[Print on Local Trust headed paper]

Patient Information Sheet – OPTIMA Study

Optimal **P**ersonalised **T**reatment of early breast cancer us**i**ng **M**ulti-parameter **A**nalysis

We would like to invite you to take part in a research study called OPTIMA

- This sheet explains why we are doing this research and what it would involve for you.
  - **Part 1** explains what will happen if you take part.
  - **Part 2** gives you more information about the study.
- A member of the research team will go through this information sheet with you.
- Please take time to read it carefully and talk it over with friends, your family and your GP if you wish. Please ask questions if there is anything that is not clear, or you would like more information.
- Joining this study is entirely up to you. If you choose not to take part, we will respect your decision and it will not affect the quality of your medical care in any way. Take your time to decide whether or not you wish to take part.

A short summary of OPTIMA

- People with your type of breast cancer are often advised to have chemotherapy
- Research suggests however, that not all people will benefit from chemotherapy. Some may do just as well with hormone treatment alone.
- We want to improve our decision making so that we give chemotherapy only to those people who could benefit from it.
- Tests have been developed to try to improve decision making. These tests tell us about how a tumour may behave in the future.
- The tests use a sample of the tumour already removed by the surgeon.
- We want to find out whether we can use one of these tests to safely and effectively make decisions about who should have chemotherapy.
- Everyone who takes part in this study will receive hormone therapy. We will use the test to decide who will receive chemotherapy.

You can also find information about OPTIMA on our website:
optimabreaststudy.com

Part 1

What is the purpose of this study?

We give chemotherapy and hormone treatment to many people as part of their breast cancer treatment. This is to reduce the risk of the cancer coming back in the breast or elsewhere.

We only offer chemotherapy to some patients with oestrogen receptor (ER) positive and HER2 negative disease. This is the type of breast cancer you are being treated for. Mostly we make decisions about advising chemotherapy or not, by looking at the tumour with a microscope and measuring its size and whether the lymph nodes are affected. These methods are not as good as we would like as we end up treating some people with chemotherapy who we think do not need it. Chemotherapy can have unpleasant short and long term side-effects. What we need is a better way to find out which patients are likely to benefit from chemotherapy and who could safely avoid it.

There are now several tests which give more accurate information about individual tumours than traditional measurements. The tests use a sample of the tumour already removed by the surgeon. We need to do more research into how best to use the tests. Some research that has already been done suggests that the tests can predict whether a tumour will benefit from chemotherapy.

The aim of this study is to investigate whether we can use a test called "Prosigna" to make safe and accurate personal decisions about chemotherapy. The study is running across the UK in over 100 hospitals and in other countries. We expect 4,500 people to take part**.**

Can you explain the test?

In recent years there has been a lot of research into new ways to understand breast cancer. Several tests have been developed that look at the genes in the breast cancer cells. The tests measure how active some of these genes are. They are sometimes called multi-parameter assays. They should improve the selection of breast cancer treatment by providing accurate information about individual tumours.

The test we are using for this study is called Prosigna. An American company developed it; you can look at their website at www.nanostring.com for more details. The test uses a specialist machine to look at the activity of 50 genes in the tumour cells.

The Prosigna test has been developed since 2009. It has been used on stored breast cancer samples from patients who were treated many years ago and for patients given chemotherapy before their surgery. The results suggest that the test could show how well chemotherapy works for different breast cancer types.

Tests like Prosigna are now widely used for patients whose cancer has not spread to lymph nodes. However, more research is needed to help decide how best to use the tests for patients with cancers that involve lymph nodes. We looked at the Prosigna test in the first part of this research involving 300 patients. Our results showed that further research into Prosigna would

be worthwhile, so we are now performing this larger study. You can look at a summary of our earlier research on the following website: tinyurl.com/y8dqo2zx

What will happen if I join OPTIMA?

The OPTIMA Trial Office will ask your medical team to send us some basic information about you. They will ask your doctor to send a sample of your tumour to a laboratory that will carry out the Prosigna test.

