MULTI-CENTRE RESEARCH ETHICS COMMITTEES

APPLICATION FORM

For official MREC Use Only	*For official MREC Use Only*
MREC/ / /	

INSTRUCTIONS: Please complete in type. Please place a circle around Yes/No options as appropriate. A version of this form is available on disc from the administrator of the MREC.

It is essential that this form is completed fully and sent with relevant enclosures. **You should not simply refer to the protocol but complete the form with the information requested.** Please refer to the accompanying Guidance Notes when completing the form and complete the checklist before sending. Where a question is not applicable it is important to make this clear and not to leave it blank. **It is important that the language used in this application is clear and understandable to lay members**. All abbreviations should be explained.

Applicant's Checklist

Please indicate if the following have been enclosed by underlining or placing a circle round Yes/No/Not applicable options.

Application Form (one copy only)	Yes	No	
Full protocol with reference details (**six** copies)	Yes	No	Not applicable
Application Fee of £1000	Yes	No	Not applicable
Research subject consent form with version number and date	Yes	No	Not applicable
Research subject information sheet with version number and date	Yes	No	Not applicable
Advertisement for research subjects	Yes	No	Not applicable
GP/consultant information sheet or letter	Yes	No	Not applicable
Interview schedules for research subjects	Yes	No	Not applicable
Letters of invitation to research subjects	Yes	No	Not applicable
Questionnaire* Finalised/Not yet finalised	Yes	No	Not applicable
Researchers brochure or data sheet for all drugs (**six** copies)	Yes	No	Not applicable
Statement regarding compensation arrangements (one copy only)	Yes	No	Not applicable
Principal Researcher c.v. (one copy only)	Yes	No	Not applicable
CTX/CTC/DDX (one copy only)	Yes	No	Not applicable
Annexe A**	Yes	No	Not applicable
Annexe B***	Yes	No	Not applicable
Annexe C****	Yes	No	Not applicable

* *Please indicate whether or not this is the final version*

** *Required if the study involves the use of a new medicinal product or medical device, or the use of an existing product outside the terms of its product licence. Annexe A is attached to the Application Form.*

*** *Required if the study includes the use of ionising, radioactive substances or X-Rays. Annexe B is attached to the Application Form.*

**** *Information concerning local researchers should always be given where possible at this stage. Annexe C is attached to the Application Form. Please make additional copies as necessary.*

SECTION 1 Details of applicant(s)

1. Short title of project (including any version dates):

MRC CLL4 trial

A randomised comparison of chlorambucil, fludarabine and fludarabine plus cyclophosphamide

Full title:

2. Principal researcher (who will be responsible for dealing with the MREC)

Surname:

Catovsky

Forename:

Daniel

Title:

Professor

Present appointment of applicant:

Head, Academic Department of Haematology and Cytogenetics, Royal Marsden Hospital and Institute of Cancer Research. Chairman, MRC CLL Working Group

Qualifications:

Dsc(Med), FRCP, FRCPath

Address:

Royal Marsden NHS Trust, 203 Fulham Road, London SW3 6JJ

Tel:

0171 352 8171, extension: 2875

Fax:

0171 351 6420

E-Mail:

d.catovsky@icr.ac.uk

3. Senior researcher at LEAD centre (if different from above)

Surname:

Forename:

Title:

Present appointment:

Qualifications:

4. Who is sponsoring the study?

Contact name:

Dr Simon H Dyer, Programme Manager

Medical Research Council (MRC)

Organisation:

20 Park Crescent, London W1N 4AL

0171 636 5422

0171 436 8112

Address:

Simon.Dyer@headoffice.mrc.ac.uk

Tel:

Fax:

E-Mail:

---

5. Drug Company Reference Number

1st January 1999, for 5 years

---

6. Will researchers be paid for taking part in the study? *No*

If so, will BMA guidelines (*Manual* II.47 - see Guidelines) **be followed?** *Yes* *No*

If not, why not?

---

7. Proposed start date and duration of the study

---

8. What other researchers are/do you intend to be involved in this project? (Details of researchers added subsequently must be notified to the MREC)
Please use the form attached at Annexe C

134 doctors at 100 centres (list attached)

SECTION 2 Details of project

*This section must be completed fully. A copy of the protocol should be enclosed with the application form, but it is **not** sufficient to complete questions by referring to the protocol.*

9. Aims and objectives of project *(Approx. 250 words)*

Main aims: To evaluate whether fludarabine (Fludara) prolongs the survival of previously untreated patients with chronic lymphocytic leukaemia (CLL) compared with the standard agent chlorambucil, and whether the combination of cyclophosphamide (Cyclo) with Fludara has additional survival benefit. The trial will also compare response rates, duration of remission and toxicity of the 3 regimens used and will investigate issues of quality of life by means of EORTC QLC-C30 questionnaires.

