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NHS

National Research Ethics Service

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28 August 2007

Professor Julia Hippisley-Cox
Professor of Clinical Epidemiology & General Practice
University of Nottingham
Division of Primary Care, 13th Floor
Tower Building, University Park
Nottingham NG7 2RD

Dear Professor Hippisley-Cox

Full title of study: **Derivation and validation of a new Cardiovascular Disease Risk Score for the UK: Validation using THIN data.**

REC reference number: **07/H0718/69**

The Research Ethics Committee reviewed the above application at the meeting held on 22 August 2007.

Ethical opinion

The Committee noted that, as the study was focusing on patients who attend GP clinics, a large cohort of non-attenders would be excluded from the study.

The Committee also questioned whether a patient's data could be present on both databases being employed, thus duplicating results.

However, after discussion, the Committee agreed to give a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation.

Ethical review of research sites

The Committee agreed that all sites in this study should be exempt from site-specific assessment (SSA). There is no need to submit the Site-Specific Information Form to any Research Ethics Committee. The favourable opinion for the study applies to all sites involved in the research.

Conditions of approval

The favourable opinion is given provided that you comply with the conditions set out in the attached document. You are advised to study the conditions carefully.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Application	1	11 July 2007
Investigator CV	CV for Professor Julia Hippisley-Cox	11 July 2007
Protocol	4.1	11 July 2007
Covering Letter	Letter to Ms Marshall from Professor Hippisley-Cox	11 July 2007
Letter from Sponsor	Letter to Professor Hippisley-Cox from Mr Brooks	18 July 2007

R&D approval

You should arrange for the R&D office at all relevant NHS care organisations to be notified that the research will be taking place, and provide a copy of the REC application, the protocol and this letter.

All researchers and research collaborators who will be participating in the research at a NHS site must obtain final approval from the R&D office before commencing any research procedures.

Membership of the Committee

The members of the Ethics Committee who were present at the meeting are listed on the attached sheet.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees (July 2001) and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

07/H0718/69	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project

Yours sincerely

pp Louise Braley

Dr T. J. Steiner
Chairman

Email: louise.braley@nwlh.nhs.uk

Enclosures: *List of names and professions of members who were present at the meeting and those who submitted written comments*
Standard approval conditions

Copy to: Dr Roger Brooks
Deputy Director
Research Innovation Services
University of Nottingham, King's Meadow Campus
Lenton Lane
Nottingham NG7 2NR

Attendance at Committee meeting on 22 August 2007

Committee Members:

Name	*Profession*	*Present*	*Notes*
Sir Adrian Baillie	Financial Invester	Yes	
Dr Sue Birtwistle	General Practitioner	Yes	
Dr Malcolm Boyce	Pharmacologist	Yes	
Dr Peter Brodrick	Consultant Anaesthetist	Yes	
Ms Juliet Dunmur	Editor	No	
Dr Ruth Harris	Research Nurse	Yes	
Ms Trudi Hilton – Co-opted	Pharmacist	No	
Dr John Keen	General Practitioner	Yes	
Dr Adrian Lambourne	Statistician	Yes	
Ms Linda McDonald	Nurse Consultant	Yes	
Ms Frances Percival	Pharmacist	No	
Dr Andy Petros	Consultant in Neonatal Intensive Care	No	
Dr Amin Rahemtulla	Consultant Haematologist	Yes	
Lady Sarah Riddell	Editor	No	
Dr Deborah Rutter	Qualitative Researcher	Yes	
Dr T. J. Steiner	Reader in Clinical Physiology	Yes	
Dr Olivia Stevenson	Clinical Trials Administrator	Yes	

In Attendance:

Name	
Ms Louise Braley	Manager
Dr Les Huson	Observer

RESEARCH IN HUMAN SUBJECTS OTHER THAN CLINICAL TRIALS OF INVESTIGATIONAL MEDICINAL PRODUCTS

Standard conditions of approval by Research Ethics Committees

1. Further communications with the Research Ethics Committee

1.1 Further communications during the research with the Research Ethics Committee that gave the favourable ethical opinion (hereafter referred to in this document as "the Committee") are the personal responsibility of the Chief Investigator.

2. Commencement of the research

2.1 It is assumed that the research will commence within 12 months of the date of the favourable ethical opinion.

2.2 In the case of research requiring site-specific assessment (SSA) the research may not commence at any site until the Committee has notified the Chief Investigator that the favourable ethical opinion is extended to the site.

2.3 The research may not commence at any NHS site until the local Principal Investigator (PI) or research collaborator has obtained research governance approval from the relevant NHS care organisation.

2.4 Should the research not commence within 12 months, the Chief Investigator should give a written explanation for the delay. It is open to the Committee to allow a further period of 12 months within which the research must commence.

2.5 Should the research not commence within 24 months, the favourable opinion will be suspended and the application would need to be re-submitted for ethical review.

