National Patient Safety Agency

National Research Ethics Service

NOTICE OF SUBSTANTIAL AMENDMENT

For use in the case of all research other than clinical trials of investigational medicinal products (CTIMPs). For substantial amendments to CTIMPs, please use the EU-approved notice of amendment form (Annex 2 to ENTR/CT1) at http://eudract.emea.eu.int/document.html#guidance.

To be completed in typescript by the Chief Investigator in language comprehensible to a lay person and submitted to the Research Ethics Committee that gave a favourable opinion of the research ("the main REC"). In the case of multi-site studies, there is no need to send copies to other RECs unless specifically required by the main REC.

Further guidance is available at http://www.nres.npsa.nhs.uk/applicants/review/after/amendments.htm.

Details of Chief Investigator:

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Full title of study:	Prospective Observational Study of the long term hazards of anti-TNF therapy in rheumatoid arthritis
Name of main REC:	North West 5 REC – Haydock Park
REC reference number:	MREC 00/8/53
Date study commenced:	October 2001
Protocol reference *(if applicable)*, current version and date:	Protocol dated 06/10/2003
Amendment number and date:	Today's date: 17/05/2012

Type of amendment (indicate all that apply in bold)

(a) Amendment to information previously given on the NRES Application Form

Yes *No*

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

(b) Amendment to the protocol

Yes ***No***

If yes, please submit either 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 to the REC and given an unfavourable opinion?

Yes ***No***

Summary of changes

Briefly summarise the main changes proposed in this amendment using language comprehensible to a lay person. Explain the purpose of the changes and their significance for the study. In the case of a modified amendment, highlight the modifications that have been made.

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 two main points:

i) An **extension of the study recruitment and follow up period**

ii) A study **invitation letter**.

i) Extension of the study follow up period

The 'extension to follow up' amendment which was approved on 06/05/2008 stated that all participants would be followed up via their consultant rheumatologist until the end of the study in 2013. However the register has been opened to additional cohorts of participants (REC approval letters dated 04/08/2010 and 20/12/2010) and it was stated that participants recruited into the newly-opened cohorts - as with all participants in the study – will be followed up for at least five years. Thus additional funding has been obtained and the follow up of all participants in the BSRBR will now continue until the study ends – there is no study end date in place but current funding will see the register continue until at least Sept 30, 2018. This will ensure that as much information is collected as possible, resulting in follow up data being collected past the 12 year mark for those patients registered within the first year of the study.

As the study is so established, there is an assumption that the follow up of participants is permanently ongoing; as stated in the 2008 extension to follow up amendment:

"In support of this proposal, the BSRBR Steering Committee (who meet on a quarterly basis), which includes a patient representative, have indicated that there was an expectation that active follow-up to the end of the study was already occurring."

As the participants consented to be involved in the study for at least five years there is no requirement to re-consent.

ii) Study invitation letter

A study invitation letter has been developed for research nurses/ staff working on the study within each hospital to send out to any potential participant before they are next due in clinic – this is optional and has been developed as some centres have asked if there is an invitation letter available for them to use. An information sheet will be included with the letter so that when the participant next comes in to clinic they can consent to be involved in the study if they so wish; consent will be witnessed by the research nurse/designated healthcare professional working on the study. It is made clear in the letter that participation in the study is optional, and choosing to decline participation will not affect the standard of care received in any way.

Any other relevant information

Applicants may indicate any specific ethical issues relating to the amendment, on which the opinion of the REC is sought.

List of enclosed documents

Document	Version	Date
Notice of Amendment	N/A	
BSRBR Invitation Letter	1	17/05/2012

Declaration

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

Signature of Chief Investigator: .....

Print name: ..... Kimme Hyrich

Date of submission: ..... 29/5/12 .....