31044 – Informed consent statement

All participants in the intervention study (BLAST) provided informed written consent prior to study enrolment. The long term follow-up of the screened individuals receiving standard care was approved as an audit by Primary Care Trusts.

I have attached

1. The patient information sheet of the BLAST study
2. A sample consent form
3. The appendix of the agreement confirming that the screening programme was an audit.

Professor Sudarshan Ramachandran

The patient information sheet of the BLAST study

1054 - VERSION 12th July 2008
Subject Information /Informed Consent

STUDY TITLE:	**Double-blind, placebo controlled, multi-center, randomized study of the effects of NEBIDO in Type 2 diabetic patients with symptomatic testosterone deficiency syndrome (TDS)**

Introduction
You are being invited to take part in the above research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

This information sheet tells you about the study in order to help you make a decision on whether or not to participate. Please take the time to read it carefully before making your decision.

If you have any questions or you are unclear about something, please discuss this with the doctor, and, if you wish, with your general practitioner or the Patient Advisory and Liaison officer (PALS) at your Primary Care Trust. (South Staffordshire Primary Care Trust, Anglesey House, Rugeley, Staffs)

Your study doctor will inform your personal GP about your participation in the study.

What is the purpose of the study?

Men with Type 2 diabetes have twice the rate of low or low normal levels of testosterone compared with non diabetic men. Recent studies have reported that treatment of low testosterone level with testosterone therapy can improve not only the symptoms associated with low testosterone (Testosterone Deficiency Syndrome – TDS) (see below) but improve the control of diabetes.

- **Diminished sexual desire and erectile quality**
- **Diminished energy**
- **Reduced sense of vitality or well-being**
- **Increased fatigue**
- **Depressed mood**
- **Impaired cognition**
- **Diminished muscle mass and strength**
- **Diminished bone density**
- **Anaemia**

The purpose of this study is to as definitely determine whether administering depot testosterone (NEBIDO) as ACTIVE TREATMENT or PLACEBO (DUMMY TREATMENT) over a period of 30 weeks will improve symptoms. Standard measures of diabetes control will be routinely carried out by your doctor.

Why have I been chosen?

Your study doctor considers that you are suitable to take part in this research study, as you have been identified as suffering from symptoms of testosterone deficiency and a low level of testosterone on a morning blood sample. NEBIDO is marketed for the treatment of men with symptomatic testosterone deficiency syndrome (TDS). Approximately 200 patients in 3 centres will take part. You have no obligation to take part in the study and your study doctors will discuss other possible treatments should you decide not to take part.

Who has reviewed the study?

A national Ethics Committee has reviewed and given their approval for this study.

Do I have to take part?

It is up to you to decide whether or not to take part. If you decide to take part you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive. If however you have experienced side effects or other discomfort, we might have to collect further information from you as it could affect the safety of others. The study and also your participation in the study may also be stopped earlier than expected, for example, for scientific or safety reasons, or if you do not follow the study or study medication schedule.

If you do decide to take part you will be given this information sheet to keep and be asked to sign a consent form. You will also be given the contact details of your study doctor. You should keep these with you at all times.

If you have questions about the study, about your rights in the study, or you have had an injury as a result of the study, please contact your study doctor. You are encouraged to ask any and as many questions as you like so that you can decide if you wish to take part or not.

What is the drug or procedure that is being tested?

The study drug will be NEBIDO (1,000 mg of testosterone undecanoate - see below) every study patient will receive either active NEBIDO or PLACEBO on a 50:50 basis... NEBIDO is fully licensed to treat symptomatic testosterone deficiency syndrome (TDS) An initial dose of 1,000 mg will be administered by

injection into the buttock, followed by a further injection at 6 weeks followed by a further injection at 3 months (3 injections in total)

Neither you nor your study doctor will be able to choose which treatment you receive because it is decided at random (like the tossing of a coin). In addition, neither you nor your doctor will know which of the two treatments you will be receiving (although, if your doctor needs to find out he/she can do so). This has been determined according to a prefixed schedule, which allows the study treatments to be assessed in a fair way. However, if your study doctor needs to know what you are taking (for example in case of emergency) it will be easy to find out. After the last patient has completed the whole study your study doctor will be told the study results. They will discuss these with you if you want. If there are issues concerning your particular health status your study doctors will discuss this with you. This will not happen immediately after you have finished taking part in the study, but will take some time due to the analysis of results.

