NHS
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: 26 October 2011

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 refers to two clinician-completed questionnaires that have been modified to better-suit the needs of the study and a clarification of consent processes

Modified Questionnaires

i) Clinical baseline form

This form has been re-formatted and has had some redundant questions removed so that clinicians are not troubled for information that is no longer required. The prior biologic exposure form has been incorporated onto the new clinical baseline form as most patients treated currently have had previous exposure to biologic therapy, and switching between therapies is common.

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Steps have been taken to ensure that personal data is always treated confidentially; the section where personal details are entered (on page one) can be detached from the rest of the questionnaire

and stored in a separate location as required.

ii) Clinical follow-up form

Previously, one follow up form was used to collect information for the first 5 years of follow up (the three-page consultant follow up form version 8: 23/10/2010) and another form was used to collect follow up information past this point (the single page extension of follow up form version 3: 04/11/2010).

It was decided that in order to streamline internal processes and at the same time simplify the data collection for the clinical team, these two forms have been merged; the new two page clinical follow up questionnaire can be used to collect clinical data throughout the study regardless of how long the patient has been in the study. Some redundant questions have been removed, but we now also ask the clinician to document the DAS28 score at the time the participant switches therapy, and also to record dates for any temporary discontinuation of therapy. This information would be documented in the participant's case notes as part of routine clinical care and would therefore take minimal additional effort to record.

This new form will be used to collect all follow up information on both participants in the biologic cohort and participants in the DMARD comparison cohort.

Consenting participants

At the time of original ethics application in 2000, it was stated that the participant must have had the information sheet for at least a week before consent is obtained but the current protocol (dated October 2003) and the substudy protocols for tocilizumab, rituximab and certolizumab recruitment do not specify that the participant must have had the information sheet for a certain amount of time. The BSRBR is an observational study which uses simple questionnaires, and the participant is free to withdraw at any time without their care being affected in any way.

There is no requirement for the participant to have had the information sheet for a length of time before they consent to be involved in the study .The participant will be given as much time as they require in which to make a decision regarding participation in this research study; this will allow the participant to decide to sign the consent form immediately if they so wish whilst not in any way detracting from the rights of those patients who wish to take longer to consider participation.

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*
Clinical Baseline form	Version 9	10/08/2011
Clinician Follow up form	Version 9	10/08/2011

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: D. P. M. Symmons

Date of submission: 27/10/2011