Professor Fang Gao Smith
Professor of Anaesthesia, Critical Care and Pain
University of Birmingham
Birmingham Clinical Trials Unit
Institute of Applied Health Research
University of Birmingham
B15 2TT

Email: hra.approval@nhs.net
Research-permissions@wales.nhs.uk

15 November 2018

Dear Professor Gao Smith

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

Study title:	**A Randomised Controlled Trial to investigate the effectiveness of ThOracic Epidural and Paravertebral Blockade In reducing Chronic Post- Thoracotomy Pain: 2**
IRAS project ID:	**248427**
Protocol number:	**RG 17_255**
REC reference:	**18/SS/0131**
Sponsor	**University of Birmingham**

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.

How should I continue to work with participating NHS organisations in England and Wales?
You should now provide a copy of this letter to all participating NHS organisations in England and Wales, as well as any documentation that has been updated as a result of the assessment.

Following the arranging of capacity and capability, participating NHS organisations should **formally confirm** their capacity and capability to undertake the study. How this will be confirmed is detailed in the "*summary of assessment*" section towards the end of this letter.

You should provide, if you have not already done so, detailed instructions to each organisation as to how you will notify them that research activities may commence at site following their confirmation of capacity and capability (e.g. provision by you of a 'green light' email, formal notification following a site initiation visit, activities may commence immediately following confirmation by participating organisation, etc.).

It is important that you involve both the research management function (e.g. R&D office) supporting each organisation and the local research team (where there is one) in setting up your study. Contact details of the research management function for each organisation can be accessed here.

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 the devolved administrations of 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) has been sent to the coordinating centre of each participating nation. You should work with the relevant national coordinating functions to ensure any nation specific checks are complete, and with each site so that they are able to give management permission for the study to begin.

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 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.

I am a participating NHS organisation in England or Wales. What should I do once I receive this letter?
You should work with the applicant and sponsor to complete any outstanding arrangements so you are able to confirm capacity and capability in line with the information provided in this letter.

The sponsor contact for this application is as follows:

Name: Ben Watkins
Email: TOPIC2@trials.bham.ac.uk

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 **248427**. Please quote this on all correspondence.

Yours sincerely

Chris Kitchen
Assessor

Email: hra.approval@nhs.net

Copy to: *Ben Watkins, University of Birmingham (Sponsor Contact)*
Ms Elizabeth Adey, Heart of England NHS Foundation Trust (R&D Contact)

List of Documents

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

Document	*Version*	*Date*
Contract/Study Agreement template [TOPIC2 Clinical Site Agreement]		
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [UMAL insurance letter]		16 July 2018
GP/consultant information sheets or letters [TOPIC2 GP Letter]	1.0	12 September 2018
HRA Schedule of Events [SoE]	1	22 October 2018
HRA Statement of Activities [SoA]	1	11 October 2018
IRAS Application Form [IRAS Form 13092018]	248427/1248998/37/484	13 September 2018
Letter from funder [TOPIC2 Letter from funder (NIHR)]		23 November 2017
Other [TOPIC2 Patient Completed Booklet Baseline V1.0a, 29-Oct-2018]	1a	29 October 2018
Other [TOPIC2 Patient Completed Booklet Acute Phase V1.0, 29-Oct-2018]	1.0	29 October 2018
Other [TOPIC2 Patient Completed Booklet 3, 6 and 12 month v1.0, 29-Oct-2018]	1.0	29 October 2018
Other [TOPIC 2 Study Audio-recording discussions and interviews PCF Clean]	2.0	12 November 2018
Other [TOPIC2 Healthcare Professional Information Study and Audio-recording Consent Form Clean]	2.0	12 November 2018
Other [Topic2 Audio-recording discussions and interviews PIS]	2.0	08 November 2018
Other [TOPIC2 Cover Letter REC conditions response 12.11.18]	1.0	12 November 2018
Other [TOPIC 2 QRI - Interview Schedule for Recruiters]	1.0	16 July 2018
Other [TOPIC2 QRI - Interview Schedule for Patients]	1.0	16 July 2018
Other [REC response cover letter 19.10.2018]	1.0	19 October 2018
Participant consent form [TOPIC2 ICF]	1.0	12 September 2018
Participant information sheet (PIS) [TOPIC2 PIS Clean]	2.0	12 November 2018
Research protocol or project proposal [TOPIC2 Protocol V1a Clean]	1a	12 October 2018
Summary CV for Chief Investigator (CI) [Prof F Gao Smith CV]	*November*	01 November 2016
Summary, synopsis or diagram (flowchart) of protocol in non technical language [TOPIC2 Trial Summary]	1.0	04 September 2018

