Participant Information Sheet

THE FAMILIAL GASTRIC CANCER STUDY

We would like to invite you to take part in a research study. Before deciding whether to take part, you need to understand why this research is being done and what it would involve for you. Please take time to read the following information carefully and talk to others about the study if you wish. Please ask us if anything is not clear or if you would like more information.

Part 1 tells you the purpose of this study and what will happen to you if you take part.
Part 2 gives you more detailed information about the conduct of the study.

Part 1

What is the purpose of the study?
We would like to try and find out more about the different causes of gastric (stomach) cancer to improve how we screen for them and how we treat people affected by them. We particularly wish to identify those families who fit the criteria for Hereditary Diffuse Gastric Cancer (HDGC) and provide long term follow-up of CDH1 positive mutation carriers. Some people have a family history of gastric cancer and do not have the mutation in the CDH1 gene so for these families we would like to search for new genes that can help us understand the disease better. We hope that this will enable local genetic centres to provide more accurate advice to families who have a history of gastric cancer and may be undergoing clinical genetic testing.

We would like to invite people who meet criteria for Hereditary Diffuse Gastric Cancer and have the CDH1 mutation to participate in the **"Hereditary Diffuse Gastric Cancer Registry"** part of the study**.** This will help us to improve our understanding of this condition as well as the impact of genetic testing, endoscopy and surgery on people's physical and mental wellbeing and health, and their quality of life. To do this we will ask you to fill out a set of brief quality of life and personality questionnaires at the beginning of your treatment, and repeat them at regular intervals during study follow. We hope that this information will help to improve the treatment and information given to individuals and families in the future.

We would also like to continue to develop an effective endoscopy screening and monitoring programme using new techniques for individuals at high risk of stomach cancer. We hope that this will help individuals make well informed choices about their own treatment options.

Why have I been invited?
You have been invited to participate in this study because you have a strong family history of gastric or lobular breast cancer, have two or more relatives with stomach cancer one diagnosed with diffuse gastric cancer, or have one relative with diffuse gastric cancer under 40 years.

Do I have to take part?

Participating in this study is completely voluntary. If you decide to participate you will be asked to sign an Informed Consent Form to show that you understand and agree to take part. However you are still free to change your mind and leave the study at any time without giving a reason. This would not affect the standard of care you receive in the future.

What will happen to me if I take part?

If you agree to participate in the study, you will be asked to sign the Consent Form at the end of this document and return to the Research Nurse.

When you attend your clinic or endoscopy appointment at Addenbrookes Hospital the Research Nurse will explain the research in more detail and there will be opportunity ask questions. We will ask you to re-sign the Consent Form at this visit. However, if your clinical care is provided elsewhere the Research Nurse will arrange a telephone consultation with you to explain the research study in more detail and to give you the opportunity to ask questions. You will be given a copy of the Consent Form for reference.

If you decide to take part you will be asked to give us some details about any cancers running in the family to the best of your knowledge. With your permission we may request additional information your clinicians about your family history including confirmations of cancer pathologies and your own medical history including of genetic test results. This will be done on the telephone, in person or in writing. We will also ask you to give permission for the research team to access pathology samples from yourself (if you have had an operation or biopsies taken in the past) or deceased members of your family who had cancer. These samples are routinely stored in the pathology department of the hospital at the time of an operation or procedure.

We may ask you to contact some of your relatives to see if they would be willing to help us with our research. If they are interested in knowing more about the research we may ask you to forward your relative a ‘permission to contact slip’ to complete and return to the Research Nurse in the pre-paid envelope which we will provide. The Research Nurse will only contact your relative on receipt of their signed permission slip. All information will remain strictly confidential and will be anonymised i.e. all information that could identify you will be removed, before being given to researchers.