What will happen to me if I take part?

Below is a list of the study visits and procedures that will happen at each visit during the study; your involvement should last for no more than 30 weeks.

What will happen to me if I take part?

Below is a list of the study visits and procedures that will happen at each visit during the study;

Visit 1 (screening)

The study doctor will take review of your medical history and your current health status, symptoms of testosterone deficiency and testosterone level. You must let him/her know what other drugs, whether prescribed by another doctor or bought from a pharmacy, you are taking. We recommend that you make a list of the drugs you are taking (whether prescribed or self-medicated) and bring it with you to each visit. You will have a full physical examination your weight, height, pulse and blood pressure recorded.

You will also be asked to fill in questionnaires about your sexual activity (International Index of Erectile Function Questionnaire), This is a well validated questionnaire recommended by several international organisations in the standard assessment of diabetic men as up to 75% experience sexual problems, such as erectile dysfunction but a few may be too embarrassed to discuss it with their physician. All doctors and nurses taking part in this study are very experienced in dealing with personal and embarrassing issues and will be able to offer all appropriate treatment or counselling if required. The Ageing Male Symptom Score (AMSS) consists of a series of questions related to symptoms that we all experience with ageing, but may also be associated with low

testosterone levels. The Hospital Anxiety and Depression Score (HADS) is a standard questionnaire used to detect depression and is a currently administered to diabetic patients as a standard requirement of your GP's contract.

You will have blood samples taken (35 ml) for hormone and diabetes tests. This will include a measurement of PSA (Prostate Specific Antigen), a widely used routine screening test for prostate cancer. It is widely accepted that up to 1% of the male population may have a tiny focus of prostate cancer and be totally unaware. If this PSA test was found to be abnormal, you may not be eligible for the study, but your doctor will offer you full standard investigation and follow up according best current practice.

Visit 2 (randomisation)

The study doctor will ask you questions to assess how you are feeling. You must let him/her know if there is any change in your health condition since the previous visit. You must let him/her know what other drugs, whether prescribed or bought from a pharmacy; you are taking or have taken since last visit.
He/she will review your diary of sexual attempts.

You will have a physical examination including your weight, pulse and blood pressure recorded. You will also be asked to fill in questionnaires about your sexual activity (International Index of Erectile Function Questionnaire), a global assessment question about study medication and another questionnaire "Ageing Male's Symptom" and HADS.

You will be given the study drug by intramuscular injection into your buttock (see NEBIDO product details)

Visit 3 and 4 and 5 (after 8 weeks and 18 and 30 weeks of treatment)

The study doctor will ask you questions to assess how you are feeling. You must let him know if there is any change in your health condition since the previous visit. You must let him/her know what other drugs, whether prescribed or bought from a pharmacy; you are taking or have taken since last visit.

He/she will review your diary of sexual attempts.

You will have a physical examination including your pulse and blood pressure recorded. You will also be asked to fill in questionnaires about your sexual activity (International Index of Erectile Function Questionnaire), a global assessment question about study medication, another questionnaire "Ageing Male's Symptom" and a HADS.

You will have blood samples taken (20 ml) which will be used for hormone analysis and Prostate specific Antigen (PSA) which is recommended as standard follow up for patients on NEBIDO.

You will be given study drug at each visit.

Premature Discontinuation Visit

Should you or the study doctor decide to stop your participation in the trial for any reason at any time before the end of 16 weeks of treatment (Visit 5), you will be asked to return to the clinic for a visit. The study doctor will ask you questions to assess how you are feeling. You must let him/her know if there is any change in your health condition since the last visit/telephone contact. You must let him/her know what other drugs, whether prescribed or bought from a pharmacy; you are taking or have taken since last visit/telephone contact.

You will have a full physical examination, and a blood test done. You will have your weight, pulse and blood pressure recorded. You will also be asked to fill in questionnaires about your sexual activity (International Index of Erectile Function Questionnaire), a global assessment question about study medication, another questionnaire "Ageing Male's Symptom". and HADS.