Secondary objectives: To assess the value of the DiSC assay to guide the response in non-responding or relapsing patients and the prognostic value of four genetic markers of CLL.

10. Scientific background of study *(Approx. 250 words)*

CLL is the most common leukaemia in adults over the age of 50. Over 1700 cases of CLL are diagnosed each year in the UK, and over 800 patients die from the disease in England and Wales alone. Studies with a new group of chemotherapeutic agents, the nucleoside analogues, have suggested that they are useful in CLL. The most promising and most commonly used, fludarabine, shows high response rates. Among patients with CLL receiving the same treatment, those with a good response have better survival. However, the question of whether the higher response rates seen with fludarabine result in longer survival has not yet been answered. The unique mode of action of fludarabine, which affects DNA and RNA synthesis, including DNA repair, has opened up the possibility of using this agent in combination to potentiate the effect of other drugs. The MD Anderson Cancer Center found cyclophosphamide, another agent with activity in CLL, to be the most promising to combine with Fludara. Laboratory data have shown these drugs to be synergistic in vitro: the DNA repair that occurs after exposure to Cyclo is blocked by Fludara by its inhibition of the DNA polymerase required for DNA repair.

11. Brief outline of project *(Approx. 250 words)*

There are few ongoing or completed trials, comparing Fludara versus chlorambucil, or versus CAP (Cyclo, doxorubicin plus prednisolone) or CHOP (CAP plus vincristine). These trials show better responses for Fludara, but are not large enough to reliably assess survival benefit. Fludara is currently used as first line in a MRC pilot study for younger patients with CLL with encouraging results and has been used as second line therapy for non-responders in MRC CLL3NR with response rates as good as first line therapy. We propose a large randomised trial comparing Fludara or Fludara plus Cyclo with chlorambucil as first line for patients with advanced CLL.

Fludara is now licensed and is significantly more expensive than chlorambucil, which has been used for the last 30 years, but its effect on survival, duration of response and quality of life are unknown. Fludarabine and the combination of Fludara plus Cyclo may be more myelosuppressive than chlorambucil. Therefore an important part of the protocol will be to address the issue of prophylaxis and treatment of infection.

This trial will also test, by randomised comparison with standard protocol guided treatment, the value of the DiSC assay for drug sensitivity in patients that require further therapy after relapse or fail to respond to the first line regimen. In addition the prognostic significance of four cytogenetic abnormalities which encompass 60-80% of CLL patients will be examined.

12. Study design (e.g. RCT, cohort, case control, epidemiological analysis)

Multicentre, prospective, randomised controlled trial.

---

13. Size of the study (including controls)

Will the study involve:

(a) Human Subjects *Yes* *No*

500

i) How many patients will be recruited?

Survival, response rate, remission duration and quality of life.

At the expected rate of about 100 patients per year, 500 patients will be randomised in 5 years.

ii) How many controls will be recruited?

Comparison of 250 patients allocated to chlorambucil with 250 allocated to fludarabine based treatment will give more than 90% power to detect an absolute difference of 15%, from 40% to 55%, in survival at 5 years using a 2-sided p-value. There will be 65% power to detect a difference of 10%.

iii) What is the primary end point?

iv) How was the size of the study determined?

v) What is the statistical power of the study?

(b) Patient Records *Yes* *No*

i) How many records will be examined?

ii) How many control records will be examined?

iii) What is the primary end point?

iv) How was the size of the study determined?

v) What is the statistical power of the study?

---

14. Scientific critique

Has the protocol been subject to scientific critique? If so, please give the following information:

If the critique formed part of the process of obtaining funding, please give the name and address of the funding organisation:

The Medical Research Council (MRC) Board banded alpha rating this proposal. The MRC review included: CLL Working Group, Adult Leukaemia Working Party, Leukaemia Steering Committee, Molecular and Cellular Medicine Board and Health Services and Public Health Board.

