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10 May 2023

Dear KAILASH KRISHNAN

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**MAnnitol for Cerebral oEdema after IntraCerebral Haemorrhage (MACE-ICH): a feasibility trial**
IRAS project ID:	**1004870**
Protocol number:	**22SR001**
REC reference:	**22/EM/0242**
Sponsor	**Nottingham University Hospitals NHS Trust**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report (including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The standard conditions document "*After Ethical Review – guidance for sponsors and investigators*", issued with your REC favourable opinion, gives detailed guidance on reporting expectations for studies, including:

- Registration of research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics, and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **1004870**. Please quote this on all correspondence.

Yours sincerely,

Abitha Paimpillichalil

Approvals Specialist

Email: approvals@hra.nhs.uk

Copy to: *Jennifer Boston, Nottingham University Hospitals NHS Trust*

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

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 [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
Organisation Information Document [Organisation Information Document]	1.0	11 August 2022
Other [mCTA]	3.0	23 March 2021
Other [NUH-UoN Tripartite Agreement]	2.0	22 April 2021
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 (tracked-changes)]	1.1	29 December 2022
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
Pharmacy Single Technical Review Form [Confirmation of Pharmacy Assurance]		
Project Information - PDF [ProjectStudyInformation]		29 September 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
Research Exposure Form [Confirmation of Radiation Assurance]		
Schedule of Events or SoECAT [SoECAT]	1.19	11 March 2020
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

IRAS project ID	1004870

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
All sites will perform the same research activities therefore there is only one site type.	Research activities should not commence at participating NHS organisations in England or Wales prior to their formal confirmation of capacity and capability to deliver the study in accordance with the contracting expectations detailed.	An Organisation Information Document has been submitted but the sponsor is intending to use a separate agreement with participating NHS organisations of this type. The sponsor has supplied the appropriate current unmodified model agreement and intends to use this with participating NHS organisations.	The sponsor has detailed its proposals with respect to whether any study funding will be provided to participating NHS organisations of this type in the Organisational Information Document and in the alternative site agreement that they propose to use as the agreement. These should be read in conjunction with the relevant Schedule of Events/SoECAT which details the cost implications of the study for participating NHS organisations.	In line with HRA/HCRW expectations a Principal Investigator should be appointed at participating NHS organisations of this type.	Where an external individual who does not already hold an NHS employment contract will be conducting any of the research activities that will be undertaken at this site type then they would be expected to hold an Honorary Research Contract. External staff holding pre-existing NHS employment contracts should obtain a Letter of Access. This should be issued be on the basis of a Research Passport (if university employed) or an NHS to NHS confirmation of pre-engagement checks letter (if NHS employed). These should confirm Occupational Health Clearance.

					These should confirm enhanced DBS checks and appropriate barred list checks.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio. Radiation Assurance is in place for this study. Pharmacy Assurance is in place for this study.