We will ask you to give us a blood (approximately 4 teaspoons in total) or a saliva sample on up to two occasions during the duration of the study. A blood or saliva sample may be collected at the same time as your research endoscopy, if the procedure is being done Addenbookes Hospital. Otherwise, a saliva kit with instructions will be sent to you in the post. The sample may be analysed in the research laboratory and help us look in more detail for alterations in genes that might be linked to cancer. If you have already had a clinical genetic test then we may contact the relevant genetic laboratory to request a DNA (extracted genetic material) sample for research purposes instead of collecting a blood or saliva sample from you. All samples will be anonymised ie. all information that could identify you will be removed

Research endoscopy

Your GP or clinician may feel it is necessary for you to have an endoscopy examination of your stomach which would be part of your routine clinical care. However, we would be able to offer this as part of the research study. We would also like to continue to develop an effective endoscopy screening and monitoring programme using new techniques for individuals at high risk of stomach cancer. Your research endoscopy will be carried out in Cambridge where we have the interest and expertise in familial gastric cancers on a specialist gastric cancer research endoscopy list. However, if it is not possible for you to come to Cambridge then your clinician or GP may be able to arrange for your endoscopy to be done your local hospital, under guidance from Cambridge. It will not be possible to reimburse your travel expenses for travel to Cambridge.

The endoscopy procedure will last approximately 30 minutes to allow for careful inspection of the stomach and to allow time to take approximately 30 biopsy samples from your stomach. These will be examined to look for changes in the cells lining your stomach. This will include the standard 24 clinical biopsies plus additional research biopsies. The clinical biopsies will be analysed by a hospital pathologist and the results will help to decide on your clinical care. Your GP will be informed of the endoscopy results. We would also like to store the biopsies viewed by the pathologist and some additional biopsies for use in cell culture as well as research relating to stomach cancer as new strategies develop. Photographs will be taken during the procedure which will also be recorded.

Genetic analysis of the research samples we collect during your endoscopy may help us to understand which areas in your stomach might change over a period of time. This may be done when you have regular endoscopies or if have you decided to have your stomach removed at some point in the future.

Around the time of each endoscopy appointment we will ask you complete a set of mental wellbeing and quality of life questionnaires. These will be sent to you in the post or done anonymously online in the fortnight before you attend the hospital or at the hospital appointment. These questionnaires will help us to assess the impact of undergoing an endoscopy on your health, wellbeing and quality of life.

Optional research endoscopy

In addition to your standard research endoscopy we would also like to incorporate new imaging techniques as they become available. One technique we would like to use is a probe-based confocal laser endo-microscopy to inspect your stomach lining. This may help provide further information about any changes in the stomach at the cellular level in the early diagnosis of diffuse gastric cancer. The procedure would be done immediately after your standard research endoscopy and take approximately an additional 5-10 minutes. However, please note that this is an optional procedure and which will be discussed with you in more detail and additional consent obtained if you agree to participate.

During the endoscopy examination, we will use a special microscope which enables us to identify changes at cellular level. This is called Cellvizio and is performed by inserting a tiny camera down the endoscope biopsy channel. The procedure requires intravenous injection of a small dose of a dye called fluorescein. Fluorescein is a safe drug already used in other medical diagnostic tests in ophthalmology. Cellvizio has been shown to detect abnormal

dysplastic cells in the oesophagus and stomach with a high degree of accuracy, but it has not been widely tested in diffuse gastric cancer. The device has been approved by the UK regulatory authorities and is CE marked however, it is not currently part of standard care.

The use of fluorescein during the Cellvizio video procedure can be associated with transient and minor side effects such as nausea and vomiting. Temporary yellowish discoloration of the skin and eye may occur following the intravenous injection of dye but it should disappear within several hours. Allergic reactions (skin rash and itching) to the fluorescein are rare and they respond well to anti-histamines or steroids. More severe side effects such as anaphylactic shock, cardiac arrest, respiratory distress or seizures are extremely rare.