If the critique took place as part of an internal process, please give brief details:

If no critique has taken place, please explain why, and offer justification for this:

If you are in possession of any referees' or other scientific critique reports relevant to your proposed research, please forward copies with your application form.

SECTION 3 Recruitment of subjects

15. How will the subjects in the study be:

i) selected?

All patients with a diagnosis of CLL fulfilling the entry criteria will be entered by Haematologist by telephoning Clinical Trial Service Unit to randomise once consent has been obtained.

ii) recruited?

Adult patients with a diagnosis of CLL that require therapy. This includes stages A progressive (lymphocyte doubling time less than 1 year, downward trend in Hb and platelets, 'B' symptoms), stage B (lymphadenopathy in 3 or more sites), stage C (anaemia and/or thrombocytopenia).

iii) what inclusion criteria will be used?

Presence of other cancers, no informed consent, renal failure, abnormal liver enzymes not due to CLL, pregnancy and incorrect diagnosis

iv) what exclusion criteria will be used?

N/A

N/A

N/A

N/A

16. How will the control subjects group (if used) be: *(Type N/A if no controls)*

i) selected?

ii) recruited?

iii) what inclusion criteria will be used?

iv) what exclusion criteria will be used?

17. Will there be payment to research subjects of any sort? *Yes* *No*

If yes, how much per subject and for what?

SECTION 4 Consent

18. Is *written* consent to be obtained? *Yes* *No*

If yes, please attach a copy of the consent form to be used.

If no written consent is to be obtained, please justify.

19. How long will the subject have to decide whether to take part in the study?

If less than 24 hours please justify.

No urgency, usually up to 1 week.

20. Please attach a copy of the written information sheet or letter to be given to the subject.

(See Guidelines page 3 and Appendix A.)

If no Information Sheet is to be given, please justify.

21. Have any special arrangements been made for subjects for whom English is not a first language? *Yes* *No* *N/A*

If yes, give details.

Patients whose first language is not English will not be excluded from taking part. This point is now clearly stated in Section 6 (page 11) of the protocol.

If no, please justify.

22. Will any of the subjects or controls be from one of the following vulnerable groups?

Children under 18 (16 in Scotland)

People with learning difficulties

Unconscious or severely ill

Other vulnerable groups e.g. mental illness, dementia

Yes *No*

If yes, please specify and justify:

23. What special arrangements have been made to deal with the issues of consent for the subjects above? *(Please see Guidelines.)*

Participating clinicians will go over the details of the information sheet with patients and explain the nature of the disease and the treatment options of the trial, explaining the possible advantages and disadvantages of the modality considered.

SECTION 5 Details of interventions

24. Does the study involve the use of a new medicinal product or medical device, or the use of an existing product outside the terms of its product licence? *(Please see Guidelines.)* *Yes* *No*

If yes, please complete Annexe A of the Application Form.

25. Will any ionising or radioactive substances or X-Rays be administered? *Yes* *No*

(NB Please ensure information in Question 14 includes exclusion criteria with regard to ionising radiation if appropriate.)

If yes, please complete Annexe B of the Application Form.

26. Please list those procedures in the study to which subjects will be exposed indicating those which will be part of normal care and those that will be additional (e.g. taking more samples than would otherwise be necessary). Please also indicate where treatment is withheld as a result of taking part in the project.

Normal care: Blood counts; bone marrow aspirates and trephine biopsies at diagnosis and at the end of treatment; chest x-ray; biochemical profile; blood immunophenotyping.

Additional test: Blood samples at diagnosis for cytogenetic (FISH) analysis, for in-vivo drug sensitivity (DiSC assay) and for cryopreservation. Further samples for DiSC assay at the time of second randomisation (non-responders, relapsing patients). These tests will not result in a delay in initiating treatment, except for the DiSC assay with second randomisation, as the result will be needed to choose the treatment; results are available between 7-10 days.

SECTION 6 Risks and ethical problems

27. Are there any potential hazards? *Yes* *No*

If yes, please give details, and give the likelihood and details of precautions taken to meet them, and arrangements to deal with adverse events.

Both Fludara and Fludara plus Cyclo are more myelosuppressive than chlorambucil and may result in infectious episodes. The protocol advises the use of low dose cotrimoxazole (Septrin) to prevent infections and gives detail account of other supportive measures to prevent and manage infections and other complications during and after treatment for all patients with CLL.

28. Is this study likely to cause any discomfort or distress? *Yes* *No*

If yes, please give details and justify.