You must return your completed diary card and the unused study medication. The reason for your discontinuation will also be recorded.

Each blood sample taken from a vein in your arm at selected visits will be approximately 20 to 35 ml (4-7 teaspoons). Your blood will be analysed for standard tests (and complete hormone analysis at the end of the study only for the patients who have completed the study).

What would I have to do?

Before taking part in the study it will be necessary to stop taking medications containing oral or injectable androgens including DHEA, anti-androgens, oestrogen, anabolic steroids,. You need also to agree not to use any new therapy for erectile dysfunction for the whole duration of the study, but existing therapy for erectile dysfunction may continue to be taken in the same manner.

You must let your study doctor know immediately if there are any major changes in your health/condition between visits/telephone contacts or if you have any concern regarding the study. If you see other doctor/nurse/healthcare persons you must tell them you are taking part in this study and that they can contact your study doctor for information. If you are admitted to hospital between study visits/telephone contacts you must inform your study doctor as soon as possible.

What are the possible benefits of taking part?

We cannot be sure you will have any benefit from the study drug. However it is expected that if you are randomly assigned to receive testosterone in this study, symptoms caused by low or low normal level of testosterone may improve. All patients, including those receiving placebo in the initial 30 weeks of treatment will be offered 12 months of treatment provided by the sponsor free of charge.

The information we receive from this study may help us to better treat future patients with low or low normal levels of testosterone.

What are the possible disadvantages and risks of taking part?

Side effects most frequently recorded on testosterone injection are explained below. Other rare side effects have been recorded as headache, alopecia, gynaecomastia (slight enlargement of the breasts), mastodynia (painful breasts), prostatic disorder, diarrhoea, dizziness, hypertension, mood disturbance, hyperaesthesia, paresthesia, increase in red blood cells number, and change in serum lipids level. These side-effects are not to be expected when patients with low levels receive treatment to restore them to normal levels.

Although the study drugs are already available on prescription, there may be side effects that are not yet known. Therefore you must notify your study doctor of any new symptoms that you may have.

Possible side effects from blood drawing include faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. There is also a slight possibility of infection. Type 2 diabetics are regularly exposed to a similar frequency of blood drawing as part of their normal care.

What if something goes wrong?

The treatment involved in this study is fully licensed for men with symptomatic testosterone deficiency and your legal rights are the same as if the drug was issued on prescription from your doctor. A no-fault compensation policy has been arranged by the sponsor to further protect the rights of participants. In the event of a research-related illness or injury, you should contact your study doctor immediately. The study procedures involved are consistent with normal diabetes care. The sponsor will not compensate you where such injury results from any procedure carried out which is not in accordance with the protocol for the study. Your right in law to claim compensation for injury where you can prove negligence is not affected. By signing the consent form you are not waiving any of your legal rights.

Will my taking part in this study be kept confidential?

If you consent to take part in the research any of your medical records may be inspected by the company sponsoring (and/or the company organising) the research for purposes of analysing the results. They may also be looked at by people from the company and from regulatory authorities to check that the study is being carried out correctly. Your name, however, will not be disclosed outside the GP surgery and your privacy will be respected.

All the information collected from you, including samples, will be identified with a number to ensure your identity will be kept confidential. Only your study doctor holds the information that allows the number to be linked to your name. This information will be kept as long as the study information is kept by the study doctor. Your records would only be kept for as long as necessary and during that time would be kept confidential. This is likely to be at least 15 years but in the case of your computer records, will be permanent.

Who is organising and funding the research?

The study is sponsored by Dr Geoff Hackett, a consultant in Sexual Medicine. Your doctor will be paid for including you in this study. The compensation will cover all extra costs for the clinic due to participation in this study. Participation will be without cost to you and you will not have to pay for your drug or for your tests, examinations or medical care required as part of this study. You will not be paid for taking part in this study.

What will happen to the results of the research study?

The information collected will be processed, analysed and reported by the sponsor (Dr Geoff Hackett) or his representative. The written study results may be given to health authorities to help them decide if the drug indication can be approved. The study results may also be published in scientific journals. You will not be identified in person in any reports or publications.