Hereditary Diffuse Gastric Cancer Registry

Participants who meet the criteria for Hereditary Diffuse Gastric Cancer and who have undergone clinical genetic testing will be invited to take part in the '**Hereditary Diffuse Gastric Cancer Registry'.** If you consent we will collect information about your genetic testing and results from your clinician which will be kept on the research database maintained in Cambridge. We would also like to collect information from you about your mental health and wellbeing, nutritional and any lifestyle changes you may make following genetic testing, endoscopy and before / after stomach removal surgery. This information will help us to measure the impact that genetic testing, endoscopy surveillance versus surgery has on your mental wellbeing and on-going quality of life. The information will be collected using wellbeing and quality of life questionnaires either in person, by post or through an anonymised internet portal.

If you decide to have an operation then we would like your consent to have any excess tissue from your stomach to be stored in Cambridge for research. This would only be after the routine examination of your stomach by the pathologist at your local hospital and would only include the tissue in excess to the requirements of the normal process. It will be used to look for any abnormalities of your stomach lining and to help with our studies of hereditary diffuse gastric cancer, including culturing the cells.

What are the possible disadvantages and risks of taking part?

Blood samples may cause momentary discomfort and occasional bruising. When possible we will try to minimise the discomfort by taking the research blood sample at the same time as any routine clinical blood samples or at the research endoscopy procedure.

There are well known risks associated with Upper GI endoscopy and your doctor will talk you through these risks and assess that you are fit to receive the procedure. You may experience discomfort or bloating during the procedure and, have a sore throat afterwards. You will already be having 24 (approx) biopsies taken during the procedure for your clinical management. As the associated risk of taking these samples is very small (less than 1 in 10000 risk of a serious problem) there will be negligible extra risk to you by taking an additional six biopsies for research. It is also possible that due to your discomfort, or technical reasons, that we cannot complete the endoscopy and do not get the samples that we need. Your safety would, however, be of utmost importance during the endoscopy.

The use of fluorescein during the **optional** Celivizo video procedure can be associated with transient and minor side effects such as nausea and vomiting. Temporary yellowish discolouration of the skin and eye may occur following the intravenous injection of dye but it should disappear within several hours. Allergic reactions (skin rash and itching) to the fluorescein are rare and they respond well to anti-histamines or steroids. More severe side effects such as anaphylactic shock, cardiac arrest, respiratory distress or seizures are extremely rare. If you are known to have severe asthma or fluorescein allergy you will not have this procedure.

What are the possible benefits of taking part?
There is no guarantee that you will benefit from taking part in this study. We hope the information we get from the research will allow us to improve the care offered to patients and their families affected with stomach cancer or who are considering having their stomach removed in the future. Your research samples and data are not intended to be used for your own diagnosis or treatment and therefore no individual results will be returned to you.

We do not plan to routinely feedback to you any genetic information from your research samples. However, you may choose whether you wish to be informed about any incidental findings or inherited gene mutations of known clinical significance for you and other family members. In this instance your local Genetic Centre will provide you with more information regarding any findings. No genetic information linked to your name will be accessible by any third party without ethical approval and your written consent.

Will I be paid for my participation in the study?
You will not receive any payment for participating in this study and we are unable to reimburse you for any expenses incurred or any travel expenses by your participation.

Will my taking part in the study be kept confidential?
Yes. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.

If you have found this information interesting and you are considering participation, please read the additional information in **Part 2** before making any decision.

Part 2: Study Conduct

What if new information becomes available?
We continuously review the latest scientific reports so if new evidence comes to light we might consider amending our study design. If this occurred, we would explain the changes to you and if you wish to continue may ask you to sign a new Informed Consent Form.

What if I decide I no longer wish to participate in the study?
If you do decide to take part in this study, you are free to leave the study at any time and you do not have to give a reason for your decision. This will not affect your current or future medical care in any way. If you withdraw from the study, we will retain any anonymised tissue samples, DNA samples, data and results of analyses that we have obtained up until the time of your withdrawal. Any information already provided, or results from tests already

performed on you or your samples will continue to be used in the study unless you indicate your wishes otherwise. However, all stored data and samples will be anonymised.

