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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|---|---|
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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 |

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|---|---|
| **Amendment number and date:** | |

**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.*

## 1. Comparability of Controls Form

One of the original concerns with this observational prospective cohort study was the potential lack of comparability between the exposed and non-exposed RA cohorts in

relation to their underlying risk of endpoint development and that the comparison cohort would be somewhat different to those in the biologic cohort. To try and help us to understand any differences between these two cohorts we are proposing to ask rheumatologists/nurses why patients submitted to the control cohort are not currently receiving anti-TNF therapy to get a better understanding of such potential differences. This will be carried out using a short one-page form (see Comparability of Controls Form_v1.doc). It is proposed that this form will be sent out to rheumatology departments for completion once a new control patient has been registered, although it will also be downloadable from the BSRBR website. For those patients who have already been recruited to this cohort, we propose to carry out a one-off mailing to rheumatology departments asking them to complete one of these forms per patient registered.

## 2. Data Validation and Audit Exercise

It is important to gain an understanding of the quality and completeness of the clinical data that is submitted to the BSRBR and thus the BSRBR are proposing to carry out a pilot source verification audit. The aim of this audit is to compare information in patient medical records to the information which is submitted on the BSRBR Consultant Baseline and Follow-up questionnaires in small proportion of hospitals that have registered patients. It is proposed for the pilot audit that 10 centres will be randomly chosen from all hospitals across the UK who have submitted patient data to the register. It is then proposed that 5 patients will be randomly chosen per hospital for the audit exercise. The audit would involve checking the original questionnaires submitted to BSRBR against the information in the patient medical records. Due to the volume of clinical data collected by the BSRBR, it is envisaged that only data key to current analysis will be verified, such as changes to drug therapy, disease severity and adverse events. This key data is shown in the Patient History Summary Sheet_v1.doc. The BSRBR would need to gain approval from each Trust and Consultant for access to patient medical records.

This audit will enable BSRBR to start addressing the important question regarding source data quality and give an idea as to whether a more detailed audit is required.

**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* |
|---|---|---|

| | | |
|---|---|---|
| Comparability of Controls Form_v1.doc | Version 1 | 01/06/2007 |
| Patient History Summary Sheet_v1.doc | Version 1 | 24/07/2007 |
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**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:* ……