APPLICANT'S CHECKLIST

All studies except clinical trials of investigational medicinal products

REC Ref:	07/MRE08/9
Short Title of Study:	BAD Biological Interventions Register
CI Name:	Professor Christopher EM Griffiths
Sponsor:	University of Manchester

Please complete this checklist and send it with your application

- Send ONE copy of each document (except where stated)
- ALL accompanying documents must bear version numbers and dates (except where stated)
- When collating please do NOT staple documents as they will need to be photocopied.

Document	Enclosed?	Date	Version	Office use
Covering letter on headed paper	(•) Yes ( ) No	14/12/2006		
NHS REC Application Form, Parts A&B – British Association of Dermatologists Biologicals Intervention Register	Mandatory			
NHS REC Application Form, Part C (SSA)	( ) Yes (•) No			
Research protocol or project proposal (6 copies) – BADBIR Protocol	Mandatory	05/12/2006	10	
Summary C.V. for Chief Investigator (CI) – BADBIR Griffiths CV	Mandatory	05/12/2006		
Summary C.V. for supervisor (student research)	( ) Yes (•) No			
Research participant information sheet (PIS) – BADBIR patient information sheet v1	(•) Yes ( ) No	08/12/2006	1	
Research participant consent form – BADBIR patient consent form v1	(•) Yes ( ) No	08/12/2006	1	
Letters of invitation to participants	( ) Yes (•) No			
GP/Consultant information sheets or letters	( ) Yes (•) No			
GP/Consultant information sheets or letters	( ) Yes (•) No			
Statement of indemnity arrangements	( ) Yes (•) No			
Letter from sponsor	(•) Yes ( ) No			
Letter from statistician – BADBIR statistics approval letter	(•) Yes ( ) No	25/10/2006		
Letter from funder	(•) Yes ( ) No			
Referees' or other scientific critique report – BADBIR scientific review	(•) Yes ( ) No	15/08/2006		
Summary, synopsis or diagram (flowchart) of protocol in non–technical language	( ) Yes (•) No			
Interview schedules or topic guides for participants	( ) Yes (•) No			
Validated questionnaire	(•) Yes ( ) No			
Non–validated questionnaire	(•) Yes ( ) No			
	(•) Yes ( ) No			

Copies of advertisement material for research participants, e.g. posters, newspaper adverts, website. For video or audio cassettes, please also provide the printed script.				

WELCOME TO THE NHS RESEARCH ETHICS COMMITTEE APPLICATION FORM

An application form specific to your project will be created from the answers you give to the following questions.

1. Is your project an audit or service evaluation?

○ Yes ◉ No

2. Select one research category from the list below:

○ Clinical trials of investigational medicinal products
○ Clinical investigations or other studies of medical devices
○ Other clinical trial or clinical investigation
○ Research administering questionnaires/interviews for quantitative analysis, or using mixed quantitative/qualitative methodology
○ Research involving qualitative methods only
◉ Research limited to working with human tissue samples and/or data
○ Research tissue bank

If your work does not fit any of these categories, select the option below:

○ Other research

2a. Please answer the following questions:

a) Will you be taking new tissue samples primarily for research purposes (i.e. excluding surplus tissue)?	○ Yes	◉ No
b) Will you be using newly obtained surplus tissue (i.e. left over from tissue taken in the course of normal clinical care)?	○ Yes	◉ No
c) Will you be using existing stored tissue identifiable to the researcher?	○ Yes	◉ No
d) Will you be using only existing stored tissue not identifiable to the researcher?	○ Yes	◉ No
e) Will you be using identifiable data?	◉ Yes	○ No
f) Will you be using only anonymised or pseudonymised data?	○ Yes	◉ No

3. Is your research confined to one site?

○ Yes ◉ No

4. Does your research involve work with prisoners?

○ Yes ◉ No

5. Does your research involve adults unable to consent for themselves through physical or mental incapacity?

○ Yes ◉ No

6. Is the study, or any part of the study, being undertaken as an educational project?

○ Yes ◉ No

NHS Research Ethics Committee NHS
Application form for research limited to working with human tissue samples and/or data

This form should be completed by the Chief Investigator, after reading the guidance notes. See glossary for clarification of different terms in the application form.

Short title and version number: (maximum 70 characters – this will be inserted as header on all forms)
BAD Biological Interventions Register

Name of NHS Research Ethics Committee to which application for ethical review is being made:
North West England

Project reference number from above REC: 07/MRE08/9
Submission date: 18/12/2006

PART A: Introduction

A1. Title of the research

Full title: British Association of Dermatologists Biological Interventions Register

Key words: Psoriasis, etanercept, efalizumab, infliximab, biological agents, patient register, pharmacovigilance

A2. Chief Investigator

Title:	Professor
Forename/Initials:	Christopher EM
Surname:	Griffiths
Post:	Professor of Dermatology
Qualifications:	MD, FRCP, FRCPath
Organisation:	The University of Manchester
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Fax:	0161 2061095
Mobile:	

A copy of a current CV (maximum 2 pages of A4) for the Chief Investigator must be submitted with the application

A3. Proposed study dates and duration

Start date: 01/01/2007
End date: 31/12/2016
Duration: Years: 10 ; Months: 0

A4. Primary purpose of the research: *(Tick as appropriate)*

- ☐ Commercial product development and/or licensing
- ☐ Publicly funded trial or scientific investigation
- ☐ Educational qualification
- ☑ Establishing a database/data storage facility
- ☐ Other

Question(s) 5 disabled.

A6. Does this research require site–specific assessment (SSA)? (Advice can be found in the guidance notes on this topic.)

◉ Yes ○ No

If No, please justify:

If Yes, Part C of the form will need to be completed for each research site and submitted for SSA to the relevant Local Research Ethics Committee. Do not submit Part Cs for other sites until the application has been booked for review and validated by the main Research Ethics Committee.

Management approval to proceed with the research will be required from the R&D Department for each NHS care organisation in which research procedures are undertaken. This applies whether or not the research is exempt from SSA.

PART A: Section 1

A7. What is the principal research question/objective? *(Must be in language comprehensible to a lay person.)*

The primary purpose of establishing a "biologicals" register for psoriasis is to follow a large cohort of patients treated with biologic agents (not more than 4,000 on each biologic agent) so that their long−term safety can be monitored. This will be done in patients receiving biologic therapy and in 4,000 patients treated with conventional therapy. This will allow us to ascertain the short, medium, and long term safety of biologic treatment as compared to traditional therapy for psoriasis.

