National Research Ethics Service

NRES Committee London - Bloomsbury
HRA NRES Centre Manchester
Barlow House 3rd Floor
4 Minshull Street
Manchester
M1 3DZ

Telephone: 0161 625 7815
Fax: 0161 625 7299

25 September 2014

Professor Hilary Critchley
University of Edinburgh
47 Little France Crescent
Edinburgh
EH16 4TJ

Dear Professor Critchley

Study title:	**Ulipristal acetate versus conventional management of heavy menstrual bleeding (HMB; including uterine fibroids): a randomised controlled trial and exploration of mechanism of action (UCON trial)**
REC reference:	**14/LO/1602**
EudraCT number:	**2014-003408-65**
IRAS project ID:	**145282**

The Research Ethics Committee reviewed the above application at the meeting held on 10 September 2014. Thank you for attending to discuss the application, together with Professor Williams and Ms Daniels, via teleconference.

We plan to publish your research summary wording for the above study on the HRA website, together with your contact details, unless you expressly withhold permission to do so. Publication will be no earlier than three months from the date of this favourable opinion letter. Should you wish to provide a substitute contact point, require further information, or wish to withhold permission to publish, please contact the REC Manager Dr Ashley Totenhofer, nrescommittee.london-bloomsbury@nhs.net.

Ethical opinion

The members of the Committee present gave a favourable ethical opinion of the above research on the basis described in the application form, protocol and supporting documentation, **subject to the conditions specified below**.

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Additional Conditions Specified by the REC:

1. Please add the study flow charts to the Participant Information Sheets.

2. Please add the list of contra-indicated medicines to the GP letter.

3. Please add a point to the Consent Form giving permission for them to be contacted about follow-up studies

You should notify the REC in writing once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which can be made available to host organisations to facilitate their permission for the study. Failure to provide the final versions to the REC may cause delay in obtaining permissions.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations.

Registration of Clinical Trials

All clinical trials (defined as the first four categories on question 2 of the IRAS filter page) must be registered on a publically accessible database within 6 weeks of recruitment of the first participant (for medical device studies, within the timeline determined by the current registration and publication trees).

There is no requirement to separately notify the REC but you should do so at the earliest opportunity e.g. when submitting an amendment. We will audit the registration details as part of the annual progress reporting process.

To ensure transparency in research, we strongly recommend that all research is registered but for non-clinical trials this is not currently mandatory.

If a sponsor wishes to contest the need for registration they should contact Catherine Blewett (catherineblewett@nhs.net), the HRA does not, however, expect exceptions to be made. Guidance on where to register is provided within IRAS.

Clinical trial authorisation must be obtained from the Medicines and Healthcare products Regulatory Agency (MHRA).

The sponsor is asked to provide the Committee with a copy of the notice from the MHRA, either confirming clinical trial authorisation or giving grounds for non-acceptance, as soon as this is available.

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Ethical review of research sites

NHS Sites

The favourable opinion applies to all NHS sites listed in the application taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Summary of discussion at the meeting

Social or scientific value; scientific design and conduct of the study

The committee noted that the application had been submitted to the NIHR and queried if funding had been provided yet.

You stated they have approved all parts, you just need to sign the contract but you can't do this until you have a Favourable Opinion from an ethics committee.

The committee queried if the NIHR had asked for any changes to the Protocol, particularly around recruitment and the use of primary care.

You stated that the primary care involvement is region specific. Some patients may be recruited from secondary care but others may be recruited directly from primary care. You confirmed that you have good engagement with Primary Care in your region. Each centre is asked to identify two patients a month which should be feasible.

Ms Daniels stated they have undertaken a similar study previously and have found it worked to use GP surgeries as Participant Identification Centres.

The committee queried if they are confident that they will be able to recruit sufficient numbers.

Ms Daniels stated they are.

The committee commented it may be beneficial to have a table setting out the possible risks to recruitment, how they may be mitigated and other strategies that may be used.

You agreed that you need to be thinking about other recruitment strategies sooner rather than later. You stated that one way of helping with recruitment is to raise awareness of the study which is why you have the poster. You stated you are aware that many women suffer from this condition but suffer without saying anything.

Favourable risk benefit ratio; anticipated benefit/risks for research participants (present and future)

The committee queried if the drug would be provided after the end of the trial.

You stated at the moment it is just licensed to be given up until surgical intervention. If participants find it acceptable you would like to continue using it but you will only be able to do this if it becomes licensed.

Care and protection of research participants; respect for potential and enrolled participants' welfare and dignity

The committee queried if travel expenses would be paid.

You stated you would pay these.

Informed consent process and the adequacy and completeness of participant information

The committee noted in private discussion that it may be helpful if the Consent Form had a point giving permission for them to be contacted about follow-up studies.

