Health Research Authority
East Midlands - Leicester Central Research Ethics Committee
Equinox House
City Link
Nottingham
NG2 4LA

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

10 May 2023

KAILASH KRISHNAN
Nottingham University Hospitals NHS Trust
Derby Road
Nottingham
NG7 2UH

Dear KAILASH KRISHNAN

Study title:	**MAnnitol for Cerebral oEdema after IntraCerebral Haemorrhage (MACE-ICH): a feasibility trial**
REC reference:	**22/EM/0242**
Protocol number:	**22SR001**
EudraCT number:	**2022-000283-22**
IRAS project ID:	**1004870**

Thank you for your letter responding to the Research Ethics Committee's (REC) request for further information on the above research and submitting revised documentation.

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.

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.

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:

- clinical trial of an investigational medicinal product
- clinical investigation or other study of a medical device
- combined trial of an investigational medicinal product and an investigational medical device

- other clinical trial to study a novel intervention or randomised clinical trial to compare interventions in clinical practice.

Failure to register a clinical trial is a breach of these approval conditions, unless a deferral has been agreed by the HRA (for more information on registration and requesting a deferral see: Research registration and 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.

CTIMPs submitted for combined review via IRAS will be registered automatically with the ISRCTN Registry. You do not need to notify the REC of the registration details. The lawful basis for processing your personal data for this purpose is official authority under the NHS Care Act 2014 (for further information please see our privacy notice).

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).

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).

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/HSC sites taking part in the study, subject to confirmation of Capacity and Capability (in England, Northern Ireland and Wales) or 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 final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Cover Letter [MHRA Submission Cover Letter]	1.0	29 September 2022
Cover Letter [Participant Six-month Questionnaire Cover Letter]	1.0	21 June 2022
Cover Letter [MHRA Response Cover Letter]	1.0	02 May 2023
Cover Letter [REC Re-submission Cover Letter]	1.0	03 May 2023
GP/consultant information sheets or letters [GP Letter]	1.0	17 May 2022
Investigator Brochure/SmPC [Mannitol SmPC]	1.0	08 July 2022
Letter from funder [Research Contract]	2/21	18 January 2022
Miscellaneous [Radiation Approval]	1.0	09 May 2022
Participant information and informed consent form [Participant Pictorial Information Sheet & Consent (tracked-changes)]	1.1	29 December 2022
Participant information and informed consent form [Participant Pictorial Information Sheet & Consent]	1.1	29 December 2022
Participant information and informed consent form [Legal Representative Pictorial Information Sheet & Consent Form	1.1	29 December 2022

(tracked-changes)]		
Participant information and informed consent form [Legal Representative Pictorial Information Sheet & Consent Form]	1.1	29 December 2022
Participant information and informed consent form [Legal Representative Consent Form (tracked-changes)]	1.1	29 December 2022
Participant information and informed consent form [Legal Representative Consent Form]	1.1	29 December 2022
Participant information and informed consent form [Participant Consent Form (tracked-changes)]	1.1	29 December 2022
Participant information and informed consent form [Participant Consent Form]	1.1	29 December 2022
Participant information and informed consent form [Legal Representative Information Sheet (tracked-changes))]	1.1	29 December 2022
Participant information and informed consent form [Legal Representative Information Sheet]	1.1	29 December 2022
Participant information and informed consent form [Participant Information Sheet (tracked-changes))]	1.1	29 December 2022
Participant information and informed consent form [Participant Information Sheet]	1.1	29 December 2022
Proof of Insurance [Sponsor Insurance]	1.0	11 August 2022
Protocol [Protocol (tracked-changes)]	1.1	24 April 2023
Protocol [Protocol]	1.1	24 April 2023
REC Application Form [Ethics]		29 September 2022
Suitability of the investigator/Investigator CV [Chief Investigator GCP Certificate]	1.0	24 March 2021
Suitability of the investigator/Investigator CV [Chief Investigator CV]	1.0	24 February 2022
Validated questionnaire [Participant Six-month Postal Questionnaire]	1.0	22 June 2022

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: 1004870 Please quote this number on all correspondence

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

Yours sincerely

Pp.

Abitha

Chair
Mrs Rita Patel
Email:leicestercentral.rec@hra.nhs.uk

Enclosures:

"After ethical review – guidance for researchers"
After ethical review – guidance for sponsors and investigators - **CTIMP Standard Conditions of Approval**

Copy to: Jennifer Boston, Nottingham University Hospitals NHS Trust

Lead Nation England: approvals@hra.nhs.uk