A8. What are the secondary research questions/objectives? *(If applicable, must be in language comprehensible to a lay person.)*

A subsidiary aim will be to collect information on the long−term efficacy of the biologic agent as compared to conventional treatments.

A9. What is the scientific justification for the research? What is the background? Why is this an area of importance?*(Must be in language comprehensible to a lay person.)*

Clinical trials for approval of new "biologic" therapies are based on data in limited numbers of patients over the short term (12−24 weeks). Psoriasis is a chronic long−term skin disease and when severe may require lifelong therapy. Current treatments cause significant side effects such as skin cancer and liver and kidney damage. Treatment of psoriasis by biologic agents requires suppression of the immune system and this is expected to increase the risk of some infections and possibly cancers. Large scale observational studies over prolonged time frames are required to establish the long term safety of new agents but are also needed for current therapies. The differential long term safety of therapies will inform better and safer management of chronic psoriasis. Establishing a nationwide surveillance scheme along similar methodology to that used for rheumatoid arthritis (British Society for Rheumatology Biologics Register, BSRBR) will provide essential data on long term safety of the new therapies. By combining data from several registers the risk of significant, but rare, side effects can be established e.g. lymphoma, a cancer of the lymph nodes.

Recently three biological interventions for psoriasis have been licensed in the UK for the treatment of psoriasis, (i)efalizumab, (ii)etanercept and (iii)infliximab.

The protocol for the register has been established in consultation with a multidisciplinary working group of the British Association of Dermatologists, including rheumatology, patient and nursing representation. The working group established comprehensive guidelines for the use of biologic therapies in psoriasis. This group and NICE feel the registration of patients in the long term is essential and this has been indicated in the guidelines. The protocol has been designed in consultation with the principal investigator of the British Society for Rheumatology Biologics Register and has been peer reviewed by them. Manufacturers of the biological agents have statutory requirements for safety evaluation and the European agency for the Evaluation of Medicinal Agents (EMEA) have recommended large scale registration studies. These important stakeholders have been consulted and, working together with the BSRBR, will ensure that the register meets with regulatory requirements for the coding and timely reporting of adverse events.

A10−1. Give a full summary of the purpose, design and methodology of the planned research, including a brief explanation of the theoretical framework that informs it. It should be clear exactly what will happen to the research participant, how many times and in what order.

This section must be completed in language comprehensible to the lay person. It must also be self−standing as it will be replicated in any applications for site−specific assessment on Part C. Do not simply reproduce or refer to the protocol. Further guidance is available in the guidance notes.

Study design
This is a prospective observational cohort study to monitor the long−term effects of biologic therapy in patients with psoriasis in the UK. The study will consist of two cohorts comparing (i) patients with psoriasis newly treated with one of the biologic therapies, to (ii) patients with similar disease characteristics treated with non−biologic systemic therapies (including PUVA, methotrexate, ciclosporin and acitretin).

Patients will have been exposed to a variety of conventional treatments each with its own risks before starting on the biologic therapies. Their severe skin disease will also affect their risks, as will lifestyle e.g. smoking, drinking habits and socio−economic status. Data on all these aspects will be recorded for patients starting biologic therapy and for an equal number of patients treated with conventional therapy. It is only by analysing differences between the two groups of patients that risks of biologic therapies in psoriasis can be identified.

Recruitment and sample size
The recruitment of the biologic cohort for any particular agent will be determined by a number of factors including (i) the recommendation by NICE that all subjects with psoriasis treated with these agents should be registered (ii) the desire by the sponsoring companies that all treated patients within the UK should be registered to satisfy the requirements of the EMEA and MHRA and (iii) the uptake of the agents by the consultant dermatologists.

Based on recruitment rates of a similar register (the British Society for Rheumatology Biologics Register or BSRBR) it is anticipated that 2000−4000 patients for each biologic therapy will be recruited over a five year period. During the same time period, a cohort of comparison patients on standard therapy will also be recruited. Due to the NICE guidelines recommending that all patients with psoriasis should be registered with a national register, it is envisaged that patients in the biologic cohort will be recruited from all dermatology departments in the UK. The comparison cohort will also be recruited from all contributing centres to reduce the risk of selection bias.

However, the one recruitment factor that is under control of the Register is the size of the comparison cohort. A total sample of 4000 patients followed for five years is required to provide 80% power at the 5% significance level with a 1:1 ratio in each cohort to detect a three or four fold increase risk of events occurring at a frequency of 1/1000 or 1/2000. This calculation will allow the register to detect at least a 3− to 4−fold increase in the risk of non−melanoma skin cancer, a particular concern in these patients who have been exposed to phototherapy.

Eligibility
For patients to be eligible for the biologic cohort, they must have a diagnosis of psoriasis, be over 16 and be about to receive biologic therapy. Eligibility for the comparison cohort includes patients with psoriasis who are being treated with standard therapy, who have active disease and who are over 16 years of age.

Consent
Once a decision is made to treat a patient with a biologic therapy, the patient is asked to sign the patient consent form. A copy of the consent form will be provided to the patient for their records and a copy will be kept in the patient hospital notes. A copy of the consent form will be stored in the investigator file.

Data collection and follow−up
Once the patient has consented to take part, consultants then complete a British Association of Dermatologists Biological Intervention Registry (BADBIR) consultant baseline questionnaire on−line. This questionnaire collects details on clinical indication, disease severity including the Psoriasis Area and Severity Index (PASI), current and past therapy and co−morbidities. These forms are then electronically submitted to BADBIR.

Patients are then posted a baseline questionnaire which collects demographic details including occupation, smoking status, and the name and address of a close contact should the patient become lost to follow−up. The patient is also sent a diary to keep for the next 6 months. This diary collects information about new hospitalisations, new referrals and new drugs during this coming period.

Patients are followed up every 6 months via the consultant for three years and then annually for two years to collect clinical information on drug changes, disease severity and the occurrence of adverse events. Patients are also sent questionnaires and a diary every 6 months (for three years) to collect measures of functional status, health and well−being.

All patients will be flagged for malignancy and mortality with the General Registry Office (GRO, which is part of the Office for National Statistics or ONS)and the Scottish and Northern Ireland General Registry Office. Underlying cause of death will be obtained from the death certificates provided by the GRO's. Details on malignancies, including date of diagnosis, site and morphology, will be obtained from the national cancer registry.

End of study
The study will end five years after the recruitment of the last patient.

A10–2. In which parts of the research have patients, members of the public or service users been involved?

- ☐ As user–researchers
- ☐ As members of a research project group
- ☐ As advisor to a project
- ☐ As members of a departmental or other wider research strategy group
- ☑ None of the above

Please provide brief details if applicable:

A10–3. Could the research lead to the development of a new product/process or the generation of intellectual property?