What if there is a problem?

If you have a concern about any aspect of this study you should ask to speak to the researchers who will do their best to answer your questions (Sue Richardson, Research Nurse, 01223 763994). The Addenbrooke's Hospital Patient Advice and Liaison Service (PALS) is also available to offer advice or support and to listen to any concerns (01223 216756). If you remain unhappy and wish to complain formally then you can do this through the NHS Complaints procedure, details can be obtained from the hospital.

Will my taking part in this trial be kept confidential?

Yes. All information collected about you as a result of your participation in the study will be kept strictly confidential. Once you have agreed to participate in this study you will be allocated a unique study number which will be used on all your study documentation and samples. This number will be linked to your personal information; however you will only be identified by this unique number. Your personal and medical information will be kept in a secure research study database on password protected computers and treated in the strictest confidence. The study meets the requirements of the Data Protection Act 2018 and the General Data Protection Regulation (GDPR) and also adheres to the NHS Code of Confidentiality. Data will only be accessible by the Research team, the multidisciplinary clinical care team, the sponsors and / or members of the NHS Trust Research and Development for audit and monitoring purposes.

Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge are the joint sponsors for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. The sponsor organisations will keep identifiable information about you for 10 years after the study has finished

Your rights to access, change or move your information are limited, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible.

You can find out more about how we use your information by contacting https://www.cuh.nhs.uk/corporate-information/about-us/our-responsibilities/looking-after-your-information and https://www.information-compliance.admin.cam.ac.uk/data-protection/general-data-protection-regulation. Further details specific to the study are also available via the following URLs:

https://www.mrc-cu.cam.ac.uk/research/rebecca-fitzgerald/clinical-studies/Familialgastriccancerstudy orhttp://www.cancerresearchuk.org/about-cancer/trials/a-study-to-find-genetic-causes-of-stomach-cancer

https://www.cuh.nhs.uk/familial-gastric-cancer-study

Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge will collect information from [you and/or your medical records] for this research study.

The sponsors will use your name, NHS number and date of birth to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Individuals from Cambridge University Hospitals NHS Foundation Trust, the University of Cambridge and regulatory organisations may look at your medical and research records to check the accuracy of the research study. The only people in the sponsor organisations who will have access to information that identifies you will be people who need to contact you to audit the data collection process. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Cambridge University Hospitals NHS Foundation Trust and the University of Cambridge will keep identifiable information about you from this study for 10 years after the study has finished.

When you agree to take part in a research study, the information about your health and care may be provided to researchers running other research studies in this organisation and in other organisations. These organisations may be universities, NHS organisations or companies involved in health and care research in this country or abroad.

This information will not identify you and will not be combined with other information in a way that could identify you. The information will only be used for the purpose of health and care research, and cannot be used to contact you or to affect your care. It will not be used to make decisions about future services available to you, such as insurance. This means that I the information collected about you will be used to support other research in the future, and may be shared anonymously with other academic and commercial researchers external to the project within the UK and beyond.

If you consent we will inform your GP of your participation in this study who will be sent the results of your endoscopy as per the normal practice.

What will happen to the results of the study?

We will store the anonymised results of the genetic analysis indefinitely in research databases which will be accessible to researchers around the world. We will share the results of the genetic analysis in an anonymised form, and the data may be used in future research or for other development purposes.

The results from analysis will be presented and discussed at scientific meetings and conferences. We will write scientific papers in medical journals explaining to others what we have learnt from our studies. In the long-term any discoveries from this research will be used to help improve clinical advice given to patients. Personal identities will not be revealed in any publications, all data will be anonymised. If you would like to obtain a copy of any articles published please contact Sue Richardson, Research Nurse, who will be able to arrange this for you.

Who is organising and funding the trial?
This study is jointly sponsored by Cambridge University Hospitals NHS Foundation Trust and The University of Cambridge. It is being supported by a grant from Cancer Research UK and by the Cambridge Cancer Centre.

