Professor Graham Collins
Churchill Hospital
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Oxford
OX3 7LE

Email: hra.approval@nhs.net

09 March 2018

Dear Professor Collins

Initial Assessment Letter

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**

Thank you for your application for HRA Approval. I am writing to provide you with the initial assessment letter for this application. Please note that **this is NOT a letter of HRA Approval** and that the research should not begin at any participating NHS organisations in England before HRA Approval is issued.

How should I work with my participating NHS organisations in England?
You should now provide a copy of this letter, as part of the local information pack, to your participating NHS organisations in England.

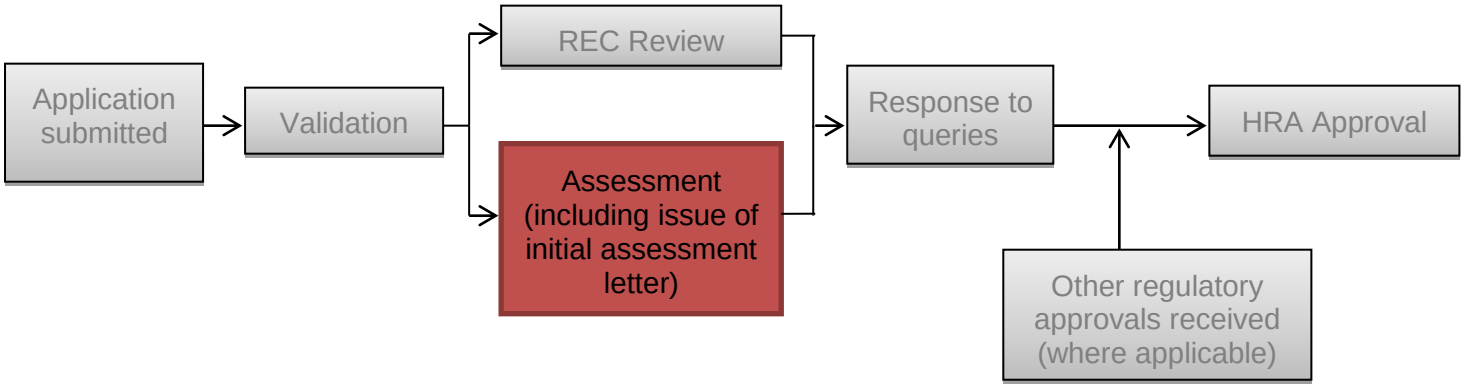
Participating NHS organisations in England should **formally confirm** capacity and capability once HRA Approval is issued. You should now work with these organisations to arrange capacity and capability whilst the HRA Approval process is ongoing. Further information to aid this process is provided in the "*Information for Sponsors and Participating NHS Organisations"* section towards the end of this document.

It is important that you involve both the research management function (e.g. R&D office and, where applicable, the Local Clinical Research Network) 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.

IRAS project ID	216147

What happens next with my application for HRA Approval?

Your application for HRA Approval is progressing. Please find below an indication of where you are in the process (indicated by the red box below).



Please note that I may separately have emailed you to request clarifications related to your application. Please respond in a timely manner, following instructions contained within the email. Once you have satisfactorily responded to any queries, once REC Favourable Opinion is in place and once any other applicable regulatory approvals are in place, we will be in a position to issue HRA Approval.

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.

I am a participating NHS organisation. What should I do once I receive this letter as part of the Local Information Pack?

You should work with the applicant and sponsor to arrange capacity and capability in line with the information provided in the "*How should I work with my participating NHS organisations in England?*" section above. I have also provided you with further information to aid study set up in the "*Information for Sponsors and Participating NHS Organisations"* section towards the end of this document.

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)

Documents received

The documents that have been received for assessment are as follows.

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]	1.0	09 March 2018
HRA Schedule of Events [Non-PET Sites]	1.0	09 March 2018
HRA Statement of Activities [PET Sites]		07 March 2018
HRA Statement of Activities [non-PET Sites]		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
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

Information for Sponsors and Participating NHS Organisations

The below provides all parties with information to support the arranging of capacity and capability with participating NHS organisations in England. This is intended to be an accurate reflection of the study at the time of issue of this letter. As part of the HRA Approval process, details may change prior to a Letter of HRA Approval being issued. NHS organisations should be assured that the HRA will continue to work with the sponsor on any HRA assessment criteria which are 'pending', and this should not impact on the arranging or 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

Section	HRA Assessment Criteria	Compliant with Standards?	Comments
			defence organisation covers the 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	Pending	Central ARSAC approval is not yet in place. HRA Approval will not be issued until this is in place. 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.