Central Office for Research Ethics Committees (COREC)

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.corec.org.uk/applicants/apply/amendments.htm.

Details of Chief Investigator:

Name: Professor Alan Silman
Address: arc Epidemiology Unit
The University of Manchester
Stopford Building
Manchester M13 9PT
Telephone: 0161 275 5037
E-mail: Alan.silman@manchester.ac.uk
Fax: 0161 275 5043

Full title of study:	Prospective observational study of the long-term hazards of biologic therapy in rheumatic conditions
Name of main REC:	North West MREC
REC reference number:	MREC 00/8/53
Date study commenced:	01/10/2001
Protocol reference *(if applicable)*, current version and date:	
Amendment number and date:	

Type of amendment (indicate all that apply in bold)

(a) Amendment to information previously given on the REC 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.

Please see attached Notice of Substantial Amendment form dated 15/01/2007 for original substantial amendment application.

This is an amendment to the original substantial amendment application in response to the Sub-Committee of the North West REC held on 30 January 2007.

To clarify the queries put forward by the Sub-Committee we present the following:

Point 1)

All of the questionnaires in the booklet are represented in their full validated form:

i. Hospital Anxiety and Depression score (HADs) (Bjelland *et al.* 2002; Zigmond *et al.* 1983)

ii. Beliefs about Medicines Questionnaire (BMQ) (Horne *et al.* 1999; Horne 1999)

iii. Coping Questionnaire (Newman *et al.* 1993; Stone *et al.* 1984)

iv. Compliance Questionnaire Rheumatology (CQR) (de Klerk *et al.* 1999; de Klerk *et al.* 2003)

There is one exception to this: the Illness Perception Questionnaire-Revised (IPQ-R) (Moss-Morris *et al.* 2002), where section 3, the cause domain has been omitted. The IPQ-R measures 9 domains: identity (a simple count score), consequence, timeline (acute/chronic and cyclical), coherence, treatment and personal control, emotional representation and causes. All domains except identity are scored on a 5-point likert scale. However the cause domain in the third and separate section of the questionnaire relates to personal ideas about the aetiology of the illness. The varied nature of the eighteen etiological factors listed in this domain means it is not appropriate to reduce the scale to a single score. In addition these items do not in anyway contribute to other domain scores. The cause domain has therefore been omitted from the study, which is inline with previously reported studies (Carlisle *et al.* 2005; Murphy *et al.* 1999).

As it was felt that it was necessary to include a number of questionnaires in the booklet, this section of the IPQ-R was removed to reduce the time taken for the completion of the booklet and reduce the burden on the patient.

All of these validated questionnaires have been put into one booklet for ease of completion by the patient. However, we do take your point and agree that the questionnaires should appear more separate than they are at present. To address your concerns, we suggest the following steps:

Proposals to address Point 1)

(i) Each individual questionnaire has now been identified under its own headings in the booklet.

(ii) Throughout the study literature, the series of questionnaires are referred to as a "booklet" rather than a "questionnaire".

(iii) A description on the covering page to the booklet now explains the booklet contains a number of different questionnaires.

Point 2)

We also take your point about the quality of life questions included which some may find to be of a sensitive nature. We propose the following:

Proposals to address Point 2)

(i) To address the introduction of questionnaires intending to collect quality of life data, there is a change to the title of the booklet from "Your views on your illness, treatment and general health" to "Your views on your illness, treatment and general health and how this impacts on your life".

(ii) The following paragraph has been added to the patient information sheet under the section "What will happen to me if I take part?"

"You may find some of the questions to be of a sensitive nature particularly in the questionnaire "Your views on your illness, treatment and general health and how this impacts on your life". You are not obliged to answer all questions. We would like to take this opportunity to reassure you that all data received will be treated with the utmost confidence."

Please note that following the end of data collection for this study, it is proposed to revert back to the original patient information sheet and consent form (currently version 5, date approved 27/11/2003).

References

Bjelland, I., Dahl, A. A., Haug, T. T., and Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res*, **52**, (2), 69-77.

Carlisle, A. C., John, A. M., Fife-Schaw, C., and Lloyd, M. (2005). The self-regulatory model in women with rheumatoid arthritis: relationships between illness representations, coping strategies, and illness outcome. *British Journal of Health Psychology*, **10**, (Pt 4), 571-587.

de Klerk, E., van der Heijde, D., Landewe, R., van der Tempel, H., and van der Linden, S. (2003). The compliance-questionnaire-rheumatology compared with electronic medication event monitoring: a validation study. *J Rheumatol*, **30**, (11), 2469-2475.

de Klerk, E., van der Heijde, D., van der Tempel, H., and van der Linden, S. (1999). Development of a questionnaire to investigate patient compliance with antirheumatic drug therapy. *J Rheumatol*, **26**, (12), 2635-2641.

Horne, R. (1999). Patients' beliefs about treatment: the hidden determinant of treatment outcome? *J Psychosom Res*, **47**, (6), 491-495.

Horne, R., Weinman, J., and Hankins, M. (1999). The beliefs about medicines questionnaire: The development and evaluation of a new mthod for assessing the cognitive representation of medication. *Psychol Health*, **14**, 1-24.

Moss-Morris, R., Weinman, J., Petrie, K. J., Horne, R., Cameron, L. D., and Buick, D. (2002). The revised Illness Perception Questionnaire (IPQ-R). *Psychol Health*, **17**, (1), 1-16.

Murphy, H., Dickens, C., Creed, F., and Bernstein, R. (1999). Depression, illness perception and coping in rheumatoid arthritis. *J Psychosom Res*, **46**, (2), 155-164.

Newman, S. P. and Revenson, T. A. (1993). Coping with rheumatoid arthritis. *Bailliere's Clinical Rheumatology*, **7**, (2), 259-280.

Stone, A. A. and Neale, J. M. (1984). New measure of daily coping: development and preliminary results. *J Pers Soc Psychol*, **46**, 892-906.

Zigmond, A. S. and Snaith, R. P. (1983). The Hospital Anxiety and Depression Scale. *Acta Psychiatr Scand*, **67**, 361-370.

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*
Views on your illness, treatment and general health and how this impacts on your life	1.1	05/03/2007
Patient 6 month follow up questionnaire	6	04/01/2007
Protocol	1	04/01/2007
Patient information sheet	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: ……………………………………