OPTIMA is what is known as a 'randomised controlled trial'. We do this type of study when doctors want to find out which treatment approach is better by comparing them in as fair a way as possible. The best way to compare the two approaches in OPTIMA is to use each of them in two similar groups of patients and compare the results. We can then be sure that any differences in results are because of the different treatment approaches, and not because the groups of patients were different from each other in some other way.

To make sure that the two groups of patients are as similar as possible, we put everyone who agrees to take part in this study into one of the two groups by chance: a process called randomisation. Randomisation is done by the OPTIMA Trial team using a computer. You will have an equal chance of being put into either of the following groups:

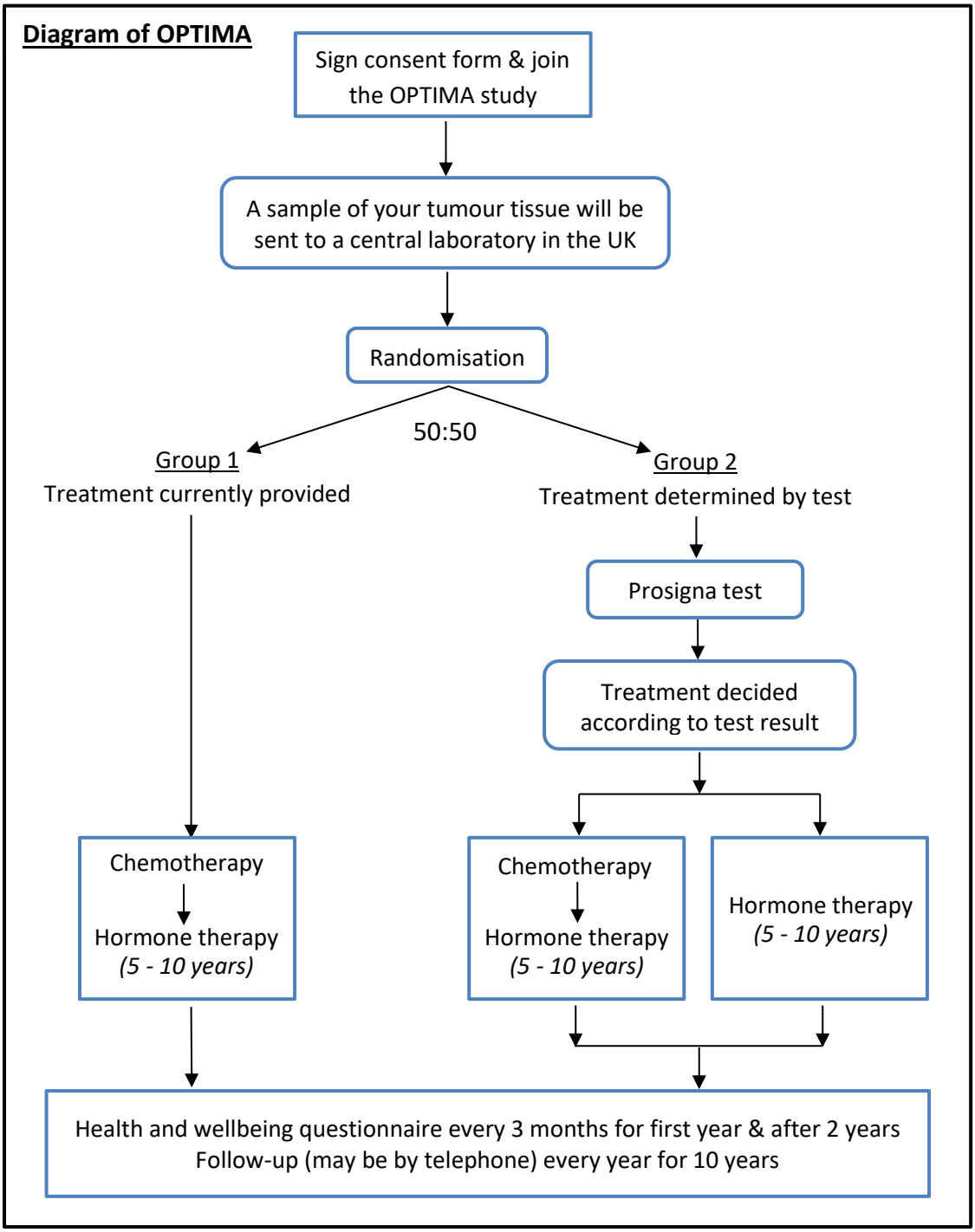
Group 1: The Prosigna test will not decide your treatment. Everybody is treated with chemotherapy followed by hormone treatment. This is the usual treatment for your type of breast cancer. Your medical team will send a sample of your tumour tissue to our laboratory where it will be examined and stored. Your team will tell you after two to three weeks when you will start chemotherapy.

