NHS
National Research Ethics Service
South East Research Ethics Committee
[redacted]
Telephone: [redacted]
Facsimile: [redacted]

23 November 2009

Professor Jonathan Grigg
[redacted]

Dear Professor Grigg

Study Title:	**Parent-determined oral montelukast therapy for preschool wheeze with stratification for arachidonate-5-lipoxygenase (ALOX5) promoter genotype.**
REC reference number:	**09/H1102/110**
Protocol number:	**1**
EudraCT number:	**2009-015626-11**

The Research Ethics Committee reviewed the above application at the meeting held on 11 November 2009. Thank you for attending to discuss the study.

Ethical opinion

The committee started by commending you on your application.

The committee stated that they had not been provided with the topics that were to be covered in the interview process.

You stated that the interview was covered in the protocol. You went on to say that the questions had been created using feedback from parents.

The committee drew your attention to the PIS and stated that it would need to be amended to contain details regarding dosage, side effects, the length of treatment and the risk of overdose.

You agreed with this and went on to state that it would also cover what would happen if a participant vomited out the drug.

The committee asked about the length of time between the start of treatment and the point at which the researcher would be contacted.

You stated that the parents / guardians of the participant would contact the researcher at the start of treatment and then contact would be made again, 7-10 days after that. Contact would subsequently be made on a monthly basis.

The committee suggested that a 'What will happen when I initiate Therapy?' section should be added to the PIS.

You agreed to this.

The committee then asked how it would be judged if the child participant really had a cold.

You stated that this would be down to the parents and suggested that they were experienced and knowledgeable enough to make the judgement. In addition to this, parents would be given training on specific triggers to watch out for.

The committee asked what would happen if the treatment was started when the child participant didn't actually have a cold.

You agreed that this could happen - but assured the committee that it was a safe medication.

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.

Ethical review of research 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).

The Committee has not yet been notified of the outcome of any site-specific assessment (SSA) for the non-NHS research site(s) taking part in this study. The favourable opinion does not therefore apply to any non-NHS site at present. I will write to you again as soon as one Research Ethics Committee has notified the outcome of a SSA. In the meantime no study procedures should be initiated at non-NHS sites.

Conditions of the favourable opinion

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

a) The PIS should indicate that travel expenses will be covered.
b) In pt. 1 of the PIS it states that steroid tablets do not work. This statement should be removed.
c) The PIS should be proofread throughout. There a few errors that need correcting (for example, the word 'sue' appears instead of the word 'use').
d) The consent form needs to have boxes inserted so that participants have definite areas to tick.
e) The PIS needs to advise parents of participants who hold private medical insurance covering the child that they should inform their insurance companies that they are taking part in the trial.
f) At A53 on the application it states that a lay summary of findings will be offered. In the PIS it states that this summary may be requested. The PIS should be amended to read that the summary will be offered.
g) The PIS is missing information relating to the possible side effects of the treatment. It also needs to provide information on the length of treatment and the possible risks of overdose.
h) A 'What will happen when I initiate Therapy?' section should be added to the PIS.

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

For NHS research sites only, management permission for research ("R&D approval") should be obtained from the relevant care organisation(s) 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 the only involvement of the NHS organisation is as a Participant Identification Centre, management permission for research is not required but the R&D office should be notified of the study. Guidance should be sought from the R&D office where necessary.

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

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 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 documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Covering Letter		19 October 2009
REC application		19 October 2009
Protocol	1	01 October 2009
Investigator CV	Prof Jonathan Grigg	
Participant Information Sheet: Parent (PartISWAIT)	1	01 October 2009
Participant Information Sheet: Child	1	01 October 2009
Participant Consent Form: Parent / Guardian (PCFWAIT)	1	01 October 2009
Letter of invitation to participant	1	01 October 2009
GP/Consultant Information Sheets	1	08 October 2009
Evidence of insurance or indemnity		19 October 2009
Sample Diary/Patient Card	1	08 October 2009
Summary of Product Characteristics	SPCmontelukast	12 March 2009
Sponsorship Approval Letter		19 October 2009

Membership of the Committee

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

Prof C Katona declared a non-specific interest in this study.

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.

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

Now that you have completed the application process please visit the National Research Ethics Service website > After Review

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.

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
- 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.

We would also like to inform you that we consult regularly with stakeholders to improve our service. If you would like to join our Reference Group please email [redacted].

09/H1102/110	**Please quote this number on all correspondence**

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

Yours sincerely

[redacted]

Dr L. Alan Ruben
Chair

Email: [redacted]

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: *Mr Gerry Leonard*