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)
Toxicity from Anti-TNF Therapy

REC details:

Name of main REC:
North West 5 Research Ethics Committee

REC Reference Number:
00/8/53

NRES form lock code:

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
	Prof Kimme Hyrich
Work Address	Arthritis Research UK Epidemiology Unit, 2nd Floor Stopford Bldg, Oxford Road, Manchester
PostCode	M13 9PL
Email	kimme.hyrich@manchester.ac.uk
Telephone	01612751679
Fax	01612751640

Full title of study:	Prospective observational study of the long term hazards of anti-TNF therapy in rheumatoid arthritis
Lead sponsor:	University of Manchester
Name of REC:	North West 5 Research Ethics Committee
REC reference number:	00/8/53
Name of lead R&D office:	Central Manchester University Hospitals NHS Foundation Trust
Date study commenced:	01/12/2000 (date of original ethical approval)
Protocol reference (if applicable), current version and date:	Main protocol dated 06/10/2003. Two current sub-study protocols: 1) certolizumab and anti-TNF (v3: 15/10/2010) tocilizumab (v1.1: 17/01/2011)
Amendment number and date:	Amendment 23: 12/07/2016

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.

This amendment covers 2 main points:

i) Study invitation letter for outreach centres
ii) Re-consenting patients directly when they switch drug cohorts

i) Outreach study invitation letter

The BSRBR-RA has a study invitation letter (v1: 17/05/2012, approved by the REC on 13/06/2012) which is an optional letter for hospitals to use if they wish to send the patient information sheet to a potential participant in advance of their next clinic visit, as each participant must be recruited within 6 months of beginning therapy with a biologic treatment to ensure we do not bias the data with only those who remained on treatment.

We have been informed by some centres that potential participants are being missed due to the clinic visits not falling within the 6 month recruitment window. As the study is observational only, we are unable to invite participants in to clinic specifically to obtain consent. This means that the patient potentially misses out on the opportunity to be involved in the research study.

A new invitation letter has been developed to be used in parallel to the existing invitation letter, named 'BSRBR-RA Outreach Consent Invitation Letter V1 12/07/2016'. This is to be used for participants who will not be seen in clinic before the end of the 6 month recruitment period. The participant has the option of signing the consent form (following a telephone call from a member of the hospital's rheumatology/research team to explain the study and discuss any questions the patient might have) and returning it to the hospital to be signed by the health care professional. A copy of the fully signed consent form will then be posted back to the participant and they will then be enrolled in the study.

ii) Re-consenting patients when they switch drugs

In addition, patients who are already in the study but then switch to a new drug which is one of our actively recruiting cohorts, can be re-registered in the study on the new drug. This allows us to re-start the patient follow-up in order for us to get a full picture of the effects of the new drug. We re-consent patients at this stage to re-start the three years of follow-up directly with the patient. However, in practice, it is proving difficult for some hospitals to obtain re-consent as they don't always see the patients in clinic when this happens and therefore we are receiving no measures of disease activity/functional status when the patient switches to the new drug.

A patient letter has been developed to be used in these instances, named 'BSRBR-RA Direct Patient Re-consent Letter V1_12/07/2016' which explains to the participant why we are seeking their consent again, and makes it clear that they are under no obligation to sign the consent form. A copy of the consent form (along with a HAQ and EQ5D) would be included which the patient could sign and return via a supplied pre-paid envelope.

If the participant does not wish to sign the consent form we ask that they return it blank.
Contact details of the study team are also provided should they wish to ask any questions or seek further explanation.

If there has been no reply two weeks after the original letter was sent, we will send one reminder letter (BSRBR-RA Direct Patient Re-consent Letter V1_12/07/2016).

Any participants who have withdrawn from the study will not be contacted.

Prior to any letters being sent, the research team at the relevant site will be contacted to ensure that we have the participant's current address and that they are not deceased as well as explaining the intention to re-consent. It is hoped that this might help alleviate some of the workload for sites that take part in the study.

Any other relevant information

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

List of enclosed documents

Document	*Version*	*Date*
BSRBR-RA Outreach Consent Invitation Letter	Version 1	12/07/2016
BSRBR-RA Direct Patient Re-consent Letter	Version 1	12/07/2016
BSRBR-RA Direct Patient Re-consent Reminder Letter	Version 1	12/07/2016

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: 6.9.16

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 Mrs Catherine Barrow on 01/09/2016 13:23.

Job Title/Post:	Research Policy Manager for Research Governance, Faculty of Biology, Medicine & Health
Organisation:	The University of Manchester
Email:	catherine.barrow@manchester.ac.uk