○ Yes ◉ No ○ Not sure

Question(s) 11–19 disabled.

A20. How will potential participants in the study be (i) identified, (ii) approached and (iii) recruited?
Give details for cases and controls separately if appropriate:

(i) Identification

Biologic cohort
The British Association of Dermatologists (BAD) is the professional body representing all dermatologists in the UK. BAD will oversee the project and own the data, with financial support from the pharmaceutical sponsors (Wyeth, Schering Plough and Serono) they will contract with the University of Manchester who will be the sponsors of the study.

The BAD guidelines for starting biologic therapy state that registering patients with a national register is mandatory and NICE confirm this in their appraisal of these agents.

Thus all dermatologists using the biologic treatments in the UK should view registration as an integral part of standard patient care for monitoring purposes. Nurses will be offered training to assist with registration.

Comparison cohort
For the control group, consultant dermatologists and specialist nurses will actively invite psoriasis patients with a similar disease severity profile but treated with conventional therapies to the comparison cohort in the same manner. The controls will be recruited from all contributing centres in the UK.

(ii) Approached and (iii) Recruited

Biologic Cohort
All patients who are eligible to start biologic therapy will be invited by the consultant dermatologist or specialist nurse to be part of the national register. A full explanation of what this involves will be given to the patient along with a copy of the patient information sheet and consent form. If a patient fulfils the criteria for biologic therapy, they must be given adequate time to consider their decision and this will also allow them time to consider participation in the national register. Further information is provided to patients in the form of BAD patient leaflets. These leaflets inform the patients of the biological therapies and also make clear the importance and value of participating in the national register.

Comparison cohort
The comparison cohort will be approached and recruited (in exactly the same way as the biologic cohort) when they have their next appointment with the dermatologist/nurse specialist. They will also be given appropriate time to consider participation in the register.

A21. Where research participants will be recruited via advertisement, give specific details.

☑ Not Applicable

If applicable, enclose a copy of the advertisement/radio script/website/video for television (with a version number and date).

A22. What are the principal inclusion criteria? *(Please justify)*

Exposed biologic cohort
1. Patients with a diagnosis of psoriasis commencing treatment with a biological agent for therapy of their skin disease.
2. Age 16 or over
3. Willingness to give informed consent for long term follow–up and access to all medical records.

Control cohort
1. Patients initiating or switching conventional therapy with PUVA, ciclosporin, methotrexate, fumarates or acitretin.
2. If not switching therapy patients must have severe psoriasis meeting the severity criteria for biological therapy as in the BAD guideline (rule of 10s)
3. Age 16 or over.
4. Willingness to give informed consent to participate in long term follow up and access to all medical records.

A23. What are the principal exclusion criteria? *(Please justify)*

Exposed biologic cohort
None

Control cohort
Patients must never have been exposed to biologic therapy

A24. Will the participants be from any of the following groups? *(Tick as appropriate)*

☐ Children under 16
☐ Adults with learning disabilities
☐ Adults who are unconscious or very severely ill
☐ Adults who have a terminal illness
☐ Adults in emergency situations
☐ Adults with mental illness (particularly if detained under Mental Health Legislation)
☐ Adults with dementia
☐ Prisoners
☐ Young Offenders
☐ Adults in Scotland who are unable to consent for themselves
☐ Healthy Volunteers
☐ Those who could be considered to have a particularly dependent relationship with the investigator, e.g. those in care homes, medical students
☐ Other vulnerable groups

Justify their inclusion.

☑ No participants from any of the above groups

Question(s) 24 1–5–25 disabled.

A26. Will informed consent be obtained from the research participants?

◉ Yes ○ No

If Yes, give details of who will take consent and how it will be done. Give details of any particular steps to provide information (in addition to a written information sheet) e.g. videos, interactive material.

If participants are to be recruited from any of the potentially vulnerable groups listed in A24, give details of extra steps taken to assure their protection. Describe any arrangements to be made for obtaining consent from a legal representative.

If consent is not to be obtained, please explain why not.

Following discussion of the register with either the consultant dermatologist or nurse specialist and with sufficient time to read the patient information sheet, the patient will be given the opportunity to ask questions and consider participation. Assenting patients will then be formally invited to provide informed written consent.

Informed consent will be obtained by the appropriate personnel who are authorised to do so by the local principal investigator. The right of the patient to refuse consent without giving reasons will be respected. It will also be emphasised to the patient (included in the patient information sheet) that a decision not to participate will not affect the quality of care that he/she receives. The patient will remain free to withdraw from the Register at any time without having to provide a reason and without prejudicing further treatment.

The original consent form will be retained at the recruiting centre and a copy will be submitted with the Consultant Baseline Form to the BADBIR in Manchester.

Copies of the written information and all other explanatory material should accompany this application.

A27. Will a signed record of consent be obtained?

◉ Yes ○ No

If Yes, attach a copy of the information sheet to be used, with a version number and date.

A28. How long will the participant have to decide whether to take part in the research?

At least 24 hours, as usually the decision to start biological treatment/conventional therapy will be a long and considered process.

A29. What arrangements have been made for participants who might not adequately understand verbal explanations or written information given in English, or who have special communication needs? *(e.g. translation, use of interpreters etc.)*

Consultant dermatologists and specialist nurses will rely on interpreters to assist with registration of non–english speaking participants. Most areas with particular ethnic groups are able to provide interpreters especially as this is necessary anyway for routine clinical care and patient education, i.e. for injecting drugs etc...

Question(s) 30 disabled.

A31. Does this study have or require approval of the Patient Information Advisory Group (PIAG) or other bodies with a similar remit?*(see the guidance notes)*

○ Yes ◉ No

Question(s) 32a–32b disabled.

A33. Will individual research participants receive any payments for taking part in this research?

○ Yes ◉ No

A34. Will individual research participants receive *reimbursement of expenses* or any other *incentives or benefits* for taking part in this research?

◉ Yes ○ No

If Yes, indicate how much and on what basis this has been decided:

The patients in the biologic and comparison cohort will not be reimbursed for participating in the national register. However, participating consultants/nurses who are registering biologic patients and control patients will receive reimbursement to their Departments as partial compensation for the time and effort involved in collecting the data.

After iterative consultation with the BAD Steering Committee, NHS R+D and a full economic costing, a compromise was reached. The consensus was that fair compensation would be £100 for registering a new patient and £50 for each of the 8 follow–up visits. This does not cover the full costs of consultant and nurse time involved but will strongly support the successful recruitment and follow–up of patients needed for the register to succeed.

