Health Research Authority

South Central - Oxford A Research Ethics Committee
Ground Floor
Temple Quay House
2 The Square
Bristol
BS1 6PN

Please note: This is the favourable opinion of the REC only and does not allow you to start your study at NHS sites in England until you receive HRA Approval

17 May 2021

Professor Philip Bath
University of Nottingham
D floor, South Block, Queen's Medical Centre
Nottingham
NG7 2UH

Dear Prof. Bath

Study title:	**COVID-19: Prophylactic therapy in care homes trial-CH**
REC reference:	**21/SC/0166**
Protocol number:	**21001**
EudraCT number:	**2021-000185-15**
IRAS project ID:	**294832**

The Research Ethics Committee (REC) reviewed the above application at the meeting held on 07 May 2021. Thank you for attending to discuss the application.

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.

Good practice principles and responsibilities

The UK Policy Framework for Health and Social Care Research sets out principles of good practice in the management and conduct of health and social care research. It also outlines the responsibilities of individuals and organisations, including those related to the four elements of research transparency:

1. registering research studies
2. reporting results
3. informing participants
4. sharing study data and tissue

Conditions of the favourable opinion

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

Number	Action required
1.	The following changes/revisions should be made to the main PIS: a) Within the sub-section "What would taking part involve?", it would be good to note the duration of the study and that Participants would be completing two questionnaires in that time. This point could be made in the Legal Representative PIS too. b) Within the sub-section "How will information about me be used?", it is noted that a Participant's date of birth may be required to link research data with medical records. If an NHS number and full name were required for this process, these identifiers should be stated there too. c) Within the sub-section "What are the trial medications?", please remove the word 'first' from the first sentence, as it could create concerns around eligibility for future trial runs, where there may be greater possible promise.
2.	The following changes/revisions should be made to the main ICF and the Legal Representative ICF: a) If it is the case that Participants, whose care home was allocated to the control arm, would still be completing the study questionnaires, then this point should be noted within Clause 3.
3.	The following changes/revisions should be made to the Email template for Personal Legal Representatives: a) On Page 2, the request is made for the ICF to be completed within one working day; please specify there whether this would be one working day from the point of email receipt, or any other time point. If it was likely this deadline would in fact be missed, it would be better to request a return "as soon as possible".

You should notify the REC once all conditions have been met (except for site approvals from host organisations) and provide copies of any revised documentation with updated version numbers. Revised documents should be submitted to the REC electronically from IRAS. The REC will acknowledge receipt and provide a final list of the approved documentation for the study, which you can make 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.

Confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland) should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements. Each NHS organisation must confirm through the signing of agreements and/or other documents that it has given permission for the research to proceed (except where explicitly specified otherwise).

Guidance on applying for HRA and HCRW Approval (England and Wales)/ NHS permission for research is available in the Integrated Research Application System.

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 management permissions from host organisations.

Registration of Clinical Trials

All research should be registered in a publicly accessible database and we expect all researchers, research sponsors and others to meet this fundamental best practice standard.

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database within six weeks of recruiting the first research participant. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Failure to register is a breach of these approval conditions, unless a deferral has been agreed by or on behalf of the Research Ethics Committee (see here for more information on requesting a deferral: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/research-registration-research-project-identifiers/

If you have not already included registration details in your IRAS application form, you should notify the REC of the registration details as soon as possible.

For CTIMPs involving both UK and EU sites a record in the EU Clinical Trials Register (other than adult Phase 1 studies) will exist and will satisfy the requirement for registration.

For CTIMPs only taking place in the UK, sponsors must register the trial on an established international registry which is a Primary Registry listed in the WHO Registry Network or the ICMJE list of registries e.g. the ISRCTN registry or ClinicalTrials.gov.

You should notify *both* the REC and the MHRA of the registration details.

