Welcome to the Integrated Research Application System

IRAS Project Filter

The integrated dataset required for your project will be created from the answers you give to the following questions. The system will generate only those questions and sections which (a) apply to your study type and (b) are required by the bodies reviewing your study. Please ensure you answer all the questions before proceeding with your applications.

Please complete the questions in order. If you change the response to a question, please select 'Save' and review all the questions as your change may have affected subsequent questions.

Please enter a short title for this project (maximum 70 characters)
BADBIR

REC details:

Name of main REC:
North West England

REC Reference Number:
07/MRE08/9

NRES form lock code: AB/98888/1

1. Select one category from the list below:

- ○ Clinical trial of an investigational medicinal product
- ○ Study only involving data or tissues not identifiable to the researcher

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

- ◉ Other study

2. Does the study involve the use of any ionising radiation?

- ○ Yes
- ◉ No

3. In which countries of the UK will the research sites be located?*(Tick all that apply)*

- ☑ England
- ☑ Scotland
- ☑ Wales
- ☑ Northern Ireland

3a. In which country of the UK will the lead NHS R&D office be located:

- ◉ England
- ○ Scotland
- ○ Wales
- ○ Northern Ireland
- ○ This study does not involve the NHS

4. Do you plan to include any participants who are children?

(●) Yes ( ) No

5. Do you plan to include any participants who are adults unable to consent for themselves through physical or mental incapacity?

( ) Yes (●) No

Answer Yes if you plan to recruit living participants aged 16 or over who lack capacity, or to retain them in the study following loss of capacity. Intrusive research means any research with the living requiring consent in law. This includes use of identifiable tissue samples or personal information, except where application is being made to the Confidentiality Advisory Group to set aside the common law duty of confidentiality in England and Wales. Please consult the guidance notes for further information on the legal frameworks for research involving adults lacking capacity in the UK.

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

( ) Yes (●) No

NOTICE OF SUBSTANTIAL AMENDMENT
Please use this form to notify the main REC of substantial amendments to all research other than clinical trials of investigational medicinal products (CTIMPs).
The form should be completed by the Chief Investigator using language comprehensible to a lay person.

Details of Chief Investigator:

	Title	Forename/Initials	Surname
	Professor	Christopher E M	Griffiths
Work Address	Dermatology Centre		
	Hope Hospital, Stott Lane		
	Salford		
PostCode	M6 8HD		
Email	christopher.griffiths@manchester.ac.uk		
Telephone	01612064392		
Fax	01612061095		

Full title of study:	British Association of Dermatologists' Biologic Interventions Register
Lead sponsor:	The University of Manchester
Name of REC:	North West England
REC reference number:	07/MRE08/9
Name of lead R&D office:	Salford Royal Hospital Foundation Trust
Date study commenced:	16/08/2007
Protocol reference (if applicable), current version and date:	Current protocol is version 16 dated 01/12/2015
Amendment number and date:	Amendment 10 01/08/2017

Type of amendment

(a) Amendment to information previously given in IRAS

◉ Yes ○ No

If yes, please refer to relevant sections of IRAS in the "summary of changes" below.

(b) Amendment to the protocol

◉ Yes ○ No

If yes, please submit <u>either</u> the revised protocol with a new version number and date, highlighting changes in bold, or a document listing the changes and giving both the previous and revised text.

(c) Amendment to the information sheet(s) and consent form(s) for participants, or to any other supporting documentation for the study

◉ Yes ○ No

If yes, please submit all revised documents with new version numbers and dates, highlighting new text in bold.

Is this a modified version of an amendment previously notified and not approved?

○ Yes ◉ No

If yes, please explain the modifications made under "Summary of changes" below

Summary of changes

Briefly summarise the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study.
If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained.

1. Addition of New Cohort to the BADBIR Study Design

Summary :

The BADBIR Steering Committee is seeking to amend the study design to include a third cohort consisting of patients with moderate-to-severe psoriasis being treated with new small molecule treatments.

