NHS
Health Research Authority

Dr Freddy Frost
Cystic Fibrosis Clinical Fellow
Liverpool Heart and Chest Hospital
Apartment 17
3 Rumford Place
L3 9BZ

Email: hra.approval@nhs.net

14 December 2016

Dear Dr Frost

Letter of HRA Approval

Study title:	**Aztreonam for inhalation for the treatment of acute exacerbations in cystic fibrosis. An open-label, randomised, cross-over pilot study of AZLI plus intravenous Colistin versus standard dual intravenous therapy.**
IRAS project ID:	**206907**
EudraCT number:	**2016-002832-34**
Protocol number:	**AZLI2016DN001**
REC reference:	**16/NW/0741**
Sponsor	**Liverpool Heart & Chest Hospital NHS Foundation Trust**

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 noted in this letter.

Participation of NHS Organisations in England

The sponsor should now provide a copy of this letter to all participating NHS organisations in England.

Appendix B provides important information for sponsors and participating NHS organisations in England for arranging and confirming capacity and capability. **Please read *Appendix B* carefully**, in particular the following sections:

- *Participating NHS organisations in England* – this clarifies the types of participating organisations in the study and whether or not all organisations will be undertaking the same activities
- *Confirmation of capacity and capability* - this confirms whether or not each type of participating NHS organisation in England is expected to give formal confirmation of capacity and capability. Where formal confirmation is not expected, the section also provides details on the time limit given to participating organisations to opt out of the study, or request additional time, before their participation is assumed.
- *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* - this provides detail on the form of agreement to be used in the study to confirm capacity and capability, where applicable.

Further information on funding, HR processes, and compliance with HRA criteria and standards is also provided.

It is critical 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 and further information about working with the research management function for each organisation can be accessed from www.hra.nhs.uk/hra-approval.

Appendices

The HRA Approval letter contains the following appendices:

- A – List of documents reviewed during HRA assessment
- B – Summary of HRA assessment

After HRA Approval

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.

In addition to the guidance in the above, please note the following:

- HRA Approval applies for the duration of your REC favourable opinion, unless otherwise notified in writing by the HRA.
- Substantial amendments should be submitted directly to the Research Ethics Committee, as detailed in the *After Ethical Review* document. Non-substantial amendments should be submitted for review by the HRA using the form provided on the HRA website, and emailed to hra.amendments@nhs.net.
- The HRA will categorise amendments (substantial and non-substantial) and issue confirmation of continued HRA Approval. Further details can be found on the HRA website.

Scope

HRA Approval provides an approval for research involving patients or staff in NHS organisations in England.

If your study involves NHS organisations in other countries in the UK, please contact the relevant national coordinating functions for support and advice. Further information can be found at http://www.hra.nhs.uk/resources/applying-for-reviews/nhs-hsc-rd-review/.

If there are participating non-NHS organisations, local agreement should be obtained in accordance with the procedures of the local participating non-NHS organisation.

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 email the HRA at hra.approval@nhs.net. Additionally, one of our staff would be happy to call and discuss your experience of HRA Approval.

HRA Training

We are pleased to welcome researchers and research management staff at our training days – see details at http://www.hra.nhs.uk/hra-training/

Your IRAS project ID is **206907**. Please quote this on all correspondence.

Yours sincerely

Michael Pate

Assessor

Email: hra.approval@nhs.net

Copy to: *Mrs Gillian Hamblin - Liverpool Heart & Chest Hospital NHS Foundation Trust – Sponsor's contact and lead NHS R&D contact.*

NIHR CRN Portfolio Applications Team.

Appendix A - List of Documents

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

Document	*Version*	*Date*
Confirmation of Clinical Trial Authorisation from MHRA and relevant correspondence [MHRA CTA]		11 November 2016
Covering letter on headed paper [REC Cover Letter]		22 September 2016
Covering letter on headed paper [REC Cover Letter]		26 October 2016
GP/consultant information sheets or letters [GP Letter]	2.0	27 September 2016
Investigator's brochure / IMP Dossier [Investigator Brochure]	14	30 September 2015
IRAS Application Form [IRAS_Form_28092016]		28 September 2016
Letter from funder [Funder's letter]		17 July 2016
Letter from sponsor [Sponsor's lett]		28 September 2016
Letter from statistician [Stats letter]		22 September 2016
Other [Clarification points from researcher re. application]		27 September 2016
Other [Email confirmation of sponsor contact]		29 September 2016
Participant consent form [Participant consent form]	2.4	14 December 2016
Participant information sheet (PIS) [Participant information sheet]	2.4	14 December 2016
Research protocol or project proposal [AZTEC-CF PROTOCOL V7.2]	7.2	28 September 2016
Research protocol or project proposal [AZTEC-CF Protocol]	7.3	26 October 2016
Summary CV for Chief Investigator (CI) [CV Professor Walshaw]		21 September 2016
Summary CV for Chief Investigator (CI) [CV FF]		
Summary CV for student [Freddy Frost]		19 September 2016
Summary CV for supervisor (student research) [Professor Winstanley]		19 September 2016
Summary CV for supervisor (student research) [Dr Fothergill]		19 September 2016
Summary of product characteristics (SmPC) [Cayston SmPC]		
Summary, synopsis or diagram (flowchart) of protocol in non technical language [Flowchart]	2.0	27 September 2016
Validated questionnaire [CFQ-R Adults]		

Appendix B - Summary of HRA Assessment

This appendix provides assurance to you, the sponsor and the NHS in England that the study, as reviewed 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 and arranging capacity and capability.

For information on how the sponsor should be working with participating NHS organisations in England, please refer to the, *participating NHS organisations*, *capacity and capability* and *Allocation of responsibilities and rights are agreed and documented (4.1 of HRA assessment criteria)* sections in this appendix.

The following person is the sponsor contact for the purpose of addressing participating organisation questions relating to the study:

Name: Mrs Gillian Hamblin

Email: Gillian.Hamblin@lhch.nhs.uk

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	Following REC favourable opinion, the information sheet and consent form were updated to bring them in line with HRA assessment standards.
3.1	Protocol assessment	Yes	The REC-approved protocol (v7.2) was updated via a non-substantial amendment to v7.3, in order to gain an MHRA CTA.
4.1	Allocation of responsibilities and rights are agreed and documented	Yes	This is a single site study that is sponsored by that site. Therefore, no agreement is expected.
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	The study is funded by Gilead. It is assumed that all secured funding adequately covers the NHS costs associated with this study.
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	Yes	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	Yes	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

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 study is a single site study; therefore, one site type, conducting activities as per the protocol. If this study is subsequently extended to other NHS organisation(s) in England, an amendment should be submitted to the HRA, with a Statement of Activities and Schedule of Events for the newly participating NHS organisation(s) in England. The Chief Investigator or sponsor should share relevant study documents with 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.

Confirmation of Capacity and Capability

This describes whether formal confirmation of capacity and capability is expected from participating NHS organisations in England.
This is a single site study sponsored by the site. The R&D office will confirm to the CI when the study can start.

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 in place at the single participating site. 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

For staff not holding a contract with the participating site, those taking consent or administering the CFQ-R would require a letter of access. Evidence of standard DBS and occupational health clearance would be expected.

For all other activities detailed in A18 and A19 of the IRAS form, staff not holding a contract with the participating site would require an Honorary Research Contract, and evidence of enhanced DBS, the appropriate barred list check, and occupational health clearance should be obtained.

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 intend to apply for inclusion on the NIHR CRN Portfolio.