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:	

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.

The British Society for Rheumatology Biologics Register (BSRBR) has been collecting data on patients receiving biologic therapy (the anti-TNF drugs etanercept, infliximab and adalimumab) for rheumatic diseases during routine clinical care since October 2001. Although the register primarily consists of patients with rheumatoid arthritis (RA) (the leading indication for prescription of these drugs),

it has also been collecting information on adult patients with other rheumatic diseases. One of these conditions is juvenile idiopathic arthritis (JIA).

JIA is a heterogeneous condition characterised by onset of arthritis prior to the 16th birthday. It is known to have 8 different subtypes, each characterised by the pattern of arthritis and well as other features of disease, including presence/absence of fevers, rashes and presence of rheumatoid factor in the blood. Unfortunately, although diagnosed in childhood, many children continue to have some disability and limitation of their activities of daily living and around 50–70% are estimated to have active disease into adulthood. The anti-TNF agents have been studied in children with JIA. However, less is known on the benefits of these therapies when prescribed to adults who have been living with JIA since childhood. The BSRBR has now recruited approximately 400 patients who had there arthritis begin prior to the age of 16 years who have been prescribed anti-TNF drugs during routine clinical use and would like to study outcomes (treatment response, drug survival and safety) in this group. The majority of data for this analysis already exists within the database from ongoing data collection. However, as the register has been primarily geared to study outcomes in RA and not JIA, the baseline questionnaires have omitted certain questions specifically related to JIA and in particular, details of the JIA subtype. Therefore, without this data, it will be unclear whether certain JIA subtypes may respond better to anti-TNF therapy, or be more prone to side effects. Understanding these differences may help direct therapy, given the increasing choice of biologic agents to patients with this condition.

Proposed changes to study:

1. Using data already collected as part of the BSR Biologics Register, identify patients with disease onset prior to the 16th birthday.
2. Send a supplementary questionnaire to the consultant rheumatologist (already participating in the study) to collect details of rheumatic disease onset to help classify the patients into one of 8 JIA subtypes. Patients have already consented to collection of further clinical information from their medical records. No additional investigations will be requested.

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*
JIA biologics consultant letter.doc	Version 1	June 2008
JIA biologics questionnaire version 1.doc	Version 1	June 2008

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: ……