Health Research Authority

London - Brighton & Sussex Research Ethics Committee
Health Research Authority
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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

22 July 2020

Miss Karina Cox
Consultant Breast and Oncoplastic Surgeon/ Honorary Senior Lecturer (University of Kent)
Maidstone and Tunbridge Wells NHS Trust
Maidstone Hospital
Hermitage Lane
Maidstone, Kent
ME16 9QQ

Dear Miss Cox

Study title:	**SENTINUS: Technical feasibility and diagnostic accuracy of intradermal microbubbles and contrast enhanced ultrasound to identify sentinel lymph node metastases in breast cancer patients following training and mentorship of imaging specialists**
REC reference:	**20/LO/0833**
Protocol number:	**MTW_2020_KC01**
EudraCT number:	**2020-000819-67**
IRAS project ID:	**274252**

Thank you for your letter of 17 July 2020, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Vice Chair, Dr John Bull.

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.

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

It is a condition of the REC favourable opinion that **all clinical trials are registered** on a publicly accessible database. For this purpose, 'clinical trials' are defined as the first four project categories in IRAS project filter question 2. Registration is a legal requirement for clinical trials of investigational medicinal products (CTIMPs), except for phase I trials in healthy volunteers (these must still register as a condition of the REC favourable opinion).

Registration should take place as early as possible and within six weeks of recruiting the first research participant at the latest. 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/

As set out in the UK Policy Framework, research sponsors are responsible for making information about research publicly available before it starts e.g. by registering the research project on a publicly accessible register. Further guidance on registration is available at:
https://www.hra.nhs.uk/planning-and-improving-research/research-planning/transparency-responsibilities/

You should notify the REC of the registration details. We will audit these as part of the annual progress reporting process.

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/

For research studies related to COVID-19, we are fast-tracking the publication of research summaries. 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 HRA 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).
[Please remove the following sentence for HRA Approval studies as the CTA status will be checked by the assessor]:
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

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 listed in the application 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*
IRAS Application Form [IRAS_Form_17072020]		17 July 2020
IRAS Application Form XML file [IRAS_Form_17072020]		17 July 2020
IRAS Checklist XML [Checklist_17072020]		17 July 2020
Letter from funder [Funding]		21 August 2019
Non-validated questionnaire [Procedure Questionnaire]	1.0	25 June 2020
Other [Answers to Part B, Section 5]		02 June 2020
Other [Response to REC]	1.0	14 July 2020
Participant consent form [Consent form]	2.0	14 July 2020
Participant information sheet (PIS) [PIS]	4.0	25 June 2020
Participant information sheet (PIS) [Privacy notice]	1.0	25 June 2020
Research protocol or project proposal [Protocol]	4.0	16 July 2020
Schedule of Events or SoECAT [SoECAT]	1.0	22 January 2020
Summary CV for Chief Investigator (CI) [CI CV]		05 May 2020
Summary of product characteristics (SmPC) [Product information]		24 April 2006
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Flow diagram]	1.0	19 December 2019

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: 274252	**Please quote this number on all correspondence**

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

Yours sincerely

PP
Dr Simon Walton
Chair

Email:brightonandsussex.rec@hra.nhs.uk

Copy to: Ms Hazel Everest