You have the right to ask to be shown what data about you has been collected and if you think anything is incorrect you may ask to have it corrected.

Contact for Further Information

Your study doctor is _____ He may be contacted for information on the study medication, the study itself or if it is necessary, in an emergency, to know which medication you are taking.

Read this entire NEBIDO leaflet carefully before you start using this medicine.

In this leaflet:

Nebido
1000 mg testosterone undecanoate, solution for injection

- The active substance is testosterone undecanoate
- The other ingredients are benzyl benzoate and castor oil, refined for parenteral use

1. What Nebido is and what it is used for

Nebido contains testosterone, a so-called androgen, as the active ingredient. Nebido is injected into a location in your body where it can be stored and gradually released over a period of time.
Testosterone is mainly produced in the testicles, and to a small extent in another gland (the adrenal cortex).
Testosterone is important for the expression of masculine characteristics during foetal, early-childhood, and pubertal development, and thereafter for maintaining masculine sex characteristics and male sex-hormone-dependent functions (e.g., creation of sperm; accessory sexual glands like the prostate, seminal vesicles, epididymis). It also performs functions in the skin, muscles, skeleton, kidney, liver, bone marrow, and central nervous system.

Insufficient production of testosterone results in male *hypogonadism*, a condition that may be characterised by infertility or impotence and smallness of testes. Other symptoms associated with male hypogonadism include decreased sexual desire, fatigue, depressive moods, underdeveloped pubic hair, and an increased risk of thinning of the bones (osteoporosis). Testosterone is given to improve the deficient hormone levels in the body and related symptoms.

Dependent on the target organ, the spectrum of activities of testosterone is mainly androgenic (e.g., the prostate, seminal vesicles, epididymis) or protein-anabolic (muscle, bone, creation of red blood cells, kidney, liver).

The effects of testosterone in some organs arise after conversion of testosterone to oestradiol (the major female sex hormone), which than binds to receptors in the target cells, e.g., the pituitary, fat, brain, bone, and testicular cells.

In hypogonadal men, androgens decrease the body fat mass, increase the body lean mass and muscle strength, and prevent bone loss. Androgens may improve sexual function and also may exert positive psychotropic effects by improving mood.

Nebido is used for testosterone replacement in primary and secondary male hypogonadism.

Pack sizes:

Glass ampoules containing 1000 mg testosterone undecanoate

2. Before you use Nebido

Do not use Nebido:

• If you are allergic (hypersensitive) to testosterone undecanoate or any of the other ingredients of Nebido,
• If you suffer from androgen-dependent cancer of the prostate or of the mammary gland (or are in doubt about this), tell your doctor,
• If you have increased calcium levels in the blood accompanying malignant tumors,
• If you suffer or have suffered from liver tumors.
Nebido is not intended for use in women.

Take special care with Nebido:

If you are older, you may be at an increased risk for the development of prostate enlargement when using androgens like Nebido. Although there is no clear evidence that androgens actually generate cancer of the prostate, these can enhance the growth of any existing cancer of the prostate. Therefore cancer of the prostate has to be excluded before starting therapy with testosterone preparations like Nebido.

As a precaution, your doctor should regularly check you're prostate.

If you are on long-term androgen therapy, your blood values (haemoglobin and hematocrit) should be checked periodically by your doctor to detect cases of an increased number of red blood cells

(polycythemia). Rarely, following the use of hormonal substances such as testosterone compounds, liver tumours have been observed to occur. Of those liver tumours that occurred, only very rarely were these malignant (cancerous). Although it is improbable that a tumour will occur, these would present a health concern. In isolated cases, internal bleeding could occur from these tumours which might endanger life. Thus you should always seek the immediate emergency attention of a doctor when you suffer severe belly pains. Not all unusual sensations you might feel in your upper abdomen can be counted as a possible sign of tumour or bleeding. Those that do not disappear within a short time should however better be brought to your doctor's attention.

Please inform your doctor if you have suffered from oedema (i.e., fluid retention which leads, e.g., to swollen legs).

Clinical trials with Nebido have so far not been conducted in children or adolescents under the age of 18.

Androgens are not suitable for enhancing muscular development in healthy individuals or for increasing physical ability.