Summary of assessment

The following information provides assurance to you, the sponsor and the NHS in England and Wales that the study, as assessed for HRA and HCRW Approval, is compliant with relevant standards. It also provides information and clarification, where appropriate, to participating NHS organisations in England and Wales to assist in assessing, arranging and confirming capacity and capability.

Assessment criteria

Section	Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	In addition to the participating organisations listed in Part C of the IRAS form, the applicant has confirmed that the following NHS organisations will participate: • Guy's and St Thomas' NHS Foundation Trust (Investigator: Dr Chang Ong) • Barts Health NHS Trust (Investigator: Dr Sibtain Anwar)
2.1	Participant information/consent documents and consent process	Yes	No comments
3.1	Protocol assessment	Yes	No comments
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	A University of Birmingham Clinical Site Agreement will form the agreement of the NHS organisation to participate. The justification for this is provided in question 5 of the Statement of Activities.
4.2	Insurance/indemnity arrangements assessed	Yes	No comments
4.3	Financial arrangements assessed	Yes	The study is funded by the NIHR. Further information on funding provisions for the participating organisations is provided in the Clinical Site Agreement and Schedule 1 of the Statement of Activities.

Section	Assessment Criteria	Compliant with Standards	Comments
5.1	Compliance with the Data Protection Act and data security issues assessed	Yes	No comments
5.2	CTIMPS – Arrangements for compliance with the Clinical Trials Regulations assessed	Not Applicable	No comments
5.3	Compliance with any applicable laws or regulations	Yes	No comments
6.1	NHS Research Ethics Committee favourable opinion received for applicable studies	Yes	No comments
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Not Applicable	No comments
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Not Applicable	No comments

Participating NHS Organisations in England and Wales

This provides detail on the types of participating NHS organisations in the study and a statement as to whether the activities at all organisations are the same or different.

This is a non-commercial study with multiple participating NHS organisations in England and Wales. Activities will be the same across sites.

The Chief Investigator or sponsor should share relevant study documents with participating NHS organisations in England and Wales in order to put arrangements in place to deliver the study. The documents should be sent to both the local study team, where applicable, and the office providing the research management function at the participating organisation. Where applicable, the local LCRN contact should also be copied into this correspondence.

If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England and Wales which are not provided in IRAS, the HRA or HCRW websites, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net or HCRW at Research-permissions@wales.nhs.uk. We will work with these organisations to achieve a consistent approach to information provision.

Principal Investigator Suitability

This confirms whether the sponsor position on whether a PI, LC or neither should be in place is correct for each type of participating NHS organisation in England and Wales, and the minimum expectations for education, training and experience that PIs should meet (where applicable).

A Principal Investigator is expected to be in place at the participating organisation.

As per the Statement of Activities, the sponsor will provide training in the use of para vertebral blockade to anaesthetists and surgical colleagues, as requested by the participating organisation. The Principal Investigator will also receive training on safety reporting requirements. Training will be included as part of the site initiation visit.

GCP training is not a generic training expectation, in line with the HRA/HCRW/MHRA statement on training expectations.

HR Good Practice Resource Pack Expectations

This confirms the HR Good Practice Resource Pack expectations for the study and the pre-engagement checks that should and should not be undertaken

For research team members that do not have existing contractual relationships with the participating organisation, Honorary Research Contracts should be in place if the activities undertaken at the NHS site involve contact with patients (e.g. to take consent), on the basis of Research passports (if University employed) or NHS to NHS confirmation of pre-engagement checks letters (if NHS employed). The pre-engagement checks should include enhanced DBS checks and Occupational Health Clearance. No specific pre-engagement checks are required to have taken place if the members of the research team are only accessing patients' data.

Other Information to Aid Study Set-up

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales to aid study set-up.

The applicant has indicated that they intend to apply for inclusion on the NIHR CRN Portfolio.