29. What particular ethical problems or considerations do you consider to be important or difficult with the proposed study?

Please give details.

No specific ethical problems. The new treatments are likely to be more effective, but may not prolong survival and may increase, slightly, the susceptibility to infection complications during the early phases of treatment.

30. Will information be given to the patient's General Practitioner? *Yes* *No*

Please note: permission should always be sought from research subjects before doing this.

If yes, please enclose an information sheet/letter for the GP.

If no, please justify:

31. If the study is on hospital patients, will consent of all consultants whose patients are involved in this research be sought? *Yes* *No*

If no, please justify:

SECTION 7 Compensation and confidentiality

Product liability and consumer protection legislation make the supplier and producer (manufacturer) or any person changing the nature of a substance, e.g. by dilution, strictly liable for any harm resulting from a consumer's (subject or patient) use of a licensed product.

---

32. Have arrangements been made to provide indemnity and/or compensation in the event of a claim by, or on behalf of, a subject for non negligent harm?
(Please indicate N/A if not applicable)

Yes *No* *N/A*

If yes, please give details of compensation arrangements with this application.

The study will adhere to the 1998 MRC guidelines for good clinical practice in clinical trials (attached). The MRC accepts responsibility for it's sponsorship. Hospital indemnity applies as all researchers are employees of NHS trusts undertaking research on NHS patients. Local management approval of the research constitutes acceptance of liability for negligence and must be obtained before trial starts.

For NHS-sponsored research, HSG(96)48 reference no. 2 refers.

For pharmaceutical company sponsored research, the company should confirm that it will abide by the most recent ABPI guidelines *(Manual V.14.1.1)*

---

33. In cases of equipment or medical devices, have appropriate arrangements been made with the manufacturer to provide indemnity?

(Please indicate N/A if not applicable) *Yes* *No* *N/A*

If yes, please give details and enclose a copy of the relevant correspondence with this application.

---

34. Will the study include the use of any of the following?

Audio/video recording *Yes* *No*

Observation of patients *Yes* *No*

If yes to either:

i) How are confidentiality and anonymity to be ensured?

ii) What arrangements have been made to obtain consent for these procedures?

---

35. Will medical records be examined by research worker(s) outside the employment of the NHS? *Yes* *No*

If yes, please see Guidelines.

36. What steps will be taken to safeguard confidentiality of personal records?

Data held on computers, at the MRC Clinical Trial Service Unit (CTSU) and with the trial coordinators, will be carefully safeguarded and password protected.

37. What steps will be taken to safeguard the information relating to specimens and the specimens themselves?

Standard current hospital procedures will apply. Information on research tests will only be used for analysis of prognostic factors during the trial and will not be available to participating clinicians.

PLEASE ENSURE THAT YOU COMPLETE THE CHECKLIST ON THE FRONT COVER OF THE APPLICATION FORM AND ENCLOSE ALL RELEVANT ADDITIONAL DOCUMENTS.

SECTION 8 Declaration

DECLARATION

The information in this form is accurate to the best of my knowledge and belief and I take full responsibility for it.

I understand it is my responsibility to obtain management approval where appropriate from the relevant NHS body before the project takes place.

I agree to supply interim and final reports on the pro forma provided, and to advise my sponsor, the MREC from which approval was granted for this proposal and any local researchers taking part in the project of any adverse or unexpected events that may occur during this project.

Signature of Principal Researcher: .....…….....

Date:.....

Annexe A — Drugs and Devices

This form is to be used if the study involves the use of a new medical product or medical device, or the use of an existing product outside the terms of its produce licence.

i) **Is a pharmaceutical or other commercial company arranging this trial?** *Yes* *No*

If no, has approval of the licensing authority been obtained by means of a DDX? *Yes* *No*

ii) **Does the drug(s) or device have a product licence(s) for the purpose for which it is to be used?** *Yes* *No*

If yes, please attach data sheet or equivalent.

iii) **Is any drug or medical device being supplied by a company with a Clinical Trial Certificate or Clinical Trial Exemption?** *Yes* *No*

Please attach CTC, CTX, or DDX.

iv) **Has a CTC, CTX or DDX been applied for but not yet received?** *Yes* *No*

If so, the application can be made but a valid CTX must be provided to the MREC before the research can proceed

v) **Details of drugs to be used** *(Please complete the table below for each drug making additional copies of this page as necessary)*

Approved Name(s):

Generic Name:

1) Chlorambucil; 2) Fludarabine phosphate; 3) Cyclophosphamide.