Nebido will be injected intramuscularly (into a muscle) by your doctor.

Driving and using machines:
Nebido has no influence on your ability to drive and use machines.

Using other medicines:
Please inform your doctor if you have diabetes, because it may be necessary for your doctor to adjust your diabetes medication (androgens such as Nebido may enhance the blood-sugar reducing effects of insulin and other
tablets taken for diabetes).

Interactions can occur with so-called enzyme-inducers, e.g. anti-epileptics, that can result in increased clearance of testosterone. Your doctor will know whether this applies to any other medicines you are using, so be sure to mention all of these.

Androgens may interfere with the way your body breaks down and removes other drugs from the body (e.g. increased oxyphenbutazone levels have been reported). Testosterone and related substances have been reported to increase the activity of oral blood thinning medication

(anticoagulants), possibly requiring dose adjustment by your doctor. Please be sure to inform your doctor if you are taking any such medication, or if you suffer from an inherited or acquired disturbance of blood clotting, because this is important for your doctor to know before deciding for an injection into a muscle.

Please inform your doctor or pharmacist if you are taking or have recently taken any other medicines, even those for which you needed no prescription to obtain.

3. How to use Nebido

Nebido (1 ampoule corresponding to 1000 mg testosterone undecanoate) will be injected by your doctor every 10 to 14 weeks. Injections with this frequency are capable of maintaining sufficient testosterone levels and without leading to excessively increased testosterone blood levels.
The injections will be administered very slowly. Nebido is strictly for intramuscular injection. Special care will be given to avoid injection into a blood vessel.

Start of treatment
Your doctor will measure your blood testosterone levels before start of treatment. The first injection interval may be reduced to a minimum of 6 weeks. With this initial shortened interval, the necessary testosterone level will be reached quickly.

Individualisation of treatment
Your doctor will measure testosterone serum levels occasionally at the end of an injection interval. Serum levels below normal range would indicate the need for a shorter injection interval. In case of high serum levels an extension of the injection interval may be considered by your doctor. The injection interval should remain within the recommended range of 10 to 14 weeks.

If you have the impression that the effect of Nebido is too strong or too weak, talk to your doctor.

Effects when treatment with Nebido is stopped:

When Nebido is stopped, symptoms of testosterone deficiency may reoccur.

4. Possible side effects

Like all medicines, Nebido can have side effects.
The following adverse events were reported in clinical trials with a suspected relationship to Nebido:

Common events:
- Diarrhoea
- Leg pain, painful joints (arthralgia)
- Dizziness, increased sweating, headache
- Respiratory disorders
- Acne, breast pain, excessive breast development (gynecomastia), itching (pruritus), skin disorders
- Testicular pain, prostate disorder
- Injection site pain, clotted blood beneath the skin (subcutaneous haematoma) at the injection site

Other events:
- Rare cases of increased number of red blood cells (polycythemia)
- Weight gain
- Muscle cramps
- Nervousness, hostility, depression
- Brief involuntary stoppage of breathing during sleep (sleep apnoea)
- In very rare cases, yellowish skin pigmentation (jaundice) and liver-function-test abnormalities
- Various skin reactions may occur including acne, seborrhoea, and balding
- Libido changes, increased frequency of erections;
- Therapy with high doses of testosterone preparations commonly interrupt or reduce creation of sperm, thereby reducing the size of the testicles; this is usually reversible
- Testosterone replacement therapy of hypogonadism can in rare cases cause persistent, painful erections (priapism)
- High-dosed or long-term administration of testosterone occasionally increases the occurrences of water retention and abnormally excessive accumulation of serous fluid in connective tissue
or in a serous cavity — called also oedema;
- Injection site reactions and hypersensitivity reactions may occur.

If you notice any side effects not mentioned in this leaflet, please inform your doctor or pharmacist.

IF YOU HAVE ANY FURTHER QUESTIONS PLEASE CONSULT YOUR DOCTOR.

A sample consent form

Dr V.C.Boss
Dr G.J.C.Bruce
Dr E.A.Odber
Dr A.A.Deshpandé
Dr M.I.King
Dr A. Meehan
Dr J. Heazlewood

ALDERGATE
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CONSENT FORM

Title of Project: Double-blind, placebo controlled, multi-center, randomized study of the effects of intra-muscular testosterone undecanoate (NEBIDO) in symptomatic hypogonadal men with type 2 diabetes.

Name of Researchers: Geoff Hackett, Dr Mark Popple, Dr Arup Deshpande and Dr Nigel Cole.

Please initial box

1. I confirm that I have read and understand the information sheet dated (version 23/5/08) for the above study and have had the opportunity to ask questions.
   [redacted]
2. I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected.
   [redacted]
3. I understand that sections of any of my medical notes may be looked at by responsible representatives of the sponsor or from regulatory authorities where it is relevant to my taking part in research. I give permission for these individuals to have access to my records.
   [redacted]
4. I understand I have the right to ask to see the data which has been collected about me and if anything is incorrect **I can ask to have it corrected. I agree to the information to be** processed and stored in coded form, so that my identity is kept confidential.
   [redacted]
5. I agree to take part in the above study and consent to study procedures including the taking of blood tests for research purposes
   [redacted]

Name of Patient [redacted] Date [redacted] Signature [redacted]

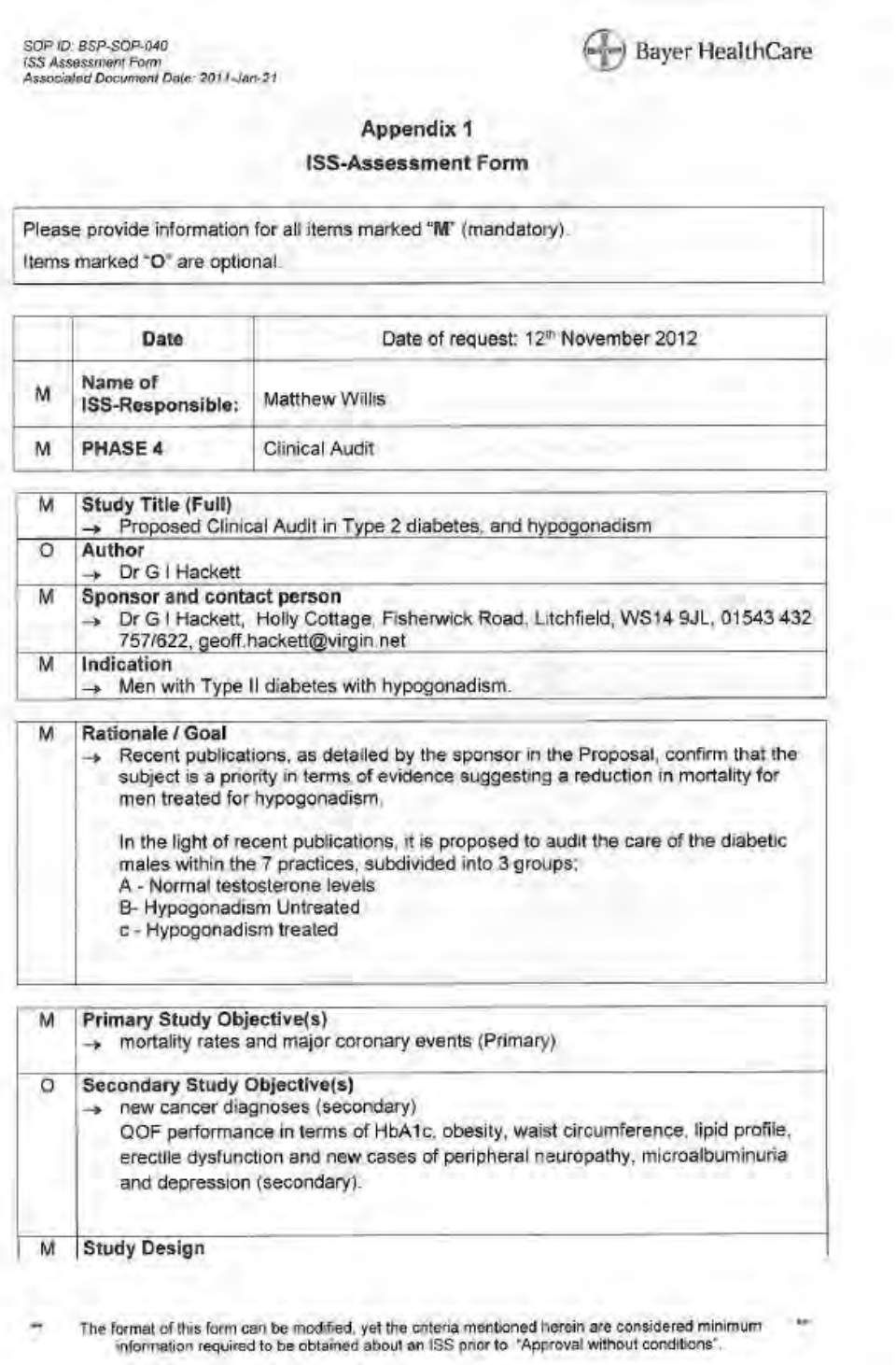
Name of Person taking consent ..... Date ..... Signature .....
(if different from researcher)

