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North Wales Research Ethics Committee - West
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Professor Tom Solomon
Head, Liverpool Brain Infections Group
University of Liverpool
Duncan Building
Daulby St, Liverpool
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01 August 2011

Dear Professor Solomon,

Study title:	**Meningitis North West: Epidemiology and outcomes in meningitis in the North of England: A prospective, observational, cohort study**
REC reference:	**11/WA/0218**
Protocol number:	**UoL000699**

Thank you for your letter of 29 July 2011 responding to the Committee's request for further information on the above research and submitting revised documentation.
The further information has been considered on behalf of the Committee by the Chairman.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Mental Capacity Act 2005

I confirm that the committee has approved this research project for the purposes of the Mental Capacity Act 2005. The committee is satisfied that the requirements of section 31 of the Act will be met in relation to research carried out as part of this project on, or in relation to, a person who lacks capacity to consent to taking part in the project.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites 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).

Conditions of the favourable opinion

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

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

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).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter		
REC application submission code: 66167/227943/1/909		06 July 2011
Protocol	2	28 July 2011
User guide to the protocol	1	30 June 2011
Letter of invitation to participant	1	30 June 2011
Patient Information Leaflet	5	28 July 2011
Participant Consent Form	4	28 July 2011
Consultee Declaration form	3	28 July 2011
Participant Information Sheet on Genital Self Swabbing	1	22 June 2011
Letter to Asymptomatic patients with HSV-2PCR positive genital swabs	1	22 June 2011
GP/Consultant Information Sheets	1	28 July 2011
Covering Letter for Questionnaires	1	21 June 2011
Questionnaire: SF-36	1992	
Questionnaire: EQ-5D	1990	
Questionnaire: A-B Neuropsychological Assessment Scale		
Questionnaire: HIT-6	1.1	
Questionnaire: TMS	1	30 June 2011
Letter from the Funder (Meningitis Research Foundation)		31 May 2009
Letter from Sponsor		20 May 2011
Evidence of insurance or indemnity		03 August 2010
Investigator CV: Chief Investigator - Prof Tom Solomon		
Investigator CV: Student - Dr Fiona McGill		24 June 2011
Response to Request for Further Information		29 July 2011

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.

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.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

11/WA/0218	**Please quote this number on all correspondence**

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

Yours sincerely

Rossela Roberts

Mr David Owen
Chairman

Email: rossela.roberts@wales.nhs.uk

Enclosures: "After ethical review – guidance for researchers"

Copy to: *Sponsor: Lindsay Carter, University of Liverpool*
R&D Office: Mrs Heather Rogers, Royal Liverpool and Broadgreen University Hospitals Trust

NHS
National Patient Safety Agency

National Research Ethics Service

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

After ethical review – guidance for sponsors and investigators

This document sets out important guidance for sponsors and investigators on the conduct and management of research with a favourable opinion from a NHS Research Ethics Committee. Please read the guidance carefully. A failure to follow the guidance could lead to the committee reviewing its opinion on the research.

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 The research must not commence at any site until the local Principal Investigator (PI) or research collaborator has obtained management permission or approval from the organisation with responsibility for the research participants at the site.

2.3 Should the research not commence within 12 months, the Chief Investigator should give a written explanation for the delay

2.4 Should the research not commence within 24 months, the Committee may review its opinion.

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.

3.2 Where the research involves the use of "relevant material" for the purposes of the Human Tissue Act 2004, authority to hold the material under the terms of the ethical approval applies until the end of the period declared in the application and approved by the Committee.

4. Progress reports

4.1 Research Ethics Committees are expected 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 www.nres.npsa.nhs.uk/applicants/after-ethical-review/).

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. The agreement of the sponsor should be sought before submitting the notice of amendment.

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

Management permission (all studies)

6.1 For all studies, management permission should be obtained from the host organisation where it is proposed to:

- include a new site in the research, not included in the list of proposed research sites in the original REC application
- appoint a new PI or Local Collaborator at a research site
- make any other significant change to the conduct or management of a research site.

In the case of any new NHS site, the Site-Specific Information (SSI) Form should be submitted to the R&D office for review as part of the R&D application.

Site-specific assessment (where required)

6.2 The following guidance applies only to studies requiring site-specific assessment (SSA) as part of ethical review.

6.3 In the case of *NHS/HSC sites*, SSA responsibilities are undertaken on behalf of the REC by the relevant R&D office as part of the research governance review. The Committee's favourable opinion for the study will apply to any new sites and other changes at sites provided that management permission is obtained. There is no need to notify the Committee (or any other REC) about new sites or other changes, or to provide a copy of the SSI Form.

6.4 Changes at *non-NHS sites* require review by the local REC responsible for site-specific assessment (SSA REC). Please submit the SSI Form (or revised SSI Form as appropriate) to the SSA REC together with relevant supporting documentation. The SSA REC will advise the main REC whether it has any objection to the new site/PI or other change. The main REC will notify the Chief Investigator and sponsor of its opinion within a maximum of 35 days from the date on which a valid SSA application has been received by the SSA REC.

Studies not requiring SSA

6.5 For studies designated by the Committee as not requiring SSA, there is no requirement to notify the Committee of the inclusion of new sites or other changes at sites, either for NHS or non-NHS sites. However, management permission should still be obtained from the responsible host organisation (see 6.1 above).

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.