Trade Name:

1) Leukeran; 2) Fludara; 3) Endoxana

	Strength	Dosage and Frequency	Route	Duration of Course
1)	2mg and 5mg tablets	10mg/m^2 every 4 weeks	By mouth	7 days
2)	50mg vials	25mg/m^2 every 4 weeks	IV	5 days (3 days, plus Cyclophosphamide)
3)	200mg and 500mg vials	250mg/m^2 every 4 weeks	IV	3 days (plus Fludara)

vi) **When Drugs not listed in the British National Formulary are being used, applicants should provide the following information on not more than 3 sides of A4 paper :**

a) **What is the formulation, purity and source of the Drug ?**

b) **What are the pharmacological actions of the Drug - including those not relevant to the proposed therapeutic indications ?**

c) Toxicology - including details of species, number of animals, doses, duration of treatment and route(s) of administration. Important findings should be summarised.

d) Clinical pharmacology in Man including :

- Extent of Use in Man
- Dosage schedules used - dose, route, duration
- Side effects and their frequency
- Information on duration of action and mechanism of elimination, if known.

e) Applicant's experience with this drug in man. Give brief information on previous studies, number and type of subjects and nature and incidence of side effects.

vi) Details of Medical Device

vii) If an electrical device, has the device been through acceptance and safety testing? *Yes* *No*

Give details:

Annexe B Radiation

This form is to be used if the study involves the use of additional ionising or radioactive substances or X-Rays.

a) RADIOACTIVE SUBSTANCES

i) Details of substances to be administered *(Please complete the table below)*

Investigation:

Radionucleide

Chemical form

Quantity of radio-activity to be administered (MBq)	Route	Frequency

ii) Estimated Effective Dose (Effective Dose Equivalent) (mSv):
(Please supply source of reference or attach calculation)

iii) Absorbed dose to organ or tissues concentrating radioactivity (mGy) (Specify dose and organ)
(Please supply source of reference or attach calculation)

b) X-RAYS

i) Details of radiographic procedures

Investigation	Organ(s)	Frequency

ii) Estimated Effective Dose (Effective Dose Equivalent) (mSv):

(Please supply source of reference or attach calculation)

Annexe C	**Local Researchers**

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the MREC Administrator by means of a copy of this form as each new researcher is recruited.)

MREC Reference Number:

Name

Professor D Catovsky
Dr E Matutes

Contact Address:

Academic Department of Haematology and Cytogenetics
The Royal Marsden NHS Trust
203 Fulham Road
London, SW3 6JJ

Location of research
(if different):

0171 352 8171, extension 2875

Telephone:

0171 351 6420

Professor Catovsky: <d.catovsky@icr.ac.uk>
Dr Matutes: <estella@icr.ac.uk>

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the MREC Administrator whenever other local researchers become involved in the future.

Annexe C — Local Researchers

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the MREC Administrator by means of a copy of this form as each new researcher is recruited.)

MREC Reference Number:

Name

Professor TJ Hamblin
Dr D Oscier

Contact Address:

Department of Haematology
Royal Bournemouth Hospital
Castle Lane East
Bournemouth, BH7 7DW

Location of research
(if different):

01202 704790

Telephone:

01202 300248

Professor Hamblin: < terjoha@aol.com>

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the MREC Administrator whenever other local researchers become involved in the future.

Annexe C **Local Researchers**

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the MREC Administrator by means of a copy of this form as each new researcher is recruited.)

MREC Reference Number:

Name

Dr JA Child

Contact Address:

Leeds General Infirmary
Great George Street
Leeds
LS1 3EX

Location of research
(if different):

0113 392 6643

Telephone:

0113 392 6349

TONYCH@pathology.leeds.ac.uk

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the MREC Administrator whenever other local researchers become involved in the future.

Annexe C	**Local Researchers**

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the MREC Administrator by means of a copy of this form as each new researcher is recruited.)

MREC Reference Number:

Name

Dr D Milligan

Contact Address:

Consultant Haematologist
Birmingham Heartlands Hospital
Bordesley Green East
Birmingham B9 5ST

Location of research
(if different):

0121 766 6611

Telephone:

0121 766 7530

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the MREC Administrator whenever other local researchers become involved in the future.

