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 MREC
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:	14/03/2008

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.

BSRBR has been recruiting and following patients receiving biologic and conventional therapy for rheumatic diseases since October 2001. We aim to have completed patient recruitment of the current biologic drugs (adalimumab, etanercept, infliximab) and the comparison cohort by 30/09/2008. The current protocol states that all patients are actively followed via the clinician using questionnaires for a period of five years from registration and via the patients themselves for three years. All patients in the register are also flagged with the national cancer and death registers for life-long follow-up.

BSRBR has funding available to complete the study by 30/09/2013. Although we will be notified by the national registers (via the Office for National Statistics) if any patient develops a cancer or dies after the active five years of follow-up, BSRBR will not be receiving drug therapy or adverse event information past this five year period from first registration. Therefore, we are proposing to extend the consultant questionnaire follow-up of all patients to the end of the study (2013). It is proposed that after the initial five years of follow-up, an annual minimum data questionnaire (see Extension to Follow-up Questionnaire_v2_01022008.doc) will be sent to the rheumatology department. Only minimum data on changes to biologic/DMARD therapy, a most recent DAS28 (where available) and any adverse events occurring would be requested. This will enable BSRBR to use the data sent by the national registers on cancer and death in drug specific analysis past the first five years of follow-up. In addition, it will also enable BSRBR to consider the risk of other serious adverse events past the initial five years. 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.

We would not need to re-consent the patients as the current patient information states “At this stage we do not know how long we will want to collect this information from you and about you. It is likely to be for at least five years” – version 6 dated 05/03/2007. In addition, the patients themselves will not be contacted directly by the BSRBR after the first three years of follow-up as specified in the current protocol (dated 06/10/2003).

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*
Extension to Follow-up	2	01/02/2008

Questionnaire_v2_01022008.doc		
Study Protocol		06/10/2003
Patient information sheet	Version 6	05/03/ 2007
Patient consent form	Version 6	05/03/2007

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: ……

Date of submission: ……..