3. Duration of ethical approval

3.1 The favourable opinion for the research generally applies for the duration of the research. If it is proposed to extend the duration of the study as specified in the application form, the Committee should be notified.

4. Progress reports

4.1 Research Ethics Committees are required to keep a favourable opinion under review in the light of progress reports and any developments in the study. The Chief Investigator should submit a progress report to the Committee 12 months after the date on which the favourable opinion was given. Annual progress reports should be submitted thereafter.

4.2 Progress reports should be in the format prescribed by NRES and published on the website (see http://www.nres.npsa.nhs.uk/applicants/review/after/progress.htm#submission)

4.3 The Chief Investigator may be requested to attend a meeting of the Committee or Sub-Committee to discuss the progress of the research.

5. Amendments

5.1 If it is proposed to make a substantial amendment to the research, the Chief Investigator should submit a notice of amendment to the Committee.

5.2 A substantial amendment is any amendment to the terms of the application for ethical review, or to the protocol or other supporting documentation approved by the Committee, that is likely to affect to a significant degree:

(a) the safety or physical or mental integrity of the trial participants

(b) the scientific value of the trial

(c) the conduct or management of the trial.

5.3 Notices of amendment should be in the format prescribed by NRES and published on the website, and should be personally signed by the Chief Investigator.

5.4 A substantial amendment should not be implemented until a favourable ethical opinion has been given by the Committee, unless the changes to the research are urgent safety measures (see section 7). The Committee is required to give an opinion within 35 days of the date of receiving a valid notice of amendment.

5.5 Amendments that are not substantial amendments ("minor amendments") may be made at any time and do not need to be notified to the Committee.

6. Changes to sites *(studies requiring site-specific assessment only)*

6.1 Where it is proposed to include a new site in the research, there is no requirement to submit a notice of amendment form to the Committee. The Site-Specific Information (SSI) form of the application form together with the local Principal Investigator's CV should be submitted to the relevant REC for site-specific assessment (SSA).

6.2 Similarly, where it is proposed to make important changes in the management of a site (in particular, the appointment of a new PI), a notice of amendment form is not required. A revised SSI form for the site (together with the CV for the new PI if applicable) should be submitted to the relevant REC for SSA.

6.3 The relevant REC will notify the Committee whether there is any objection to the new site or Principal Investigator. The Committee will notify the Chief Investigator of its opinion within 35 days of receipt of the valid application for SSA.

6.4 For studies designated by the Committee as exempt from SSA, there is no requirement to notify the Committee of the inclusion of new sites.

7. Urgent safety measures

7.1 The sponsor or the Chief Investigator, or the local Principal Investigator at a trial site, may take appropriate urgent safety measures in order to protect research participants against any immediate hazard to their health or safety.

7.2 The Committee must be notified within three days that such measures have been taken, the reasons why and the plan for further action.

8. Serious Adverse Events

8.1 A Serious Adverse Event (SAE) is an untoward occurrence that:

(a) results in death
(b) is life-threatening
(c) requires hospitalisation or prolongation of existing hospitalisation
(d) results in persistent or significant disability or incapacity
(e) consists of a congenital anomaly or birth defect
(f) is otherwise considered medically significant by the investigator.

8.2 A SAE occurring to a research participant should be reported to the Committee where in the opinion of the Chief Investigator the event was related to administration of any of the research procedures, and was an unexpected occurrence.

8.3 Reports of SAEs should be provided to the Committee within 15 days of the Chief Investigator becoming aware of the event, in the format prescribed by NRES and published on the website.

8.4 The Chief Investigator may be requested to attend a meeting of the Committee or Sub-Committee to discuss any concerns about the health or safety of research subjects.

8.5 Reports should not be sent to other RECs in the case of multi-site studies.

9. Conclusion or early termination of the research

9.1 The Chief Investigator should notify the Committee in writing that the research has ended within 90 days of its conclusion. The conclusion of the research is defined as the final date or event specified in the protocol, not the completion of data analysis or publication of the results.

9.2 If the research is terminated early, the Chief Investigator should notify the Committee within 15 days of the date of termination. An explanation of the reasons for early termination should be given.

9.3 Reports of conclusion or early termination should be submitted in the form prescribed by NRES and published on the website.

10. Final report

10.1 A summary of the final report on the research should be provided to the Committee within 12 months of the conclusion of the study. This should include information on whether the study achieved its objectives, the main findings, and arrangements for publication or dissemination of the research including any feedback to participants.

11. Review of ethical opinion

11.1 The Committee may review its opinion at any time in the light of any relevant information it receives.

11.2 The Chief Investigator may at any time request that the Committee reviews its opinion, or seek advice from the Committee on any ethical issue relating to the research.

12. Breach of approval conditions

12.1 Failure to comply with these conditions may lead to suspension or termination of the favourable ethical opinion by the Committee.