Rationale :

The management of patients with psoriasis has significantly changed in the ten years since the inception of BADBIR. In this time period more biologic therapies have become available as well as non-biologic 'small molecule' targeted treatments (e.g. apremilast) and more are expected on the market over the next few years. The importance of treatment evaluation both in term of effectiveness and safety in a real world population is increasingly emphasised. Currently, patients starting therapy on the newer biologics are included in BADBIR. Within the framework of the current study design this opportunity is not available for the new small molecule therapies. The BADBIR Steering Committee would like to rectify this situation by including small molecule therapeutics as a third cohort, so that these treatments can be similarly evaluated. Data collection and procedure will remain identical as that for the existing biologic and conventional cohorts (see BADBIR Protocol section 3.2.3 page 9 for inclusion criteria).

This change will ultimately benefit patients by allowing safety data to be collected on the full range of psoriasis treatments that are used for moderate to severe psoriasis, which will inform patient choice. The new cohort will ultimately result in more information being available for clinical decisions on treatment options to be made.

Summary of Changes:

The protocol has been updated with the scientific justification and inclusion / exclusion criteria for this new cohort.

---

2. Increase to Cohort Maximum Cap

Summary:
Increase recruitment size of biologic and small molecule targeted therapies to n = 6000 patients.

Rationale:
Firstly, as a result of a lower take up of Remicade (infliximab) (final recruitment n = 220) and Enbrel (etanercept) (final recruitment n = 1578), the overall target (n= 12,000) for the anti TNF group will not be achieved.

Additionally, it has been noted that there is attrition from all of the cohorts over time. Therefore, increasing the registration target will allow for more person years of follow-up to be collected, negating the impact of patients lost to

follow-up and increased power to detect rarer events.

Secondly, in anticipation of the inclusion of the new biologic therapies (e.g. brodalumab, guselkumab etc.) a contemporaneous cohort of patients is desirable as this is likely to be more representative of current prescribing patterns.

Thirdly, as outlined previously in Amendment 8, there is a dearth of information on long-term safety of biologic agents in children. Thus continuing recruitment to this cohort will allow for the collection of further data in this small but important sub-group of patients. The BADBIR protocol (Section 3.2, page 6) has been amended to reflect the proposed change in recruitment numbers

---

3. Update to the Patient Information Sheet (PIS) and Consent Form

Rationale:

The primary aim of BADBIR is to evaluate the long-term safety of new drugs for the treatment of psoriasis. Thus, accurate and complete reporting and recording of adverse events is vital. To this end, BADBIR has established linkage with organisations across the UK and Republic of Ireland for malignancy and death data. This ensures that if a patient is lost to follow up key outcome data are not missing. The utility of this approach has been illustrated in a recent publication at the International Conference on Pharmacoepidemiology & Therapeutic Risk Management in 20161. Currently, all other adverse events are captured directly via the dermatology team on the BADBIR. However, an audit of 358 patient records undertaken in 125 U.K. hospitals contributing data found that only 67% of serious adverse events (SAEs) were reported correctly as part of routine study procedure. An attempt to address this through education of the clinical teams is ongoing. However, there is still scope for adverse events not to be reported as despite the best efforts of the clinical team, it is not uncommon for patients to receive treatment at another health care facility and these data will be missed. Therefore, we propose linkage to the Inpatient Admission data services (where available, currently Wales, Scotland and England). This would ensure completeness of reporting, triangulation of SAEs already reported and ultimately allow a more accurate assessment of drug safety to be conducted and thus be available to patients.

To this end, BADBIR has already acquired the data from the Welsh and Scottish services as these organisations were satisfied that the permissions were implicit. However, NHS Digital advised that permission would need to be sought via Section 251 approval to link to the Hospital Episodes Statistics service. This has been supplied under the terms of a conditional approval (attached) such that all new participants would need to provide consent on the basis of a PIS and Consent Form that has been deemed acceptable by NHS Digital (patients currently in the study would need to be informed but not re-consented). We have subsequently engaged with the Information Governance Team at NHS Digital (formerly HSCIC) to agree on the content of a revised PIS and Consent Form and after extensive negotiation, the attached have been agreed.

Summary of changes to PIS and Consent Form: We have liaised with the Information Governance team at NHS Digital to update the PIS in line with their recommendations which has resulted in the following changes:
• Expanded description of the process of the BADBIR study linking to a participants record with a linkage service
• Details of the linkage organisations involved included as an appendix
• Greater clarity on potential third party access to anonymised data

References:
1 - Mason, K et al. 2016, 'Completeness of reporting of basal cell carcinoma and squamous cell carcinoma to a pharmacovigilance register and the Health and Social Care Information Centre.' 32nd International Conference on Pharmacoepidemiology & Therapeutic Risk Management, Dublin, Ireland, 25/08/16 - 28/08/16.