Further guidance on registration is available at: https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

Publication of Your Research Summary

We will publish your research summary for the above study on the research summaries section of our website, together with your contact details, no earlier than three months from the date of this favourable opinion letter.

Should you wish to provide a substitute contact point, make a request to defer, or require further information, please visit: https://www.hra.nhs.uk/planning-and-improving-research/application-summaries/research-summaries/

N.B. If your study is related to COVID-19 we will aim to publish your research summary within 3 days rather than three months.

During this public health emergency, it is vital that everyone can promptly identify all relevant research related to COVID-19 that is taking place globally. If you haven't already done so, please register your study on a public registry as soon as possible and provide the REC with the registration detail, which will be posted alongside other information relating to your project. We are also asking sponsors not to request deferral of publication of research summary for any projects relating to COVID-19. In addition, to facilitate finding and extracting studies related to COVID-19 from public databases, please enter the WHO official acronym for the coronavirus disease (COVID-19) in the full title of your study. Approved COVID-19 studies can be found at: https://www.hra.nhs.uk/covid-19-research/approved-covid-19-research/

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

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).

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, including early termination of the study
- Final report
- Reporting results

The latest guidance on these topics can be found at https://www.hra.nhs.uk/approvals-amendments/managing-your-approval/.

Ethical review of research sites

NHS/HSC Sites

The favourable opinion applies to all NHS sites taking part in the study, subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or NHS management permission (in Scotland)being obtained from the NHS/HSC R&D office prior to the start of the study (see “Conditions of the favourable opinion” below).

Non-NHS/HSC sites

I am pleased to confirm that the favourable opinion applies to any non-NHS/HSC sites listed in the application, subject to site management permission being obtained prior to the start of the study at the site.

Approved documents

The documents reviewed and approved at the meeting were:

Document	*Version*	*Date*
Copies of materials calling attention of potential participants to the research [Participant poster]	Draft 0.2/Final 1.0	01 April 2021
Copies of materials calling attention of potential participants to the research [Participant video]	1.0	27 April 2021
Covering letter on headed paper [HRA REC Cover Letter]		28 April 2021
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Sponsor Clinical Trials Insurance]		20 July 2020
GP/consultant information sheets or letters [GP eligibility check letter]	Draft 0.1/Final 1.0	21 April 2021
GP/consultant information sheets or letters [GP IMP letter]	Draft 0.1/Final 1.0	21 April 2021
GP/consultant information sheets or letters [GP standard care letter]	Draft 0.1/Final 1.0	21 April 2021
Investigator's brochure / IMP Dossier [Ciclesonide IMPD stability data]	April 2021	01 April 2021
Investigator's brochure / IMP Dossier [Ciclesonide IMPD]	1.0	26 April 2021
Investigator's brochure / IMP Dossier [Niclosamide IMPD 2.2 Nonclinical data]	1.0	26 August 2020
Investigator's brochure / IMP Dossier [Niclosamide IMPD 2.7.2.5]	2.0	03 March 2021
Investigator's brochure / IMP Dossier [Niclosamide IMPD 2.7.2.4]	1.0	26 August 2020
Investigator's brochure / IMP Dossier [Niclosamide IMPD 2.1P]	4.0	03 March 2021
Investigator's brochure / IMP Dossier [Niclosamide IB]	1.0	26 August 2020
IRAS Application Form [IRAS_Form_29042021]		29 April 2021
Other [IMP Appendix A (ciclesonide)]	Draft 0.6/Final 1.0	27 April 2021
Other [IMP Appendix B (niclosamide)]	Draft 0.5/Final 1.0	27 April 2021
Other [Sponsor professional indemnity letter]	N/A	20 July 2020
Other [Legal Representative Consent Letter 1]	Draft 0.5/Final 1.0	23 April 2021
Other [Legal Representative Participation Update Letter 2]	Draft 0.1/Final 1.0	22 April 2021