A35. Insurance/indemnity to meet potential legal liabilities

Note: References in this question to NHS indemnity schemes include equivalent schemes provided by Health and Personal Social Services (HPSS) in Northern Ireland.

A35–1. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the *sponsor(s)* for harm to participants arising from the *management of the research*?

Note: Where a NHS organisation has agreed to act as the sponsor, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For all other sponsors, describe the arrangements and provide evidence.

○ NHS indemnity scheme will apply
◉ Other insurance or indemnity arrangements will apply (give details below)

Employers liability held by the University of Manchester

Please enclose a copy of relevant documents.

A35–2. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of the *sponsor(s) or employer(s)* for harm to participants arising from the *design of the research*?

Note: Where researchers with substantive NHS employment contracts have designed the research, indemnity is provided through NHS schemes. Indicate if this applies (there is no need to provide documentary evidence). For other protocol authors (e.g. company employees, university members), describe the arrangements and provide evidence.

○ NHS indemnity scheme will apply to all protocol authors
◉ Other insurance or indemnity arrangements will apply (give details below)

Employers liability held by the University of Manchester

Please enclose a copy of relevant documents.

A35–3. What arrangements will be made for insurance and/or indemnity to meet the potential legal liability of *investigators/collaborators* and, where applicable, *Site Management Organisations*, arising from harm to participants in the *conduct of the research*?

Note: Where the participants are NHS patients, indemnity is provided through NHS schemes or through professional indemnity. Indicate if this applies to the whole of the study (there is no need to provide documentary evidence). Where non–NHS sites are to be included in the research, including private practices, describe the arrangements which will be made at these sites and provide evidence.

- (●) All participants will be recruited at NHS sites and NHS indemnity scheme or professional indemnity will apply
- ( ) Research includes non–NHS sites (give details of insurance/indemnity arrangements for these sites below)

Indemnity is provided through NHS schemes or through professional indemnity and applies to the whole study.

Please enclose a copy of relevant documents.

Question(s) 36 disabled.

A37. How is it intended the results of the study will be reported and disseminated? *(Tick as appropriate)*

- [x] Peer reviewed scientific journals
- [x] Internal report
- [x] Conference presentation
- [ ] Other publication
- [x] Submission to regulatory authorities
- [x] Access to raw data and right to publish freely by all investigators in study or by Independent Steering Committee on behalf of all investigators
- [x] Written feedback to research participants
- [ ] Presentation to participants or relevant community groups
- [ ] Other/none e.g. Cochrane Review, University Library

A38. How will the results of research be made available to research participants and communities from which they are drawn?

Newsletters will give progress reports to all participants to highlight results and engage investigators. These will also be shared with patient groups. Definitive results to share with participants are not likely to be available until completion of the study and dermatologists/specialist nurses will be encouraged to provide feedback to participating patients under their care.

A39. Will the research involve any of the following activities at any stage (including identification of potential research participants)? *(Tick as appropriate)*

- [ ] Examination of medical records by those outside the NHS, or within the NHS by those who would not normally have access
- [x] Electronic transfer by magnetic or optical media, e–mail or computer networks
- [x] Sharing of data with other organisations
- [ ] Export of data outside the European Union
- [x] Use of personal addresses, postcodes, faxes, e–mails or telephone numbers
- [ ] Publication of direct quotations from respondents
- [ ] Publication of data that might allow identification of individuals

- ☐ Use of audio/visual recording devices
- ☑ Storage of personal data on any of the following:
  - ☐ Manual files including X−rays
  - ☑ NHS computers
  - ☐ Home or other personal computers
  - ☑ University computers
  - ☐ Private company computers
  - ☑ Laptop computers

Further details:

Patient identifiable data including: name, address and date of birth, will be held separately in a secure location in the University of Manchester using unique identifiers. All data shared with companies manufacturing the particular biologic agent and with regulatory authorities (MHRA, EMEA) will be anonymous. Patient identifiable data will only be held for the purposes of ensuring patient follow up and linkage to cancer and death registries whereby the project team would be automatically informed of serious adverse events collected in this way.

The databases that contain this data will be password protected and data will be stored according to the requirements of the Data Protection Act 1998.

A40. What measures have been put in place to ensure confidentiality of personal data? Give details of whether any encryption or other anonymisation procedures have been used and at what stage:

The BADBIR data management team will comply with all aspects of the Data Protection Act 1998. Data will be captured primarily as web−based data entry by the consultant/nurse specialist. Appropriate training will be provided for users to enter the data. This data will then be electronically encrypted before being transferred to the University of Manchester. Paper forms will be available as a substitute for those unable to use the web−based interface.

The database containing patient identifying information will be separate from that compiling the clinical data. Both databases will be securely locked via password protection so that only those members of the data management team dealing directly with patient follow up will have access.

A41. Where will the analysis of the data from the study take place and by whom will it be undertaken?

At the University of Manchester by the study team. The analysis will be completed in consultation with the BAD Steering Committee and the independent Data Monitoring and Ethics Committee (DMEC).

A42. Who will have control of and act as the custodian for the data generated by the study?

The British Association of Dermatologists

A43. Who will have access to research participants' or potential research participants' health records or other personal information? *Where access is by individuals outside the normal clinical team, justify and say whether consent will be sought.*

Each company will have access to aggregated data on patients exposed to the drug they manufacture and to the control data. Anonymised individual adverse events will be reported in timely controlled fashion to EMEA and MHRA according to the standards required by them.

A44. For how long will data from the study be stored?

15 Years Months

Give details of where they will be stored, who will have access and the custodial arrangements for the data:

In the custody of the University of Manchester. Data will be under the ownership of the BAD who will control access to data through the BAD Steering Committee and the principal investigators.

A45–1. How has the scientific quality of the research been assessed? *(Tick as appropriate)*

- [x] Independent external review
- [x] Review within a company
- [ ] Review within a multi–centre research group
- [x] Review within the Chief Investigator's institution or host organisation
- [ ] Review within the research team
- [ ] Review by educational supervisor
- [ ] Other

Justify and describe the review process and outcome. If the review has been undertaken but not seen by the researcher, give details of the body which has undertaken the review:

The protocol was drawn up in consultation with a working group comprising experts, patients representatives, nurses, rheumatologists, epidemiologists and dermatologists through 12 drafts and was peer reviewed by Professor Nils Feltelius (Stockholm) and by experts in epidemiology, pharmacovigilance and risk management within the pharmaceutical industry. The protocol has also been approved by the EMEA. Feedback from peer review has been incorporated into the design of the study.