---

4. Protocol Revision

The following changes have been made:

Page 1
• The study team has been updated

Section 1- Background

• Update on the current status and expected developments in available therapies for moderate/severe psoriasis
• Minor grammatical corrections

Section 2 - Rationale
• Addition of a third study cohort (new small molecule therapies) as described above

Section 3 - Methods
• Minor corrections and the addition of the third study cohort (as described in point 1 of this summary of changes)
• Increase to cohort recruitment cap (as described in point 2 of this summary of changes)
• A more detailed description of links to national data services for malignancy, mortality and inpatient admission has been added (3.2.1).

Section 7 - Baseline Data
• This section have been re-ordered and formatted to reflect the flow of the data collection questionnaires.

Section 8 – Follow-up Data
• This section have been re-ordered and formatted to reflect the flow of the data collection questionnaires.
• Height of patients < 16 years old will be collected at each follow-up in order to observe growth. For younger participants, there is a desire to monitor the impact, if any the exposure to psoriasis treatments has on development and growth.

---

5. Changes to supporting Documentation

The following supporting documents have been updated:

Consent Materials (all dated 01/08/2017):
• Patient Consent Form v5
• Information Sheet v5
• Patient Assent Form v5
• Parent or Guardian Consent Form v5
• Participant Information Sheet for very young children, guide: under 6 v2
• Participant Information Sheet for young children, guide: 6-10 v2
• Participant Information Sheet for children, guide: 11-16 v2

Questionnaires (all dated 01/08/2017):
• Clinical Baseline Questionnaire v9
• Clinical Follow-up Questionnaire v9 - One new item of data collection added (height for patients <16 years old)

Any other relevant information

Applicants may indicate any specific issues relating to the amendment, on which the opinion of a reviewing body is sought.

11 documents are enclosed in support:

1. Protocol v17
2. Conditional approval to access Hospital Episodes Statistics data
3. Patient Consent Form v5
4. Information Sheet v5
5. Patient Assent Form v5
6. Parent or Guardian Consent Form v5
7. Participant Information Sheet for very young children, guide: under 6 v2
8. Participant Information Sheet for young children, guide: 6-10 v2
9. Participant Information Sheet for children, guide: 11-16 v2
10. Clinical Baseline Questionnaire v9
11. Clinical Follow-up Questionnaire v9

List of enclosed documents

Document	*Version*	*Date*

Protocol	17	01/08/2017
Conditional approval to access Hospital Episodes Statistics data		24/03/2016
Patient Consent Form	5	01/08/2017
Information Sheet	5	01/08/2017
Patient Assent Form	5	01/08/2017
Parent or Guardian Consent Form	5	01/08/2017
Participant Information Sheet for very young children, guide: under 6	2	01/08/2017
Participant Information Sheet for young children, guide: 6-10	2	01/08/2017
Participant Information Sheet for children, guide: 11-16	2	01/08/2017
Clinical Baseline Questionnaire	9	01/08/2017
Clinical Follow-up Questionnaire	9	01/08/2017

Declaration by Chief Investigator

1. *I confirm that the information in this form is accurate to the best of my knowledge and I take full responsibility for it.*
2. *I consider that it would be reasonable for the proposed amendment to be implemented.*

Date of submission:.....

Signature:.....

Declaration by the sponsor's representative

I confirm the sponsor's support for this substantial amendment.

Signature: .....

Print Name:

Post:

Organisation:

Date: *(dd/mm/yyyy)*

Does this amendment involve new types of exposure or increased exposure to ionising radiation?

○ Yes ◉ No

If Yes, please provide details below:

Does this amendment involve inclusion of adults lacking capacity or a change to the arrangements relating to adults lacking capacity?

○ Yes ◉ No

If Yes, please provide details below:

Declaration by Sponsor's Representative

This section was signed electronically by Lynne MacRae on 07/08/2017 15:21.

Job Title/Post:	Faculty Research Practice Governance Coordinator
Organisation:	University of Manchester
Email:	lynne.macrae@manchester.ac.uk