Group 2: The Prosigna test will decide your treatment. Your medical team will send a sample of your tumour tissue to our laboratory for testing. The Prosigna test will be performed. Depending on the result of the test, you will start chemotherapy followed by hormone treatment OR receive hormone treatment without chemotherapy. Most patients in Group 2 will not have chemotherapy and can go straight to hormone therapy.

If you do receive chemotherapy we will not tell you or your doctor whether you are in Group 1 or Group 2. This means that you will not know if the Prosigna test decided your treatment. You may have chemotherapy because you are in Group 1 (usual treatment) or you may be one of the patients in Group 2 for whom the Prosigna test predicts a benefit from chemotherapy. We do this because we do not want the test result to influence either you or your doctor. This helps us to fairly compare Group 1 and Group 2.

It usually takes between two and three weeks to decide your treatment if you join OPTIMA. We know that it is safe to wait this length of time.

The diagram below is to help you understand how OPTIMA works.



How long will treatment last?

Chemotherapy is given as an injection into the vein usually every three weeks over three to five months. We have asked your doctor to discuss chemotherapy and the possible side effects with you. This is so that you can start treatment as soon as possible if you are to have chemotherapy.

All patients will receive hormone therapy because we know that this is a very important part of treatment for patients with your type of breast cancer. Your hormone treatment is a daily tablet, usually for ten years.

If you are a woman and have not had your menopause we will also ask you to have monthly hormone injections for several years. These will stop your menstrual periods and are part of your hormone treatment. New research shows that the injections improve the results of hormone tablets. We will do this even if with chemotherapy your periods stop because sometimes they return. The reason for giving the injections is to make sure that everyone in the OPTIMA study receives the best treatment and the same hormone treatment.

During and after your treatment your doctor will follow you up to assess your progress. This will be once a year for ten years. For some of the longer term follow up, you may find it more convenient for the research doctor or nurse to contact you by telephone or email instead of asking you to come to the hospital. Most patients will have regular mammograms for at least five years. Mammograms are part of usual care. We will ask your doctors how you are, including your GP. We will also collect information about your health from central healthcare registries. As well as finding out about your health, we will ask you to fill in questionnaires about your experience of the study and its impact for you at the time you join and then after 3, 6, 12 and 24 months.

Why have I been invited to take part?

We are asking people with breast cancer who would usually receive both chemotherapy and hormone treatment to take part. This includes people with cancer which has spread to the lymph nodes and some people with larger tumours but no lymph node spread. The information we have suggests that the Prosigna test, like similar tests, works well for such people but we need better information before we can be confident enough to offer testing to all patients.

Do I have to take part?

No. It is entirely up to you to decide whether to take part. If you change your mind, you can withdraw at any time without giving a reason.

Your standard of care will not be affected in any way if you do not enter the study.

What are the side effects of any treatment received when taking part?

Some side effects may occur with any cancer treatment. Your doctor will discuss these with you. If you join the study and have chemotherapy, the side-effects would be exactly the same as if you were treated outside the study. This is because standard chemotherapy is used in the OPTIMA study.

You may experience symptoms of the menopause if you have injections to stop your menstrual periods. These symptoms may go away when you stop the injections, but this depends on how old you are. Many women will get these symptoms anyway if they have chemotherapy. If your periods stop early because of the injections, you are more likely to develop osteoporosis (thinning of the bones) as you get older. This is also true for women whose periods stop because of chemotherapy. We often prescribe osteoporosis medicines as part of cancer treatment. This helps protect against both breast cancer and osteoporosis. Osteoporosis medicines need to be combined with the injections for younger women to work properly.