A45–2. How have the statistical aspects of the research been reviewed? *(Tick as appropriate)*

- [x] Review by independent statistician commissioned by funder or sponsor
- [ ] Other review by independent statistician
- [ ] Review by company statistician
- [ ] Review by a statistician within the Chief Investigator's institution
- [x] Review by a statistician within the research team or multi–centre group
- [ ] Review by educational supervisor
- [ ] Other review by individual with relevant statistical expertise

In all cases give details below of the individual responsible for reviewing the statistical aspects. If advice has been provided in confidence, give details of the department and institution concerned.

Title:	Forename/Initials:	Surname:
Dr	Chris	Roberts

Department:	Biostatistics Group, Division of Epidemiology and Health Sciences
Institution:	The University of Manchester
Address:	Stopford Building Oxford Road Manchester
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Fax:	0161 275 1637
Mobile:	
E–mail:	Chris.Roberts@manchester.ac.uk

Please enclose a copy of any available comments or reports from a statistician.

Question(s) 46–47 disabled.

A48. What is the primary outcome measure for the study?

To examine the long–term risks of adverse events (such as cancer, demyelinating disease and tuberculosis) with biological therapies compared to exising second–line therapies for psoriaisis.

A49. What are the secondary outcome measures?*(if any)*

(i) To assess the relative long–term efficacy of biological therapies compared to conventional therapies.
(ii) To examine factors determining increased risk of adverse events, e.g. previous drug exposure, previous cumulative ultraviolet light exposure, drug combinations.

A50. How many participants will be recruited?
If there is more than one group, state how many participants will be recruited in each group. For international studies, say how many participants will be recruited in the UK and in total.

The aim is to recruit 4,000 subjects on conventional treatments and 2,000 to 4,000 on each biological intervention (depending on the uptake of these drugs in clinical practice). There are currently three biologic agents (etanercept, efalizumab, infliximab) licensed for use in psoriasis in the UK but one (etanercept) is likely to be used much more than the others due to the NICE guidelines recommending it to be the first drug of choice in psoriasis.

A51. How was the number of participants decided upon?

Based on likely numbers of patients to be treated with these agents and thereby the number of patient years data we can collect, experience of the BSR Biologics Register for rheumatoid arthritis and the estimated incidence of adverse events. From this a table was generated for the likelihood of finding significant differences between the biologicals and conventional treatments.

If a formal sample size calculation was used, indicate how this was done, giving sufficient information to justify and reproduce the calculation.

4,000 patients in each group would, steadily entered over 5 years give an exposure of 12,000 patient years in each group. This would give power to detect at least a 3–4 fold increase in risk of events occurring at a frequency of 1 in a 1000 or 1 in 2000 patients. Rarer events would be detected if the relative risks were higher. nQuery Advisor (version 5, JD Elashoff) was used to calculate the person years of follow–up required using a 95% confidence level and 80% power with a 1 to 1 ratio in each cohort. This would be sufficient to detect for example the risk of non–melanoma skin cancer a particular concern in these patients who have been exposed to phototherapy.

A52. Will participants be allocated to groups at random?

○ Yes ◉ No

A53. Describe the methods of analysis (statistical or other appropriate methods, e.g. for qualitative research) by which the data will be evaluated to meet the study objectives.

The initial analyses will consist of comparisons in baseline status between the individuals in the treatment cohorts. For the purposes of analysis (initially) follow up time will be censored in each group if there is switching to another class of biologic therapy and censored in the comparison group if there is switching to a biologic agent. The adverse events of interest are calculated per person time of follow up, following the start

of therapy. Depending on the adverse events, separate analyses are undertaken (i) restricting consideration to time on drug, which includes the period within 90 days of last injection and (ii) all person time following start of therapy (for events such as malignancy). Time−dependent regression analyses will be undertaken to compare event rates between groups after adjusting for baseline and other differences.

A54. Where will the research take place? *(Tick as appropriate)*

- [x] UK
- [ ] Other states in European Union
- [ ] Other countries in European Economic Area
- [x] Other

If Other, give details:

Eire may contribute data (as members of the British Association of Dermatologists).

A55. Has this or a similar application been previously rejected by a Research Ethics Committee in the UK, the European Union or the European Economic Area?

- ○ Yes
- ◉ No

A56. In how many and what type of host organisations (NHS or other) in the UK is it intended the proposed study will take place?

Indicate the type of organisation by ticking the box and give approximate numbers if known:

	Number of organisations
[x] Acute teaching NHS Trusts	20
[x] Acute NHS Trusts	176
[x] NHS Primary Care Trusts or Local Health Boards in Wales	3
[ ] NHS Trusts providing mental healthcare	
[x] NHS Health Boards in Scotland	14
[x] HPSS Trusts in Northern Ireland	11
[ ] GP Practices	
[ ] NHS Care Trusts	
[ ] Social care organisations	
[ ] Prisons	
[ ] Independent hospitals	
[ ] Educational establishments	
[ ] Independent research units	
[ ] Other (give details)	

Other:

Question(s) 57−57a disabled.

A58. Has external funding for the research been secured?

(●) Yes ( ) No

If Yes, give details of funding organisation(s) and amount secured and duration:

Organisation:	Wyeth
Address:	Huntercombe Lane South Taplow Maidenhead
Post Code:	SL6 OPH
UK contact:	Nina Kola
Telephone:	01628 414979
Fax:	01628 540020
Mobile:	
E−mail:	kola@wyeth.com
Amount (£):	280K pa Duration: 60 Months

Organisation:	Serono Ltd
Address:	Stanwell Road, Feltham Middlesex
Post Code:	TW14 8NX
UK contact:	Paul Runeckles
Telephone:	0208−818 7278
Fax:	208−8187222
Mobile:	
E−mail:	Paul.Runeckles@serono.com
Amount (£):	280K pa Duration: 60 Months

Organisation:	Schering−Plough Ltd
Address:	Shire Park Falcon Way, Welwyn Garden City Herts.
Post Code:	AL7 1TW
UK contact:	Dr Brihad Abhyankar
Telephone:	+44 (0) 1707 363606
Fax:	
Mobile:	
E−mail:	brihad.abhyankar@spcorp.com
Amount (£):	280K pa Duration: 60 Months

A59. Has the funder of the research agreed to act as sponsor as set out in the Research Governance Framework?

( ) Yes (●) No

Has the employer of the Chief Investigator agreed to act as sponsor of the research?

