry on, your research doctor will make arrangements for your care to continue as per usual standard of care. If you decide to continue in the trial your doctor will provide you with a new information sheet similar to this one and ask you to sign an updated informed consent form to confirm you are happy to continue in the study.

#### **10. WHAT ARE THE POSSIBLE BENEFITS OF TAKING PART?**

We cannot promise the trial will help you but the information we get from this trial may help improve the treatment of people with tracheal malacia or stenosis in the future. We are hoping that this trial proves that the method of using a donor trachea along with a patient's own cells could offer patients an alternative, potentially curative treatment which could eliminate the need for repeated surgeries that have limited success. Even if this new technique is not completely curative you could still benefit from an improvement in your quality of life.

#### **11. WHAT ARE THE POSSIBLE DISADVANTAGES AND RISKS OF TAKING PART**

As well as the possible side effects and discomforts listed above, there may be other adverse effects from participating in the trial that we are not aware of. The visits will take a lot of your time, requiring time away from work and your family.

As this is the first time this new technique has been used, we are unsure if there are any other disadvantages.

## **12. DO I HAVE TO STAY IN THE TRIAL?**

You may choose to stop being in the trial at any time, without giving a reason. Your decision will not affect future medical care you receive. However, we may also contact your family doctor later for information to help understand the safety of the experimental treatment.

The Sponsor, regulatory authority or trial doctor may choose to stop the trial at any time. The trial doctor will explain the reason and arrange for continuing medical care.

Whether the trial is stopped, or you choose to stop the trial early, we ask you to return to the clinic to complete safety trial tests and examinations.

If you withdraw your consent, no more information will be collected about you. But all information collected before you left will still be used for the trial.

## **13. WHAT HAPPENS WHEN THE TRIAL FINISHES?**

After the long term follow up period you will no longer be required to discuss the study with your trial doctor or care team. However, once the results of the trial are available, the trial doctor can provide them to you if you ask for them. However, you will not be told of the results until the whole study has been completed and the data has been reviewed.

The Sponsor of the study, may wish to publish the results of the study in a scientific paper. You will not be identified in any report or publication.

When the study ends, normal care given by your family doctor will resume. You may discuss this with the trial doctor at any time.

## **14. WHAT IF THERE IS A PROBLEM?**

If you have a concern about any aspect of this trial, you should ask to speak to the trial doctor who will do their best to answer your questions on **07464 498 629**. If you remain unhappy and wish to complain formally, you can do this via the Patient Advice and Liaison Service (PALS) on **020 3447 3042** or via email to [PALS@uclh.nhs.uk](mailto:PALS@uclh.nhs.uk). If you wish to speak with someone who is independent of this research trial, or if you have questions about your rights, you can contact the UK Clinical Trials Gateway via email to [ukctg@nih.ac.uk](mailto:ukctg@nih.ac.uk)

Cell Therapy Catapult is the Sponsor for this study and has received funding to conduct this study from an Innovate UK Grant.

Innovate UK will also pay University College London for including you in this trial. This will be to cover any costs associated with the assessments being done.

### **Complaints:**

Complaints will be handled initially by a member of the research team who will try to rectify the problem.

### **Harm:**

In the event that something does go wrong and you are harmed during the research and this is due to someone's negligence then you may have grounds for a legal claim for compensation from Cell Therapy Catapult (the trial sponsor) but you may have to pay your legal costs.

This trial is sponsored by Cell Therapy Catapult and appropriate insurance has been obtained before patient recruitment.

### **15. WILL MY TAKING PART IN THE TRIAL BE KEPT CONFIDENTIAL?**

All information collected during the trial will be kept strictly confidential and any information that leaves the hospital with your personal details such as your name or address will be anonymised. For this trial, you will be given a unique code number which will not include your name or other information that could directly identify you.

Only authorised persons from the study team, the Sponsor and its representatives, regulatory authorities and those responsible for monitoring the quality of the research will have access to your medical records and data collected during the trial. These people will treat your information as strictly confidential. Other doctors in this hospital treating you and your own family doctor will be told of your participation in this study.

The Sponsor will be free to use the coded information and to share with other researchers working on this new technique to better understand tracheal stenosis/malacia and other diseases and conditions.

Data collected (not including your name and address) may be sent to associated research or contracted parties working for the Sponsor or regulatory authorities in countries where the laws do not protect your privacy to the same extent as in your country. In these cases, the Sponsor will take all reasonable steps to protect your privacy.

### **16. INVOLVEMENT OF THE FAMILY DOCTOR**

Your family doctor (or other health care professional) will be notified of your participation in this trial as it may be important that they know you are taking part in a medical research trial.

By signing the consent form, you are giving permission for the trial doctor to notify your family doctor or other specialists involved in your care.