All other treatment is the same whether you are in the study or not.

What are the possible benefits of taking part?

If you are in the group having the Prosigna test, the results may predict that you are unlikely to benefit from chemotherapy. This means that you would avoid chemotherapy and its possible side effects. You would start hormone treatment straight away. The test could also predict that you should have chemotherapy.

We are doing this study to work out who can safely avoid chemotherapy and go straight on to start hormone treatment, and who would benefit from both treatments. We believe that using tests to help make decisions about chemotherapy treatment will become part of usual NHS practice in the future. When this happens many fewer people will need to go through chemotherapy so many people will be spared unnecessary side effects when there is minimal benefit.

Everyone in this study will be followed up closely. Nowadays patients are often discharged quite soon after their chemotherapy ends. In many hospitals there is no follow up after the first year. In the OPTIMA study, the follow up continues for ten years. Some of this can be by telephone. A research nurse or researcher will keep a check on you during this follow up period.

What are the potential disadvantages of taking part?

We are still in the early years of learning the best way to use these new tests. We have evidence from many thousands of patients that the tests seem to be reliable. But many of these people had smaller tumours that had not spread to the lymph nodes. The test might not work so well for patients with involved lymph nodes or larger tumours. We do not believe this to be the case. However, we might find out in the future that chemotherapy could have offered additional benefit to a few people who received hormone treatment alone.

If you join the study, it usually takes two to three weeks to receive your treatment decision. There is good evidence to show that this time period is safe and should not increase the risk for people with your type of breast cancer. We appreciate that waiting to find out about your breast cancer treatment may cause you anxiety.

We will ask you to complete questionnaires which will take some of your time.

What happens if the research study stops?

The study might end before your treatment is complete. This is unlikely. If it does happen your treatment will continue as planned. If you were not treated with chemotherapy you can discuss whether you should have this with your doctor. Your progress will be followed up in the same way.

Who to contact if you would like further information

- *Principal Investigator (Name/contact.no.) ……*

- *Research Nurse/coordinator (Name/contact.no.) ……*

If you would like some independent advice, we suggest that you contact either of the following:

Your breast clinical nurse specialist is there to help you decide about treatment.

Macmillan Cancer Support is a useful source for further information. They can provide information on breast cancer, its treatment, and clinical trials. You can find this at **macmillan.org.uk** .

Alternatively, you can call them on 0808 808 0000 (freephone), and they will send you information leaflets in the post free of charge.

Other contacts you may find helpful are:

Breast Cancer Care: Tel: 0808 800 6000 (freephone) Web: breastcancercare.org.uk

Cancer Research UK: Tel: 0808 800 4040 (freephone) Web: cancerhelp.org.uk

This completes Part 1 of the Information Sheet.
If you think you might join the study, please take time to read Part 2 before making your decision.

Part 2

What if new relevant information becomes available while I am on the study?

We may get new information from other research that is important for the OPTIMA study. We might want to change the study as a result. Any change we make is unlikely to affect you but if it does, your doctor will discuss this with you. You can decide whether or not to continue on the study. If you decide not to continue, your doctor will arrange your future care. If you do continue, you may be asked to read a new information sheet. You might also be asked to sign a new consent form.

What happens if I don't want to carry on with the study?

If you decide that you do not want to carry on with the study, we will only use the information that you have already given us to that point. If you choose to withdraw from the study, we would still like to keep your tumour sample. This will be useful to our research. If you have any objection to this, please let your doctor know.

Who is organising and funding the research?

This research is run by University College London (UCL). UCL is Sponsor for the research. The Warwick Clinical Trials Unit (WCTU) at the University of Warwick (UoW) is supporting UCL.

This study is funded by UK citizens through our taxes. The National Institute for Health Research (NIHR)'s Health Technology Assessment Programme is paying for it (project number 10/34/501). This is part of the Department of Health – the NHS funding body. The NHS and NanoString Technologies, Inc. (the owner of the Prosigna test) are paying for Prosigna testing.

Your hospital will be paid a small sum for entering you into the study. This is to cover administration costs. Your local hospital will cover the costs of your treatment and follow-up care.

What if there is a problem?

If you wish to complain or have any concerns about any aspect of the way you have been treated by members of staff whilst taking part in this research, the NHS or UCL complaints mechanisms are available to you. Your doctor can provide more information.

In the unlikely event that you are harmed by taking part in this study, compensation may be available. If you suspect that the harm is the result of the Sponsor's (UCL) or the hospital's lack of care, you may be able to claim compensation. After discussing with your doctor, please write to Professor Rob Stein, the Chief Investigator for the OPTIMA study. His address is University College London Hospitals, 250 Euston Road, London NW1 2PG. You also have the right to take independent legal action. You may have to bear the costs of this initially. You should talk with a lawyer about this.

Will my taking part in this study be kept confidential?

All personal information we collect for OPTIMA is strictly confidential and is subject to the UK Data Protection Act 2018 and GDPR.

When you join OPTIMA, we will give you a unique study number. Your hospital will know who you are from this information, but the OPTIMA Trial Office will not. When your hospital contacts the Trial Office about you they will use this number together with your initials. They will not use your name.

We will ask your doctor and nurse to provide information about you and your treatment to the WCTU. We need the information as part of our research.

Some of this information could be used to identify you. We collect your date of birth and histology numbers as extra checks to make sure that the right tumour sample has been sent to our laboratory. The Health and Social Care Information Centre (HSCIC), Office of National Statistics (ONS) and other bodies collect long-term information about all NHS patients. We will ask them about your health status in the future. We will store your national health number so we can do this. Depending on where you live in the UK, this number is called one of the NHS (National Health Service), the CHI (Community Health Index) or the HSC (Health & Social Care) number. We will not use your identifiable information for any other purpose.

The information about you which we store at the WCTU is stored securely and can only be accessed by authorised trial personnel. Our laboratory also keeps all information about patients secure.

Your doctor will inform other doctors and nurses who look after you that you are in OPTIMA. This includes your GP.

Sometimes we may want to check that the OPTIMA study data is accurate. This is usually routine. Individuals from the WCTU, UCL, regulatory organisations and your hospital trust may visit your hospital and check your medical and research records. The visitors are responsible and will not disclose any personal information about you outside of your hospital.

There is more information about how we process your information and about your legal rights in the OPTIMA Data Transparency Statement (version 1.0, 8 November 2018) which accompanies this information sheet.

What will happen to my tumour samples?

We want to use the sample of your tumour for research to help improve tests like Prosigna and to see how other tests compare to Prosigna. This is a very important part of our study. In order to do this, we need to store the tumour samples because this research will not happen straight away.

All samples will be stored with your study number, initials and date of birth and will not have your name or other details. They will be kept in a secure place by the Chief Investigator or his deputies.

It is possible that some of the research results from this study might be used by companies. If this happens, neither you nor your doctors will benefit financially. None of the doctors or scientists involved in this trial have any financial interest in it.

Will you do any other research on my samples?

We would like to use your samples for other research in the future. We may need to ask your hospital for additional stored samples, including lymph nodes to do this. Some of this research may be done by scientists who are not involved in OPTIMA.

As part of our research we may want to do genetic tests on your tumour samples. The genetic tests are performed on the cancer cells, not on you. They do not predict risk of inheritance. They will not affect insurance.

Our research is trying to help us understand how breast cancers develop and how we can improve and personalise treatment.

We ask if you will give us the remainder of your tumour sample as a gift for this purpose. Your tumour sample would be returned to your hospital if you or your doctor ever needed it. You can refuse permission to have your samples used in this way at any time. It will not affect you taking part in this study.

Will my data be shared with anybody else?

In the future we plan to make the results of the research available to other doctors and scientists. Sometimes we can learn more about cancer treatment by combining the results of more than one study. We will not share any personal information.

Data from your samples might be shared to help other scientists. Skilled scientists have sometimes been able to identify individuals from such data. Any data that we share will be protected by a legally enforceable contract to prevent this.

What will happen to the results of the research study?

The results of the research will be published in scientific journals. We expect that some results will be ready for publication in 2023. Further results will be available in the late 2020's and early 2030's. You will not be identified in any report of this study. If you wish, you can ask your doctor to send you a copy of the report when it is published.