( ) Yes (●) No

Lead sponsor *(must be completed in all cases)*

Name of organisation which will act as the lead sponsor for the research:

University of Manchester

Status:

○ NHS or HPSS care organisation ◉ Academic ○ Pharmaceutical industry ○ Medical device industry ○ Other

If Other, please specify:

Address:

Post Code:
Telephone:
Fax:
Mobile:
E−mail:

Sponsor's UK contact point for correspondence with the main REC *(must be completed in all cases)*

Title: Dr Forename/Initials: Kath Surname: Watson

Address: ARC Epidemiology Unit
The University of Manchester, Stopford Building
Oxford Road, Manchester
Post Code: M13 9PT
Telephone: 0161 275 7390
Fax: 0161 275 1640
Mobile:
E−mail: Kath.Watson@manchester.ac.uk

Co−sponsors

Are there any co−sponsors for this research?

○ Yes ◉ No

A60. Has any responsibility for the research been delegated to a subcontractor?

○ Yes ◉ No

A61. Will individual *researchers* receive any personal payment over and above normal salary for undertaking this research?

○ Yes ◉ No

A62. Will individual *researchers* receive any other benefits or incentives for taking part in this research?

○ Yes ◉ No

A63. Will the host organisation or the researcher's department(s) or institution(s) receive any payment or benefits in excess of the costs of undertaking the research?

◉ Yes ○ No

If yes, give details including the amount of any monetary payment or the basis on which this will be calculated:

The arc Epidemiology Unit (The University of Manchester) who is hosting the data collection and analysis will recieve from the BAD sposorship money calculated on a basis of £215 per patient. Dermatology departments contributing data will receive £100 on registering and £50 for each follow up form.

A64. Does the Chief Investigator or any other investigator/collaborator have any direct personal involvement (e.g. financial, share−holding, personal relationship etc.) in the organisations sponsoring or funding the research that may give rise to a possible conflict of interest?

◉ Yes ○ No

If yes, give details including the amount of any monetary payment or the basis on which this will be calculated:

Dr Ormerod and Professor Griffiths have participated as investigators for the sponsoring companies clinical trials and as lecturers at sponsored events. Professor Griffiths has been involved as a member of advisory boards to all of these companies and Professor Alan Silman and Professor Deborah Symmons run the British Society for Rheumatology Biologics Register (BSRBR) with funding from Wyeth, Schering−Plough, Abbott and Amgen via the British Society for Rheumatology (BSR).

A65. Research reference numbers: *(give any relevant references for your study):*

Applicant's/organisation's own reference number, e.g. R&D (if available):
Sponsor's/protocol number:
Funder's reference number:
Project website: www.bad.org.uk

A66. Other key investigators/collaborators *(all grant co−applicants or protocol co−authors should be listed)*

Title: Dr Forename/Initials: Anthony Surname: Ormerod

Post:	Reader in Dermatology and Hon Consultant Dermatologist
Qualifications:	MBChB MRCP MD FRCPEdin FRCPLond
Organisation:	University of Aberdeen
Address:	Department of Medicine and Therapeutics Polwarth Building, Foresterhill Aberdeen
Postcode:	AB24 2ZD
Telephone:	01224 553955
Fax:	01224 550555
Mobile:	
E−mail:	a.d.ormerod@arh.grampian.scot.nhs.uk

Title: Prof Forename/Initials: Alan J Surname: Silman

Post:	Professor of Rheumatic Disease Epidemiology
Qualifications:	MSc MD FRCP FFPHM

Organisation:	arc Epidemiology Unit, The University of Manchester
Address:	Stopford Building Oxford Road Manchester
Postcode:	M13 9PT
Telephone:	0161 275 5041
Fax:	0161 275 5043
Mobile:	
E−mail:	alan.silman@manchester.ac.uk

Title: Prof Forename/Initials: Deborah PM Surname: Symmons

Post:	Professor of Rheumatology and Musculoskeletal Epidemiology
Qualifications:	MD MFPH FRCP
Organisation:	ARC Epidemiology Unit, The University of Manchester
Address:	Stopford Building Oxford Road Manchester
Postcode:	M13 9PT
Telephone:	0161 275 5044
Fax:	0161 275 5044
Mobile:	
E−mail:	deborah.symmons@manchester.ac.uk

Title: Dr Forename/Initials: Kath D Surname: Watson

Post:	BSRBR Study Co−ordinator
Qualifications:	PhD
Organisation:	ARC Epidemiology Unit, The University of Manchester
Address:	Stopford Building Oxford Road Manchester
Postcode:	M13 9PT
Telephone:	0161 275 7390
Fax:	0161 275 1640
Mobile:	
E−mail:	kath.watson@manchester.ac.uk

Question(s) 67 disabled.

PART A: Summary of Ethical Issues

A68. What are the main ethical issues with the research?

Summarise the main issues from the participant's point of view, and say how you propose to address them.

The main ethical issue with this study relates to data protection and data confidentiality. All data will be stored in accordance with the Data Protection Act 1998. Patients consent to their specialist providing data to the Register from their medical records and also for the National Health Service Central Register to access the records. Patients will also be asked to complete questionnaires about their health. All data received by the BADBIR will be stored in a secure database and patient identifying information will be held seperately from clinical data.

No−one outside of the research team will have access to this data. Patients are free to withdraw from the study at any time and this will in way affect the standard of care received.

Indicate any issues on which you would welcome advice from the ethics committee.

Question(s) 69−71 disabled.

PART B: Section 1 – List of proposed research sites

List below all research sites you plan to include in this study. The name of the site is normally the name of the acute NHS Trust, GP practice or other organisation responsible for the care of research participants. In some cases it may be an individual unit, private practice or a consortium – see the guidance notes.

Principal Investigators at other sites should apply to the relevant local Research Ethics Committee for site–specific assessment (SSA) using Part C of the application form. Applications for SSA may be made in parallel with the main application for ethical review (once the main REC has validated the application), or following issue of a favourable ethical opinion. Approval for each site will be issued to you by the main REC following SSA.

1. Name of the research site:

NHS Grampian

Principal Investigator for the study at this site:

Title: Dr Forename/Initials: A.D. Surname: Ormerod

Post: Reader in Dermatology and Honorary Consultant
Address: Depatment of Medicine and Therapeutics
Polwarth Building, University of Aberdeen,
Foresterhill, Aberdeen
Postcode: AB24 2ZD

PART B: Section 7 – Declarations

Declaration by Chief Investigator

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

– I undertake to abide by the ethical principles underlying the Declaration of Helsinki and good practice guidelines on the proper conduct of research.

– If the research is approved I undertake to adhere to the study protocol, the terms of the full application of which the main REC has given a favourable opinion and any conditions set out by the main REC in giving its favourable opinion.