The committee commented that the flow diagrams in the Protocol are helpful and would be beneficial if these could be added to the Participant Information Sheets.

You agreed this would be a good idea.

Ms Daniels said they had not used this before but could add a simplified version

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Copies of advertisement materials for research participants [UCON Clinic Poster]	1.0	19 August 2014
Covering letter on headed paper		19 August 2014
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [ACCORD]		29 July 2014
GP/consultant information sheets or letters	1.0	19 August 2014
Letter from sponsor [Accord/NHS Lothian]		18 August 2014
Non-validated questionnaire [UCON Follow-up Questionnaire]	1.0	19 August 2014
Non-validated questionnaire [UCON Follow Up Menstrual Blood Loss Diary]	1.0	19 August 2014
Non-validated questionnaire [UCON Baseline Questionnaire]	1.0	19 August 2014
Non-validated questionnaire [UCON Baseline Menstrual Blood Loss Diary]	1.0	19 August 2014
Non-validated questionnaire [UCON Follow-up Questionnaire (incl. UFSQOL)]	1.0	19 August 2014
Non-validated questionnaire [UCON Baseline Questionnaire (incl. UFSQOL)]	1.0	19 August 2014
Other [email clarification]		21 August 2014
Other [email clarification]		21 August 2014
Other [GCP Certificate]	Hilary Critchley	25 June 2014
Participant consent form [UCON Participant Consent Form (Edinburgh)]	1.0	19 August 2014
Participant consent form [UCON Participant Consent Form]	1.0	19 August 2018
Participant information sheet (PIS) [UCON PIS (Edinburgh)]	1.0	19 August 2014
Participant information sheet (PIS) [UCON PIS]	1.0	19 August 2014
REC Application Form	3.5	19 August 2014
Referee's report or other scientific critique report [UCON Comments from Board]		
Research protocol or project proposal [UCON Protocol]	1.0	19 August 2014
Summary CV for Chief Investigator (CI) [Professor Hilary Critchley]		
Summary of product characteristics (SmPC) [Mirena 20mcg]		11 June 2013
Summary of product characteristics (SmPC) [Esmya 5mg Tablets]		05 September 2012
Summary, synopsis or diagram (flowchart) of protocol in non		

technical language [Flowchart]		

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

This Committee is recognised by the United Kingdom Ethics Committee Authority under the Medicines for Human Use (Clinical Trials) Regulations 2004, and is authorised to carry out the ethical review of clinical trials of investigational medicinal products.

The Committee is fully compliant with the Regulations as they relate to ethics committees and the conditions and principles of good clinical practice.

After ethical review

Reporting requirements

The attached document "After ethical review – guidance for researchers" gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

User Feedback

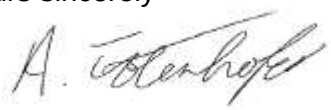
The Health Research Authority is continually striving to provide a high quality service to all applicants and sponsors. You are invited to give your view of the service you have received and the application procedure. If you wish to make your views known please use the feedback form available on the HRA website: http://www.hra.nhs.uk/about-the-hra/governance/quality-assurance/

HRA Training

We are pleased to welcome researchers and R&D staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

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

Yours sincerely



Signed on behalf of:
Dr Joe Brierley
Chair

Email: nrescommittee.london-bloomsbury@nhs.net

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

"After ethical review – guidance for researchers"

Copy to: Dr Annya Smyth – University of Edinburgh

Ms Karen Maitland - NHS Lothian

Mr Lee Priest – University of Birmingham

NRES Committee London - Bloomsbury

Attendance at Committee meeting on 10 September 2014

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Joe Brierley (Chair)	Consultant Intensivist	Yes	Chaired the meeting
Ms Sally Doganis	Executive Producer and Media Consultant	Yes	
Dr Rashmi Gandhi	Neonatal registrar	No	
Professor Faith Gibson (Alternate Vice-Chair)	Clinical Professor of Children and Young People's Cancer Care	Yes	
Ms Claire Khalil	Pharmacist	No	
Dr Rachel L Knowles	Clinical Research Fellow	No	
Dr Leah Li	Statistician	No	
Dr Vincenzo Libri	Consultant in Clinical Pharmacology	Yes	
Reverend Jim Linthicum (Vice-Chair)	Lay member - Hospital Chaplain	Yes	
Ms Clare Madin	Retired Clinical Data Management Manager	No	
Ms Michelle McPhail	Lecturer in Management Studies	Yes	
Dr Katie Elizabeth Myers Smith	Health Psychologist	No	
Ms Nabila Youssouf	Clinical Trials Manager	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Miss Regina Caden	REC Assistant
Dr Ashley Totenhofer	REC Manager