#### **17. WHAT WILL HAPPEN TO ANY SAMPLES I GIVE?**

After your trial samples have been analysed, they will stay in a freezer or refrigerator on behalf of Cell Therapy Catapult for at least 3 months after the trial has been completed, but in principal no longer than 1 year before being destroyed. The reason for keeping the samples up to 1 year after the end of the trial is that sample re-analyses may be needed.

Additionally, to gain more insight, understanding and knowledge about the nature of Tracheal stenosis/malacia and to further develop potential treatments for these particular medical conditions, we may wish to keep some samples for more than 1 year.

You will be asked to sign a separate consent [Appendix 3] to allow the samples to be kept for longer than 1 year for any intended future use.

#### **18. WILL ANY GENETIC TESTS BE DONE?**

No genetic tests will be carried out during this study or after it has finished.

#### **19. FURTHER INFORMATION AND CONTACT DETAILS**

We hope this information is sufficient to decide whether you want to take part in the trial. If you decide to take part, you must sign the consent forms. If you have any questions about this study, please ask the trial team before signing the consent forms.

If you have any questions or medical problems during the study, or if you believe that you have suffered any injury as a result of taking part in this study, please contact one of the trial clinicians on **07464 498 629**.

## **20. APPENDIX 1 - TRIAL TESTS AND PROCEDURES**

- 1) Informed Consent: If you choose to, you will sign consent before starting the trial.
- 2) Medical History & Eligibility: The doctor will ask you questions and report prior medical history.
- 3) Physical Exam: The doctor will examine you and record your blood pressure, temperature and your breathing.
- 4) Electrocardiogram (ECG 12-lead): a test to measure your heart.
- 5) Height and Weight: the nurse will measure your height and weight.
- 6) Bone Marrow Aspirate: This will be performed to collect the required cells to multiply and use for the new tracheal graft.
- 7) Blood tests: tests to check for your safety.
- 8) Urine tests: tests to see how well your kidneys are working, and pregnancy tests if applicable.
- 9) CT Scan: used so that a complete image can be obtained of your trachea both before and after the replacement surgery.
- 10) Flexible/Rigid Bronchoscopy: used to look inside the lungs airways.
- 11) Pulmonary function tests: tests carried out to check on how well your lungs and windpipe function.
- 12) Quality of life questionnaires: A short questionnaire to capture how well you feel.

Schedule of Activities

Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14
Day/Week/Month	-8w	-6w	-2w	D0	D1	D2	D3	D7	D14	D21	D28	D35	D42	D49/ Wk7
Study Phase	Screening + Manufacture of IMP			Surgery (on D0) plus follow up										
Physical Examination	X	X	X	X	X	X	X	X	X	X	X		X	
Vital Signs	X	X	X	X	X	X	X	X	X	X	X		X	
ECG	X		X	X	X	X	X							
Echocardiograph	X													
FEES/Stroboscopy	X								X		X		X	
Serology	X	X												
HLA Antibodies	X										X			
Pregnancy Test	X													
Biochemistry/haematology	X		X	X	X	X	X	X	X	X	X		X	
Pulmonary function tests	X		X	X		X			X		X			
CT scan	X				X								X	
Rigid Bronchoscopy under GA	X			X										

Visit	V1	V2	V3	V4	V5	V6	V7	V8	V9	V10	V11	V12	V13	V14
Day/Week/Month	-8w	-6w	-2w	D0	D1	D2	D3	D7	D14	D21	D28	D35	D42	D49/ Wk7
Study Phase	Screening + Manufacture of IMP			Surgery (on D0) plus follow up										
Flexible bronchoscopy under sedation					X	X	X		X		X			
Bone marrow aspirate for harvest of autologous MSCs		X												
Laparoscopy to mobilise omentum				X										
Surgical Implant of IMP				X										
QOL questionnaires	X		X	X				X	X	X	X			
Inpatient hospitalisation		X		X	X	X	X	X	X	X				

Visit	V15	V16	V17	V18	V19	V20	V21	V22	V23	V24	V25	V26	V27	V28
Day/Week/Month	D56/ Wk8 +/- 1wk	D63/ Wk9	D70/W k10	D77/W k11	D84/ Wk12	D91/ Wk13	D98/ Wk14	D105/ Wk15	D112/ Wk16	Wk24 M6	Wk32 M8	Wk52 M12	Wk104 M24	Wk260 M60
Study Phase	Surgery (on D0) plus follow up									Long term FUP				
Physical Examination	X	X	X		X		X		X	X	X	X	X	X
Vital Signs	X	X	X		X		X		X	X	X	X	X	X
ECG	X													
FEES/Stroboscopy									X		X			
Biochemistry/haematology	X	X	X		X		X		X	X	X			
Pulmonary function tests including flow volume loops	X	X	X		X		X		X	X	X	X	X	X
CT scan									X	X	X	X	X	X
Rigid Bronchoscopy under general anaesthetic	X								X	X	X			
Flexible bronchoscopy under sedation			X		X		X							
Stent placement / replacement / removal	X								X	X				
Inpatient hospitalisation	X								X	X				



## APPENDIX 2 – INFORMED CONSENT FORM

**Protocol title:** A Phase I open-label study to assess the safety, tolerability and efficacy of a novel tracheal replacement consisting of a tissue-engineered decellularised tracheal scaffold with seeded autologous mesenchymal cells in subjects with severe tracheal stenosis or malacia.

