NHS

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:	Prof. Costantino Pitzalis
Address:	Centre for Experimental Medicine and Rheumatology 2nd Floor, Sir John Vane Science Centre William Harvey Research Institute Barts and The London School of Medicine and Dentistry Charterhouse Square London EC1M 6BQ
Telephone:	(0)20 7882 8191
E-mail:	c.pitzalis@qmul.ac.uk
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Full title of study:	**Lymphoid Neogenesis In Rheumatoid Arthritis: The histomorphological pattern of the synovial membrane (SM) predicts disease outcome.**
Name of main REC:	**Kings College Hospital Research Ethics Committee**
REC reference number:	05/Q0703/198
Date study commenced:	01/12/2006
Protocol reference *(if applicable)*, current version and date:	Version 2 - 11th September 2009
Amendment number and date:	2nd amendment application - 11th September 2009

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.

The first 5 amendments we feel are minor however number 6 and 7 are likely to be substantial amendments

1.Re-naming of the project title and ethics submission

As already mentioned, this project has recently received funding from the MRC (approval letter attached). The project is aimed at developing a cohort of patients with early inflammatory arthritis to gather both clinical and biological information to better characterise their disease process, with the long term goal of developing better prognostic tools to predict outcome and potentially guide therapeutic intervention based on pathobiology (similarly to other conditions such as renal diseases or cancer). This project is entirely based upon the ethics submission above. It is on that basis, we desire to change the name of our ethics submission to **P**athobiology of **E**arly **A**rthritis **C**ohort (**PEAC**). We have submitted a new Patient information sheet and consent form with the title modified to reflect the above. We believe this will remove the opportunity for confusion when patients are

being recruited and consented as well as with in our respective R&D departments at each trust.

2. New Principal Investigator at the Kings College Hospital Site
At the time of the original Ethics submission, the PI (Prof C. Pitzalis) was based at King's College London hence the application to Kings Ethics Committee. Following his relocation to St Bartholomew's and the Royal London in 2007, Dr. Ernest Choy (who is one of the co-investigators on the MRC initiative) has taken over the position of PI at the Kings site. Dr Choy, of course, will make sure that the PIS will be put onto KCH headed paper and provides the relevant local contacts for patients.

His contact details are below.
Dr. Ernest Choy
Consultant Rheumatologist
Sir Alfred Baring Garrod Clinical Trials Unit
Academic Department of Rheumatology
King's College London
Weston Education Centre
Cutcombe Road
London SE5 9RJ

3.Change to Prof. Pitzalis' contact number
We have updated the PIS to reflect the updated contact telephone number for Prof. Pitzalis and his research team.

4.Removal of text from PIS
We have updated the PIS by removing the text relating to Consumers for Ethics in Research (CERES). This organisation no longer exists and continued inclusion in the Patient Information Sheet would be potentially confusing for the patient.

5.Modification of the PIS to include venepuncture
The original ethics submission agreed to patients undergoing venepuncture, however there is no specific mention of this on the latest version of the Patient Information Sheet. We have added a paragraph to the PIS in the spirit of transparency and in keeping with good clinical practice.

6.The inclusion of Ultrasound data routinely collected from patients with early inflammatory arthritis.
The use of ultrasound imaging has emerged over the past few years as an excellent method of assessing non-invasively patients with inflammatory arthritis. Specifically, there is evidence to suggest that it more sensitive that clinical examination in detecting on-going inflammatory disease in patients who previously have been classified as being in clinical remission. Whilst ultrasound imaging has not been validated as a tool to guide therapeutic intervention it is routinely performed on our patients as part of the inflammatory arthritis care pathway. This data is acquired on all patients who present to our clinic and follow the inflammatory arthritis care pathway.

We ask, that at inception, we are able to seek permission from patients to use this information routinely acquired during their clinic visits. We plan to incorporate this data into a regression analysis model along with clinical and biological data already recorded. Our ultimate aim is to identify imaging, clinical and biological factors, which correlate with poor disease outcome. The use of the ultrasound imaging data will not influence treatment decisions or affect the standard of care provided to all patients recruited to this study.

7.Retention of urine samples
Patients attending clinic routinely donate urine samples. These samples, after having 'dip-stick' analysis performed are discarded. We ask the committee's permission to seek patients consent to retain theses samples for the scientific purposes (metabolomic analysis).

Any other relevant information

Applicants may indicate any specific ethical issues relating to the amendment, on which the opinion of the REC is sought.

We do not fee there are any significant ethical issues with these amendments. The change of study name will standardise documentation for this project and reduce the opportunity for confusion when patients are being consented and enrolled.

Incorporating the use of ultrasound imaging in to this project adds significant value to the research project. Patients routinely receive US examinations whilst attending our early arthritis clinic. The information from this imaging modality will **not** be used to alter patient management and so will only be used retrospectively in trying to better characterise patients with inflammatory arthritis and their clinical outcome.

Similarly, the retention of a urine specimen, which has already been donated for testing at a clinic, would also add value to this project. The patient would not be required to provide any further specimens than is routinely requested in the clinic and subsequently discarded.

List of enclosed documents

Document	*Version*	*Date*
PIS	Version 6	11 September 2009
Consent	Version 6	11 September 2009
Document outlining Protocol modification	Version 2	11 September 2009
Cover letter		11 September 2009

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: Professor Costantino Pitzalis

Date of submission: 13th September 2009 .....