Researcher Dr. A. Deshpande Date 28/1/09 Signature .....

1 for patient; 1 for researcher; 1 to be kept with notes

The appendix of the agreement confirming that the screening programme was an audit

As the screened population was part of an audit consent was not required – please see 'inclusion criteria (detailed)' which confirms this (this section is highlighted in yellow).



SOP ID: BSP-SOP-040
ISS Assessment Form
Associated Document Date: 2011-Jan-21

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Appendix 1

ISS-Assessment Form

Please provide information for all items marked "**M**" (mandatory).
Items marked "**O**" are optional.

	Date	Date of request: 12th November 2012
M	**Name of ISS-Responsible:**	Matthew Willis
M	**PHASE 4**	Clinical Audit

M	**Study Title (Full)** → Proposed Clinical Audit in Type 2 diabetes, and hypogonadism
O	**Author** → Dr G I Hackett
M	**Sponsor and contact person** → Dr G I Hackett, Holly Cottage, Fisherwick Road, Litchfield, WS14 9JL, 01543 432 757/622, geoff.hackett@virgin.net
M	**Indication** → Men with Type II diabetes with hypogonadism.

M	**Rationale / Goal** → Recent publications, as detailed by the sponsor in the Proposal, confirm that the subject is a priority in terms of evidence suggesting a reduction in mortality for men treated for hypogonadism. In the light of recent publications, it is proposed to audit the care of the diabetic males within the 7 practices, subdivided into 3 groups: A - Normal testosterone levels B- Hypogonadism Untreated c - Hypogonadism treated

M	**Primary Study Objective(s)** → mortality rates and major coronary events (Primary)
O	**Secondary Study Objective(s)** → new cancer diagnoses (secondary) QOF performance in terms of HbA1c, obesity, waist circumference, lipid profile, erectile dysfunction and new cases of peripheral neuropathy, microalbuminuria and depression (secondary).
M	**Study Design**

** The format of this form can be modified, yet the criteria mentioned herein are considered minimum information required to be obtained about an ISS prior to "Approval without conditions". **