**Please put your initials against each statement to indicate you consent to the following and by signing below I consent that:**

I have read, or have had read to me, and I understand the Participant Information Sheet.	
I have been given sufficient time to consider whether or not to participate in this trial and have had the opportunity to ask questions. I am satisfied with the answers I have been given regarding the trial and I have a copy of this consent form and information sheet	
I understand that taking part in this trial is voluntary (my choice) and that I may withdraw from the trial at any time without giving any reason and without this affecting my medical care or legal rights.	
I understand my responsibilities as a trial participant.	
I understand that Cell Therapy Catapult, trial staff and others may have access to my medical and personal information, as described in this form	
I agree with collection, processing, reporting and transfer of personal and sensitive data, as described in this form	
If I decide to withdraw from the trial, I agree that the information collected about me up to the point when I withdraw may continue to be processed.	
I understand that the trial doctor will need to continue to report information about me until the end of this trial to learn about the safety of the experimental treatment	
I understand that I need to use applicable methods of contraception during the first 6 months of this trial.	
I understand that my samples may be retained for up to 1 year after the trial has completed	
I understand the compensation provisions in case of injury during the trial.	
I know who to contact if I have any questions about the trial in general.	

### Declaration by participant:

I hereby consent to take part in this trial.

Participant's name:

Signature:

Date:

### Declaration by member of trial staff:

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it. I believe that the participant understands the trial and has given informed consent to participate.

Trial doctor's name:

Signature:

Date:

## **21. APPENDIX 3 - PROLONGED STORAGE AND AUTHORISATION FOR USE OF BIOLOGICAL SAMPLES FOR MEDICAL SCIENTIFIC RESEARCH**

As described in the Information sheet, we would like to ask you if University College London Hospital can keep any remaining biological samples to use for other tests to learn more about tracheal stenosis and malacia [disease] and other diseases.

You can change your mind about permitting the use of your biological sample(s) at any time. If you wish to withdraw your consent for the sample(s) to be stored for future use, please advise trial team clinicians on **07464 498 629**, who will contact University College London Hospital. Once your request has been received, University College London Hospital will have 30 days to destroy any remaining biological sample, and you will be advised in writing that this has been done. If some of the sample has already been used, it will not normally be possible to withdraw consent for the use of any results already generated.

Your biological sample(s) will be stored anonymously and your identity will be protected at all times. Your biological sample(s) can be identified only by a code and procedures will be in place to keep these codes confidential and private.

If you agree, specific details about you will be sent to Cell Therapy Catapult; these details will be:

- age when the biological sample(s) was (were) taken
- ethnic group

All of the information will be provided anonymously and your identity will be protected at all times in the same way as for the biological sample(s).

Your biological sample(s) will only be used for research by University College London Hospital and not by any other third party.

**Informed consent form** Prolonged Storage and Authorisation for Use of Biological Samples for Medical Scientific Research

**Protocol title:** A Phase I open-label study to assess the safety, tolerability and efficacy of a novel tracheal replacement consisting of a tissue-engineered de-cellularised tracheal scaffold with seeded autologous mesenchymal cells in subjects with severe tracheal stenosis or malacia.

**Please put your initials against each statement to indicate you consent to the following**

By signing below, I show that:

I have read and understood this information about prolonged storage and authorisation for use of biological samples for medical scientific research.	
I have been given the opportunity to ask questions, and they have been answered to my satisfaction.	
I consent to my biological samples to be sent to University College London Hospital and to be stored there for the purposes of medical scientific research.	
I consent to my biological samples being used for medical scientific research, until there is no sample left subject to ethical approval.	
I consent to the specific details stated in the information letter being forwarded to University College London Hospital.	

I understand and agree that the left-over biological sample(s) (such as, but not restricted to biopsy, blood samples and urine samples) obtained from me for University College London Hospital trial D-00173-CT2013002 could be used for disease specific research, until there is no sample left	
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**Declaration by participant:**

I hereby consent to take part in this trial.

**Participant's name:**

Signature:

Date:

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**Declaration by member of trial staff:**

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the trial and has given informed consent to participate.

**Researcher's name:**

Signature:

Date: