NHS
Health Research Authority

Professor Graham Collins
Churchill Hospital
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Oxford
OX3 7LE

Email: hra.approval@nhs.net

13 April 2018

Dear Professor Collins

Letter of HRA Approval

Study title:	**A phase II study of nivolumab monotherapy in patients with relapsed/refractory Hodgkin lymphoma, fit for autologous stem cell transplant, who fail to reach complete metabolic remission after first or second line salvage therapy**
IRAS project ID:	**216147**
EudraCT number:	**2017-002544-32**
Protocol number:	**UCL/15/0515**
REC reference:	**18/LO/0204**
Sponsor	**University College London**

I am pleased to confirm that **HRA 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 from the HRA.

How should I continue to work with participating NHS organisations in England?
You should now provide a copy of this letter to all participating NHS organisations in England, 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 HRA 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, Scotland and Wales?
HRA Approval does not apply to NHS/HSC organisations within the devolved administrations of Northern Ireland, Scotland and Wales.

If you indicated in your IRAS form that you do have participating organisations in one or more devolved administration, the HRA has sent the final document set and the study wide governance report (including this letter) 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 Northern Ireland, Scotland and Wales.

How should I work with participating non-NHS organisations?
HRA 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. 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: Mr Oliver Schofield
Email: ctc.animate@ucl.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 **216147**. Please quote this on all correspondence.

Yours sincerely

Thomas Fairman
HRA Assessor

Email: hra.approval@nhs.net

Copy to: *Mr Oliver Schofield, University College London, (Sponsor Contact)*
Ms Heather House, Oxford University Hospitals NHS Foundation Trust, (Lead NHS R&D Contact)

List of Documents

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

Document	*Version*	*Date*
Contract/Study Agreement template [Site agreement - master copy]		10 January 2018
Covering letter on headed paper [Cover Letter]	N/A	11 January 2018
Details of any Data Monitoring Committee [IDMC membership list]		15 December 2017
Evidence of Sponsor insurance or indemnity (non NHS Sponsors only) [Insurance letter from Sponsor and Policy document]		06 November 2017
GP/consultant information sheets or letters [GP Letter]	1.0	04 January 2018
HRA Schedule of Events [PET Sites]	4.0	03 April 2018
HRA Schedule of Events [Non-PET Sites]	2.0	03 April 2018
HRA Statement of Activities [PET Sites]	1.0	07 March 2018
HRA Statement of Activities [non-PET Sites]	1.0	07 March 2018
Investigator's brochure / IMP Dossier [Nivolumab Investigator Brochure]	16	23 June 2017
IRAS Application Form [IRAS_Form_11012018]		11 January 2018
Letter from funder [Funding confirmation letter]		29 December 2016
Letter from sponsor [Confirmation of Sponsorship letter]		06 November 2017
Letter from statistician [Letter from statistician]		13 December 2017
Other [MHRA CTA Approval Letter]		27 February 2018
Other [FW ARSAC PRA REC acknowledegment]		08 March 2018
Participant consent form [Consent Form (Main)]	1.0	04 January 2018
Participant consent form [Pregnancy Monitoring Consent Form (Partners)]	1.0	04 January 2018
Participant information sheet (PIS) [Patient Information Sheet (Main)]	1.0	04 January 2018
Participant information sheet (PIS) [Pregnancy Monitoring Information Sheet (Partners)]	1.0	04 January 2018
Referee's report or other scientific critique report [Peer reviews (independent, statistics and CSG)]		10 January 2018
Research protocol or project proposal [Protocol]	1.0	04 January 2018
Sample diary card/patient card [Patient Contact Card]	1.0	04 January 2018
Summary CV for Chief Investigator (CI) [Graham Collins CV]		08 January 2018

Summary of HRA assessment

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

HRA assessment criteria

Section	HRA Assessment Criteria	Compliant with Standards	Comments
1.1	IRAS application completed correctly	Yes	No comments
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	There are two site types participating in the study PET Sites and Non-PET Sites. The sponsor has submitted a Statement of Activities for each site type but has indicated that they do not intend for this to form the agreement between the sponsor and participating sites. The sponsor proposes to use the UCL CTC Clinical Trial Site Agreement (CTSA), which pre-dated the mNCA but was updated in line with the mNCA, will be used for sites in this trial. The sponsor is not requesting, and does not require any additional agreements.
4.2	Insurance/indemnity arrangements assessed	Yes	Where applicable, independent contractors (e.g. General Practitioners) should ensure that the professional indemnity provided by their medical defence organisation covers the

Section	HRA Assessment Criteria	Compliant with Standards	Comments
			activities expected of them for this research study
4.3	Financial arrangements assessed	Yes	No application for external funding has been made. External study funding has been secured from Bristol-Myers Squibb Pharmaceuticals Ltd. Study funding will be provided to sites, as detailed at Schedule 1 of the relevant Statement of Activities documents.
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	REC Favourable Opinion was issued on the 1st March 2018.
6.2	CTIMPS – Clinical Trials Authorisation (CTA) letter received	Yes	MHRA CTA was issued on the 28th February 2018.
6.3	Devices – MHRA notice of no objection received	Not Applicable	No comments
6.4	Other regulatory approvals and authorisations received	Yes	Central ARSAC approval was issued on the 11th April 2018. Where the study involves administration of exposures which are additional to normal care the sponsor should ensure that the participating NHS organisation and local administering practitioners hold relevant licences under The Ionising Radiation (Medical Exposure)

Section	HRA Assessment Criteria	Compliant with Standards	Comments
			Regulations 2018 (IR(ME)R).

Participating NHS Organisations in England

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.
There are two site types participating in the study. All sites will conduct the same study activities with the exception of the PET scans. If participants are recruited from an organisation without the facilities to conduct this scan then this will be conducted at different site. The Chief Investigator or sponsor should share relevant study documents with all participating NHS organisations in England 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. For NIHR CRN Portfolio studies, the Local LCRN contact should also be copied into this correspondence. For further guidance on working with participating NHS organisations please see the HRA website. If chief investigators, sponsors or principal investigators are asked to complete site level forms for participating NHS organisations in England which are not provided in IRAS or on the HRA website, the chief investigator, sponsor or principal investigator should notify the HRA immediately at hra.approval@nhs.net. The HRA 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 the minimum expectations for education, training and experience that PIs should meet (where applicable).
A Principal Investigator should be appointed at all study sites. GCP training is not a generic training expectation, in line with the HRA 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
As a non-commercial study undertaken by local staff, it is unlikely that letters of access or honorary research contracts will be applicable, except where local network staff employed by another Trust (or University) are involved (and then it is likely that arrangements are already in place). Where arrangements are not already in place, network staff (or similar) undertaking any of the research activities listed in A18 or A19 of the IRAS form (except for administration of questionnaires

or surveys), would be expected to obtain an honorary research contract from one NHS organisation (if university employed), followed by Letters of Access for subsequent organisations. This would 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 enhanced DBS checks, including appropriate barred list checks, and occupational health clearance.

For research team members only administering questionnaires or surveys, a Letter of Access based on standard DBS checks and occupational health clearance would be appropriate.

Other Information to Aid Study Set-up

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