Who has reviewed the study?

All research in the NHS is reviewed by an independent group of people, called a UK National Research Ethics Committee, which is there to protect your safety, rights, wellbeing and dignity. The study has been reviewed and approved by the South East Coast – Surrey Research Ethics Committee (Integrated Research Application System 'IRAS' reference: 95626). Patient representatives from Independent Cancer Patients Voice and from other groups have been involved in the study's development from the start and have approved it. Several patient groups including ICPV have helped develop this information sheet. You can find out more about ICPV at

independentcancerpatientsvoice.org.uk. Every participating hospital will also have examined the details of the study before deciding to take part.

What to do if you wish to take part in the study?

If you wish to join this study, you will be asked to sign a consent form. There will be further discussion with the doctor before you sign it. You will also be given a copy of this information sheet and your signed consent form.

If you decide not to take part, your care will not be affected in anyway.

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

You can also find information about OPTIMA on our website:
optimabreaststudy.com

[Print on Local Trust headed paper]

Consent Form – OPTIMA Study

Study Title:	**O**ptimal **P**ersonalised **T**reatment of early breast cancer us**i**ng **M**ulti-parameter **A**nalysis
Study Number:	ISRCTN42400492 IRAS ref. 95626
Study Doctor Name:	
Study Site:	

Patient statement and signature	*Please **initial** boxes below if you agree*
1. I have received and read the OPTIMA Patient Information Sheet (version 6.3, dated 21st November 2019). I fully understand what is involved in taking part in this study and have had an opportunity to ask questions, and all my questions have been answered.	
2. I understand that my participation is voluntary and that I am free to withdraw from the study at any time without giving a reason and without my medical care or legal rights being affected.	
3. I understand that samples of my cancer removed at the time of surgery will be used for research as part of the OPTIMA study.	
4. I give permission for some personal details to be collected as part of the study. These include my date of birth, national health number and pathology number. I understand that this information will be used to ensure that the results of the study are accurate and to find out about my future health status. I understand that all information about me will be stored securely and will only be accessible by authorised personnel.	
5. I understand that relevant sections of my medical notes and study data collected during the study may be looked at by authorised individuals from Warwick Clinical Trials Unit, University College London (the Sponsor of the study) Regulatory Authorities and from my hospital trust, to check that the study is being carried out correctly. I give permission for these individuals to have access to my records.	
6. I give permission for a letter to be sent to my General Practitioner informing them of my participation in the OPTIMA study.	
7. I understand that some of this research may generate information that companies may use in future for commercial gain.	

8. OPTIONAL: I give permission for data collected about me in the OPTIMA study to be used for future research. I understand that nobody will be able to identify me from this data.	
9. OPTIONAL: I agree to donate the remainder of my tumour sample to future research projects. I also agree that my hospital can be asked to provide additional stored samples for this research. I understand that these tumour samples will be returned to my hospital if needed for my future care. I understand that donating samples is a gift for this research, that it is entirely voluntary and that I am free to withdraw my approval for use of the samples at any time without giving a reason. I understand that my medical treatment or legal rights will not be affected by this voluntary donation.	
10. OPTIONAL: I agree to being contacted in the future about other research studies.	
11. I voluntarily agree to participate in this study.	

Your signature confirms that you have had an opportunity to ask questions and that all of your questions have been answered. [You will be given a signed and dated copy of this consent form to take away with you]

Patient name (print):	Patient Signature:	Date signed:
_____	_____	_____

Investigator Statement and Signature

To be completed by the investigator or designee taking consent

I have discussed this clinical research study with the patient and/or his or her authorised representative using a language that is understandable and appropriate. I believe that I have fully informed the participant of the nature of this study and the possible benefits and risks of taking part. I believe the participant has understood this explanation.

Investigator name (print):	Investigator signature:	Date signed:
_____	_____	_____

The completed Patient Information Sheet / Consent Form must be kept in the OPTIMA site file, a copy given to the patient and copy filed in hospital notes.

Do not send the completed Consent Form to the OPTIMA Trial Office or OPTIMA Central Laboratory.