– I undertake to seek an ethical opinion from the main REC before implementing substantial amendments to the protocol or to the terms of the full application of which the main REC has given a favourable opinion.

– I undertake to submit annual progress reports setting out the progress of the research.

– I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Officer.

– I understand that research records/data may be subject to inspection for audit purposes if required in future.

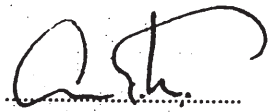
– I understand that personal data about me as a researcher in this application will be held by the relevant RECs and their operational managers and that this will be managed according to the principles established in the Data Protection Act.

– I understand that the information contained in this application, any supporting documentation and all correspondence with NHS Research Ethics Committees or their operational managers relating to the application:

- Will be held by the main REC until at least 3 years after the end of the study.
- May be disclosed to the operational managers or the appointing body for the REC in order to check that the application has been processed correctly or to investigate any complaint.
- May be seen by members of a peer review or other panel appointed by the Central Office for Research Ethics Committees to undertake accreditation of the REC.
- Will be subject to the provisions of the Freedom of Information Acts and may be disclosed in response to requests made under the Acts except where statutory exemptions apply.

Optional – please tick as appropriate:

☐ I would be content for members of other RECs to have access to the information in the application in confidence for training purposes. All personal identifiers and references to sponsors, funders and research units would be removed.

Signature: 

Print Name: C.E.M.Griffiths

Date: 19/12/2006

Declaration by the sponsor's representative

If there is more than one sponsor, this declaration should be signed on behalf of the co–sponsors by a representative of the sponsor nominated to take the lead for the REC application.

I confirm that: *(tick as appropriate)*

☑ This research proposal has been discussed with the Chief Investigator and agreement in principle to sponsor the research is in place.

☑ An appropriate process of scientific critique has demonstrated that this research proposal is worthwhile and of high scientific quality.*

☑ Any necessary indemnity or insurance arrangements, as described in question A35, will be in place before this research starts.

☑ Arrangements will be in place before the study starts for the research team to access resources and support to deliver the research as proposed.

☑ Arrangements to allocate responsibilities for the management, monitoring and reporting of the research will be in place before the research starts.

☑ The duties of sponsors set out in the NHS Research Governance Framework for Health and Social Care will be undertaken in relation to this research.**

* Not applicable to student research (except doctoral research).
** Not applicable to research outside the scope of the Research Governance Framework.

Signature: Karen Shaw

Print Name: KAREN SHAW

Post: HEAD OF RESEARCH OFFICE

Organisation:

Date: (dd/mm/yyyy) 20/12/2006

PART C: Site–Specific Assessment (SSA)

This form should be completed by the Principal Investigator for each site (see glossary)

Part C should be completed and sent with the relevant enclosures to each NHS Research Ethics Committee, which needs to consider site–specific issues. See guidance notes at the COREC website for further information about the application procedure.

The data in this box is populated from Part A.

Short title and version number:
BAD Biological Interventions Register

Name of NHS Research Ethics Committee to which application for ethical review is being made:
North West England

Project reference number from above REC: 07/MRE08/9

Name of NHS REC responsible for SSA:

SSA reference (for REC office use only):

Questions C1, C4, C5, C6, C7, C8 and C13a correspond to questions A1, A2, A65, A10, A12, A13 and A29 on main application form respectively and will populate automatically:

C1. Title of the research *(Populated from A1)*

Full title: British Association of Dermatologists Biological Interventions Register

Key words: Psoriasis, etanercept, efalizumab, infliximab, biological agents, patient register, pharmacovigilance

C2. Who is the Principal Investigator for this study at this site?

Title:

Forename/Initials:

Surname:

Post:

Qualifications:

Organisation:

Address:

Post Code:

E–mail:

Telephone:

Fax:

Mobile:

A copy of a current CV (maximum 2 pages of A4) for the Principal Investigator(s) must be submitted with the application

C2–1. Give the names and posts of other investigators or members of the research team responsible to the local Principal Investigator for this site.
Include all staff with a significant research role. If the site is a network or consortium, list all participating investigators below.

Title:
Forename/Initials:
Surname:
Position:
Qualifications:
Role in the research team:

C3. Indicate the number of trials/projects within the organisation that the local Principal Investigator has been involved with in the previous 12 months:

How many are still current (active or recruiting)?

C4. Chief Investigator *(Populated from A2)*

Title:	Forename/Initials:	Surname:
Professor	Christopher EM	Griffiths

Post:	Professor of Dermatology
Qualifications:	MD, FRCP, FRCPath
Organisation:	The University of Manchester
Address:	Dermatology Centre
	Hope Hospital, Stott Lane
	Salford
Post Code:	M6 8HD
E–mail:	christopher.griffiths@manchester.ac.uk
Telephone:	0161 2064392
Fax:	0161 2061095
Mobile:	

C5. Research reference numbers: *(Populated from A65)*

Applicant's/organisation's own reference number, e.g. R&D (if available):
Sponsor's/protocol number:
Funder's reference number:
Project website: www.bad.org.uk

C6. Give a full summary of the purpose, design and methodology of the planned research, including a brief explanation of the theoretical framework that informs it. It should be clear exactly what will happen to the research participant, how many times and in what order.
(Populated from A10–1)

Study design
This is a prospective observational cohort study to monitor the long−term effects of biologic therapy in patients with psoriasis in the UK. The study will consist of two cohorts comparing (i) patients with psoriasis newly treated with one of the biologic therapies, to (ii) patients with similar disease characteristics treated with non−biologic systemic therapies (including PUVA, methotrexate, ciclosporin and acitretin).

Patients will have been exposed to a variety of conventional treatments each with its own risks before starting on the biologic therapies. Their severe skin disease will also affect their risks, as will lifestyle e.g. smoking, drinking habits and socio−economic status. Data on all these aspects will be recorded for patients starting biologic therapy and for an equal number of patients treated with conventional therapy. It is only by analysing differences between the two groups of patients that risks of biologic therapies in psoriasis can be identified.

Recruitment and sample size
The recruitment of the biologic cohort for any particular agent will be determined by a number of factors including (i) the recommendation by NICE that all subjects with psoriasis treated with these agents should be registered (ii) the desire by the sponsoring companies that all treated patients within the UK should be registered to satisfy the requirements of the EMEA and MHRA and (iii) the uptake of the agents by the consultant dermatologists.