	→ A follow on audit will be conducted involving patients from 4 different sources 1. 536 patients screened for the BLT study in 2009 2. 211 patients recruited into the BLAST study in 2009 including (50% with placebo) on which 106 patients entered into the open label follow on study 3. 250 patients diagnosed with hypogonadism and treated for up to 4 years in the andrology clinic at Good Hope Hospital Andrology service 4. 180 patients screened for hypogonadism as part of the recent EDS study none of whom were treated with testosterone. This will provide a cohort of 450 patients treated with testosterone for a minimum of 2 years and a maximum of 5 years plus an untreated hypogonadal cohort of 250 and a eugonadal cohort of 300 and a total population of 1000 patients.
M	**Study Organization** → The study will take place in the UK alone, in 6 GP centres in the West Midlands and at Good Hope Hospital Sutton Coldfield and the University of Bedfordshire. The 6 Practices involved will be Atherstone surgery (Dr T Gooding, Aldergate surgery Tamworth (Dr A Deshpande), Cloisters Practice Lichfield (Dr N Cole), Langton Grange Health Centre Lichfield (Dr A Hall) Manor Practice Sutton Coldfield (Dr R Flacks) and Hazlewood Practice, Coleshill (Dr T Wildbore) A lead GP / Registrar in Diabetes Dr Mithun Bhartia and Clinical Assistant, Alice Blakey with developed IT skills will be identified to supervise the audits across the 6 practices.
M	**Study Population** → The target population represents the approximately 900 men with type 2 diabetes already screen to produce 435 men with defined hypogonadism and around 230 men treated for hypogonadism with testosterone supplementation for 2-3 years.
M	**Inclusion Criteria (detailed)** → Patients with type 2 Diabetes or Glucose Intolerance on the Diabetic Register of the practices have been screened for hypogonadism as defined by the presence of clinical symptoms defined by the Ageing Male symptom Score (AMS) and biochemical evidence of hypogonadism as defined by either a Total testosterone lof 8nmol/l or less or a Free Testosterone of 250 pmol/l or less on 2 separate occasions. These patients will be either treated or untreated. Those treated as part of the BLAST study provided written informed consent at the time. Of the study but further consent is not required as this study is an audit of normal ongoing care and this has been agreed by the R and D department of South Staffs PCT. The cohort without hypogonadism will be followed up using data from subsequent QOF visits recorded in the GP records. In terms of the cohort from the clinic at Good Hope Hospital, this audit would form part of routine follow up of patients in line with good clinical practice.

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M	**Exclusion Criteria** → Patients with severe intercurrent illness or psycholocal circumstances where the GP felt that inclusion would be inappropriate.
M	**Test Treatment(s) (Description)** → In the light of recent publications, it is proposed to audit the care of the diabetic males within the 7 practices, subdivided into 3 groups; A - Normal testosterone levels B- Hypogonadism Untreated c - Hypogonadism treated

O	**Test Treatment(s) or Investigated Treatment(s) for Non-Interventional Studies: Rationale for unusual or novel approaches** → N/A
M	**Request for Study Drug Delivery** → N/A
M	**Reference Treatment or Modality / Treatment or Modality of Comparison (Description)** → N/A
O	**Standard of Reference / Standard of Truth*** → N/A
M	**Rationale for selection of reference** → N/A
M	**Assignment of subjects to study arms or groups (Randomization / Stratification)** → Audit – patients are not to be randomised.
M	**Blinding** → N/A
M	**Concomitant Treatment(s)** → Not applicable, this is an audit of normal clinical care.
M	**Primary Outcome variables** → The primary outcome measures will be (a) diabetes control according to HbA1c or equivalent and (b) Cardiovascular and all cause mortality and major cardiovascular and all cause morbid events.

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O	**Secondary Outcome variables** → Changes in Weight, BMI and waist circumference, Total, LDL HDL cholesterone and trigylcerides, total and free testosterone erectile function, HADS and Ageing male symptom score. As these form part of normal follow up care in these patients.
M	**Safety Variables** → As this is clinical audit of normal care, there will be no specific safety measures imposed.)
O	**Measurement of results (How assessed)** →

M	**Visit schedule** → The visit schedule will that that which constitutes the normal clinical follow up of these patients.
M	**Follow-up period** → Data will be collected between September 2012 and April 2013 and be assessed relative to baseline and interim assessments visits.
M	**Statistical & Analytical Plan and Methodology** → Statistical analysis will be conducted by Wilkinson associates in line with the Methodology already described within the BLAST protocol to allow comparison between cohort A - Normal Testosterone, B Hypogonadism UNTREATED C Hypogonadism TREATED
O	**Criteria for selection of evaluable cases** → As GP practices currently achieve greater than 90% attendance for visits and this forms an important component of the terms of service, it is expected that data will be available on at least 90% of patients. As this is an audit and not a clinical trial, no further efforts will be made to retrieve data..

M	**Interim Analyses (if applicable)** → Wilkinson associates will perform statistical analysis on an annual basis.
M	**Sample Size Assumptions / Target Number of Valid Cases** → IAs this is clinical audit, then sample size assessment is not applicable. The intention is to provide the maximum size population possible.

M	**Health Economic Variables (if applicable)** → It is outside the scope of this audit to collect health economic data other than the cost of medications prescribded, readily available from practice prescribing data.