Annexe C	**Local Researchers**

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the MREC Administrator by means of a copy of this form as each new researcher is recruited.)

MREC Reference Number:

Name

Dr S Schey,

Contact Address:

Consultant Haematologist
Guy's Hospital
St Thomas Street
London
SE1 9RT

Location of research
(if different):

0171 955 4003

Telephone:

0171 955 4002

s.schey@umds.ac.uk

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the MREC Administrator whenever other local researchers become involved in the future.

Annexe C	**Local Researchers**

OTHER RESEARCHERS INVOLVED IN THIS STUDY

Please provide the name and contact details of other researchers involved in this study. Please include your own name and centre if you are also a local researcher.

(Please copy and complete this page for each researcher. You must inform the MREC Administrator by means of a copy of this form as each new researcher is recruited.)

MREC Reference Number:

Name

Dr AG Smith

Contact Address:

Haematology Department
Royal South Hants Hospital
Graham Road
Southampton
SO9 4PR

Location of research
(if different):

01703 825335

Telephone:

01703 825338

agsmith@tcp.co.uk

Fax:

E-Mail:

Please retain a blank copy of this form, complete it and send to the MREC Administrator whenever other local researchers become involved in the future.

Annexe D Supplementary Form for LRECs

SUPPLEMENTARY FORM FOR LOCAL ARRANGEMENTS

To be completed by the local researcher or principal researcher if appropriate (please see guidelines) once MREC approval has been obtained.

Please send this signed and completed form to the appropriate LREC administrator together with the **appropriate number** of copies of::

the MREC application form
the MREC letter of approval
the signed MREC response form.
the local researcher's c.v.
the consent form and information sheet

together with **one** copy of the protocol

If you require help with the address of your appropriate LREC please seek advice from the MREC Administrator.

1 MREC Reference Number:

2. Short title of project

3. Details of lead of local investigator:

Surname:

Forename:

Title:

Present Appointment:

Qualifications:

4. Please give an approximate figure for the number of trials/studies in which the principal researcher has been involved over the past year

5. Proposed start date and duration of project

6. Names, titles and qualifications of other local researchers working on this project

7. Location of project

8. Funding

Please give full details where applicable of:

a) Payment to subjects

b) Payment to Trust/practice/research funds

c) Personal payment or personal benefit to researcher

Is payment:

i) A block grant *Yes* *No*

ii) Based on the number of research subjects recruited? *Yes* *No*

If yes, how much per patient:

d) Details of other benefits, e.g. equipment

e) Will the costs incurred by the institution be covered by the payment? *Yes* *No*

9. Local Recruitment of Subjects

a) How many subjects are being studied locally?

b) **Are any of these subjects involved in existing research or have been involved in any recent research in the last six months?** *Yes* *No*

If yes, please justify their use in this project

c) **Will any of the subjects involved be in a dependent relationship with the researcher?** *Yes* *No*

If yes, please ensure you comply with local recruitment arrangements

d) **Will any of the subjects involved be medical students?** *Yes* *No*

If yes, please obtain signed agreement of the Principal of the Medical School:

Signature of Principal of Medical School: .....

10. Local Safety Requirements

a) **Are you going to administer radioisotopes?** *Yes* *No*

i) **If yes, do you have an ARSAC certificate?** *Yes* *No*

ii) **Have you informed the local radiation officer?** *Yes* *No*

Signature of Radiation Safety Officer: .....

b) **If you are going to administer drugs what arrangements have you made to store, code and administer them?**

Signature of Hospital Pharmaceutical Officer: .....

c) **Local emergency contact details:**

d) **Local independent adviser details:**

DECLARATION

I have read and understood the MREC form and the supplementary form for LRECs, the protocol, guidelines and all documents pertaining to this research approved by the MREC that I now enclose. The information therein and above is accurate to the best of my knowledge and belief and I take full responsibility for it.

I understand it is my responsibility to obtain management approval where appropriate from the relevant NHS body before the project takes place.

I confirm that this research will comply with all relevant UK legislation, including the Data Protection Act and the Access to Medical Records Act.

I agree to supply interim and final reports to my LREC as required.

I agree to advise my sponsor, the LREC and MREC from which approval was granted for this proposal of any adverse or unexpected events that may occur during this project. I also agree to advise the LREC if this is withdrawn or not completed.

Signature of Local Investigator: …….....……..

Date: …….....……