Based on recruitment rates of a similar register (the British Society for Rheumatology Biologics Register or BSRBR) it is anticipated that 2000−4000 patients for each biologic therapy will be recruited over a five year period. During the same time period, a cohort of comparison patients on standard therapy will also be recruited. Due to the NICE guidelines recommending that all patients with psoriasis should be registered with a national register, it is envisaged that patients in the biologic cohort will be recruited from all dermatology departments in the UK. The comparison cohort will also be recruited from all contributing centres to reduce the risk of selection bias.

However, the one recruitment factor that is under control of the Register is the size of the comparison cohort. A total sample of 4000 patients followed for five years is required to provide 80% power at the 5% significance level with a 1:1 ratio in each cohort to detect a three or four fold increase risk of events occurring at a frequency of 1/1000 or 1/2000. This calculation will allow the register to detect at least a 3− to 4−fold increase in the risk of non−melanoma skin cancer, a particular concern in these patients who have been exposed to phototherapy.

Eligibility
For patients to be eligible for the biologic cohort, they must have a diagnosis of psoriasis, be over 16 and be about to receive biologic therapy. Eligibility for the comparison cohort includes patients with psoriasis who are being treated with standard therapy, who have active disease and who are over 16 years of age.

Consent
Once a decision is made to treat a patient with a biologic therapy, the patient is asked to sign the patient consent form. A copy of the consent form will be provided to the patient for their records and a copy will be kept in the patient hospital notes. A copy of the consent form will be stored in the investigator file.

Data collection and follow−up
Once the patient has consented to take part, consultants then complete a British Association of Dermatologists Biological Intervention Registry (BADBIR) consultant baseline questionnaire on−line. This questionnaire collects details on clinical indication, disease severity including the Psoriasis Area and Severity Index (PASI), current and past therapy and co−morbidities. These forms are then electronically submitted to BADBIR.

Patients are then posted a baseline questionnaire which collects demographic details including occupation, smoking status, and the name and address of a close contact should the patient become lost to follow−up. The patient is also sent a diary to keep for the next 6 months. This diary collects information about new hospitalisations, new referrals and new drugs during this coming period.

Patients are followed up every 6 months via the consultant for three years and then annually for two years to collect clinical information on drug changes, disease severity and the occurrence of adverse events. Patients are also sent questionnaires and a diary every 6 months (for three years) to collect measures of functional status, health and well−being.

All patients will be flagged for malignancy and mortality with the General Registry Office (GRO, which is part of the Office for National Statistics or ONS)and the Scottish and Northern Ireland General Registry Office. Underlying cause of death will be obtained from the death certificates provided by the GRO's. Details on

malignancies, including date of diagnosis, site and morphology, will be obtained from the national cancer registry.

End of study
The study will end five years after the recruitment of the last patient.

Question(s) C7–C8 disabled.

C9a. Give the name of the research site for which the PI is responsible: *(Please give the name only. Further details of locations should be given in C10. The name of the site is normally the name of the acute NHS Trust, GP practice or other organisation responsible for the care of research participants. In some cases it may be an individual unit, private practice or consortium – see the guidance notes. Each GP practice is a separate site unless a formal consortium/network is in place.)*

If you wish to add further information about the definition of the site, please do so below:

C9b. Give the name of the NHS or other organisation with which the PI holds the necessary contract (substantive or honorary) to undertake the research at this site:

C9c. For NHS sites, give the name and contact details of the Research Governance contact for the research site at the care organisation or consortium:

Title: Forename/Initials: Surname:

Address:

Postcode:
Telephone:
Fax:
Mobile:
E–mail:

C9d. For non–NHS sites, give details of the arrangements for the management and monitoring of the research at this site:

C10. Specify all locations or departments at which research procedures will be conducted at this site.
Include details of any centres at other NHS care organisations where potential participants may be seen and referred for inclusion in the research at this site. Give details of any research procedures to be carried out off site, for example in participants' homes.

C11. How many research participants/samples is it anticipated will be recruited/obtained from this organisation in total?

C12a. Give details of who will be responsible for obtaining informed consent locally, their qualifications and relevant expertise and training in obtaining consent for research purposes:

C13a. What arrangements have been made for participants who might not adequately understand verbal explanations or written information given in English, or who have special communication needs? *(e.g. translation, use of interpreters etc.) (Populated from A29)*

Consultant dermatologists and specialist nurses will rely on interpreters to assist with registration of non−english speaking participants. Most areas with particular ethnic groups are able to provide interpreters especially as this is necessary anyway for routine clinical care and patient education, i.e. for injecting drugs etc...

C13b. What local arrangements have been made to meet these requirements (where applicable)?

☐ Not Applicable

C14. In addition to informing the GP (if required), what arrangements have been made to inform those responsible for the care of the research participants in the host care organisation of their involvement in the research?

C15. Are the facilities and staffing available locally adequate to perform any necessary procedures or interventions required for the study, and to deal with any unforeseen consequences of these?*(This should include consideration of procedures and interventions in both control and intervention arms of a study.)*

◉ Yes ○ No

If Yes, give the information necessary to justify your answer. If No, indicate what arrangements are being made to deal with the situation:

C16a. Give brief details of a contact point where participants may obtain further information about the study.

C16b. What is the contact point for potential complaints by research participants?

C16c. Is there a local source where potential participants can obtain independent information about being involved in a research study?*See guidance notes.*

C16d. Please specify the headed paper to be used for the participant information sheet.

C17. If any extra support might be required by research participants as a result of their participation, what local arrangements are being made to provide this?

PART C: Declaration

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

– I undertake to abide by the ethical principles underpinning the Declaration of Helsinki and good practice guidelines on proper conduct of research.

– If the research is approved I undertake to adhere to the study protocol, the terms of the full application of which the main REC has given a favourable opinion and any conditions set out by the main REC in giving its favourable opinion.

– I am aware of my responsibility to be up to date and comply with the requirements of the law and relevant guidelines relating to security and confidentiality of patient or other personal data, including the need to register when necessary with the appropriate Data Protection Controller.

– I understand that research records/data may be subject to inspection for audit purposes if required in future.

– I understand that personal data about me as a researcher in this application will be held by the relevant RECs and their operational managers and that this will be managed according to the principles established in the Data Protection Act.

– I understand that the information contained in this application, any supporting documentation and all correspondence with Research Ethics Committees relating to the application will be subject to the provisions of the Freedom of Information Acts. The information may be disclosed in response to a request under the Acts except where statutory exemptions apply.

Signature of the local Principal Investigator * .....

Date: (dd/mm/yyyy)

Print Name:

** The Chief Investigator should sign where s/he is also the local Principal Investigator for this research site.*

***PART C IS NOW COMPLETE AND SHOULD BE SUBMITTED** to the NHS Research Ethics Committee responsible for the site–specific assessment.*