Who has reviewed this trial?
All research within the NHS is reviewed by an independent group of people called a Research Ethics Committee, to protect your interests. This study has been reviewed and given favourable opinion by the East of England - Cambridge South Research Ethics Committee.

Further information and contact details
If you would like further information on this study or have any queries relating to the study please contact Sue Richardson at the following address:

Susan Richardson
Research Nurse and HDGC Coordinator
University of Cambridge
Dept. of Oncology
Box 279 (S4)
Addenbrooke's Hospital
Hills Road
Cambridge CB2 0QQ

Tel: 01223 763994
Email: susan.richardson@addenbrookes.nhs.uk

Thank you for taking the time to read this information sheet.

INFORMED CONSENT FORM

Study Title: Familial Gastric Cancer Study **Participant Study Number:**

If you agree with each sentence below, please initial the box

		INITIALS
1	I have read and understood the Participant Information Sheet version 13, dated 29/11/2017 for the above study and have had the opportunity to consider the information and ask questions and discuss the study.	
2	I understand that my participation in this trial is voluntary and that I am free to withdraw at any time, without giving a reason and without my medical care or legal rights being affected.	
3	I understand that samples, which will be anonymised, and specific personal data will be securely stored by the research team at the Department of Oncology and Strangeways Research Laboratory in accordance with the Data Protection Act. I understand that relevant sections of my medical notes and data collected during the study may be looked at by responsible individuals from the research team, regulatory authorities or the NHS Trust where it is relevant to my taking part in this research. I give permission for these individuals to have access to my records.	
4	I consent to the Research Nurse obtaining copies of my medical notes and pathology reports, from the cancer registry, the relevant hospital or genetic centre. All this information will remain confidential.	
5	I consent to the research team obtaining pathology samples and previously extracted DNA from the relevant hospital or genetic centre for myself and deceased family members.	
6	I consent to my personal and family information, provided to the Research Nurse, being recorded for the study and to completing the mental wellbeing and quality of life questionnaires.	
7	I agree to my GP and hospital consultant responsible for my clinical care being informed of my participation in the research study.	
8	I agree to the collection and storage of blood, saliva and tissue samples for the Familial Gastric Cancer Study and for future research studies which may include cell culture.	
9	I consent to the research team collecting additional research biopsy samples when I have my HDGC endoscopy if I chose to have one, and to the storage of images recorded during the procedure. These research biopsies will be in addition to any clinical biopsies taken during the endoscopy procedure.	
10	I understand this research may include looking at the whole DNA sequence of my blood, saliva or tissue samples.	
11	I understand that my anonymised coded genetic information may be held indefinitely on international databases with controlled access for researchers worldwide.	
12	I agree that the researchers can re-contact me in the future, if necessary.	
13	I agree to participate in this trial.	

OPTIONAL **INITIALS**

		YES	NO
14	If you meet the criteria for Hereditary Diffuse Gastric Cancer and have undergone clinical genetic testing you are invited to take part the '**Hereditary Diffuse Gastric Cancer Registry'.** I consent to information about my genetic testing and results to be stored on the register held on the research study database maintained in Cambridge.		
15	If I have a gastrectomy I consent to the research team obtaining my stomach, in the form of pathology specimens which will be stored in Cambridge. This would only be after the routine examination of my stomach by the pathologist and would only include the tissue in excess to the requirements of the normal process.		
16	I agree to endoscopic examination using a probe-based confocal laser endo-microscopy to inspect my stomach lining and to the storage of images from the procedure. This endoscopic examination will be done at the same time as my HDGC research endoscopy.		
17	I wish to be informed if research on my blood, saliva or tissue DNA reveals genetic information that might affect me or members of my family. If, due to exceptional circumstances, I am unable to receive the information I give permission for this to be shared with my next of kin. This will be done via the NHS counselling service.		

Name of patient	Signature	Date
Name of person taking consent	Signature	Date