Other [Legal Representative Consent Letter 3]	Draft 0.4/Final 1.0	23 April 2021
Other [Legal Representative Eligibility & Randomisaion Confirmation Letter 4]	Draft 0.1/Final 1.0	23 April 2021
Other [Legal Representative E-mails]	Draft 0.8/Final 1.0	23 April 2021
Other [Ciclesonide dosing instructions]	Draft 0.2/Final 1.0	27 April 2021
Other [Niclosamide dosing instructions]	Draft 0.2/Final 1.0	27 April 2021
Other [Consent and eligibility overview]	Draft 0.2/Final 1.0	23 April 2021
Other [Flowchart from point of outbreak (PEP)]	Draft 0.3/Final 1.0	21 April 2021
Other [Safety reporting flowchart]	Draft 0.2/Final 1.0	16 April 2021
Participant consent form [Participant Informed Consent Form]	Draft 0.6/Final 1.0	27 April 2021
Participant consent form [Legal Represent Consent Form]	Draft 0.6/Final 1.0	27 April 2021
Participant information sheet (PIS) [Participant Information Sheet]	Draft 0.11/Final 1.0	27 April 2021
Participant information sheet (PIS) [Legal Representative Information Sheet]	Draft 0.6/Final 1.0	27 April 2021
Research protocol or project proposal [Trial Protocol]	Draft 0.9/Final 1.0	27 April 2021
Summary CV for Chief Investigator (CI) [Chief Investigator CV]		
Summary of product characteristics (SmPC) [SmPC ciclesonide]		29 June 2020
Validated questionnaire [QoL (EQ5D5L)]	1.0	07 April 2021
Validated questionnaire [QoL (EQ5D5L) proxy]	1.0	07 April 2021

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.

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

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/

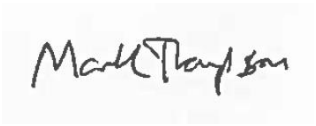
HRA Learning

We are pleased to welcome researchers and research staff to our HRA Learning Events and online learning opportunities– see details at: https://www.hra.nhs.uk/planning-and-improving-research/learning/

IRAS project ID: 294832	**Please quote this number on all correspondence**

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

Yours sincerely



On behalf of Dr Hugh Davies
Chair

E-mail: oxforda.rec@hra.nhs.uk

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" [SL-AR]

Copy to: Ms Angela Shone

South Central - Oxford A Research Ethics Committee

Attendance at Committee meeting on 07 May 2021

Committee Members:

Name	*Profession*	*Present*	*Notes*
Dr Katie Bonner	Clinical Research Fellow	Yes	
Ms Jane Cheeseman	Research Nurse	Yes	
Dr Hugh Davies (Chair)	Consultant Paediatrician / HRA Training Adviser	Yes	
Mr Adrian Hampshire	Managing Director (retired) of clinical research data services company	Yes	
Dr Stephanie Jones	Postdoctoral Research Scientist	Yes	
Dr Pamela Laurie	(Retired) Consultant Anaesthetist	Yes	
Miss Jennifer Lawson	Trials Manager	No	
Dr Fraser Macfarlane	Retired Senior Lecturer - Health Care Management	Yes	
Ms Morag McCormick-Power	Research Contracts Specialist	No	
Ms Christine Montague-Johnson	Paediatric Nurse	Yes	
Mr Barry Muir	Retired NHS Management Consultant	No	
Dr Altar Munis	Postdoctoral Research Scientist	Yes	
Dr Karen Pulford	Freelance medical/scientific writer and the honorary title of Emeritus Reader of Immunodiagnostics, NDCLS	Yes	
Ms Kay Symons	Publishing consultant and trainer	Yes	
Mr Nicholas Way	Former Director General - Historic Houses Association	Yes	

Also in attendance:

Name	*Position (or reason for attending)*
Mrs Sharon Northey	Approvals Manager
Ms Anfal El-Awaisi	Approvals Administrator
Mr Mark Thompson	Approvals Officer