## IRAS PROJECT ID 281958, REC Reference 20/SC/0158 Confirmation of favourable opinion for substantial amendment

berkshire.rec@hra.nhs.uk <noreply@harp.org.uk>

Mon 3/15/2021 11:45

**To:** Christopher Butler <christopher.butler@phc.ox.ac.uk>; CTRG Sponsorship Correspondence <ctrg@admin.ox.ac.uk>
**Cc:** gram.nrspcc@nhs.scot <gram.nrspcc@nhs.scot>; research-permissions@wales.nhs.uk <research-permissions@wales.nhs.uk>; Hannah Swayze <hannah.swayze@phc.ox.ac.uk>

1 attachments (122 KB)

IRAS 281958 SL32_Favourable_opinion_of_a_substantial_amendment.pdf;

Dear Professor Butler

| | |
|---|---|
| **IRAS project ID:** | 281958 |
| **REC reference:** | 20/SC/0158 |
| **Short Study title:** | PRINCIPLE [COVID-19] [UPH] |
| **Date complete amendment submission received:** | 09 March 2021 |
| **Amendment No./ Sponsor Ref:** | **SA 13** |
| **Amendment Date:** | **22 February 2021** |
| **Amendment Type:** | **Substantial** |
| **Outcome of HRA Assessment** | **This email also constitutes HRA and HCRW Approval for the amendment, and you should not expect anything further.** |

I am pleased to confirm that this amendment has been reviewed by the Research Ethics Committee and has received a Favourable Opinion. Please find attached a copy of the Favourable Opinion letter.

**HRA and HCRW Approval Status**

As detailed above, **this email also constitutes HRA and HCRW Approval for the amendment**. No separate confirmation of HRA and HCRW Approval will be issued.

**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/.

If you require further information, please contact me.

Kind regards

**Alison Doherty**
**Approvals Administrator**
Bristol REC Centre | Whitefriars | BS1 2NT
**T.** 020 7104 8049
**E.** berkshire.rec@hra.nhs.uk
**W.** www.hra.nhs.uk

Medicines & Healthcare products Regulatory Agency

MHRA

**MHRA**
10 South Colonnade
Canary Wharf
London
E14 4PU
United Kingdom

**gov.uk/mhra**

Prof C Butler
UNIVERSITY OF OXFORD
NUFFIELD DEPARTMENT OF PRIMARY CARE HEALTH SCIENCES,
RADCLIFFE OBSERVATORY QUARTER, WOODSTOCK ROAD
OXFORD
OX2 6GG
UNITED KINGDOM

09/03/2021

Dear Prof C Butler,

**THE MEDICINES FOR HUMAN USE (CLINICAL TRIALS) REGULATIONS 2004 S.I. 2004/1031**

| | |
|---|---|
| Our Reference: | CTA 21584/0426/001-0011 |
| Eudract Number: | 2020-001209-22 |
| Product: | Plaquenil-Hydroxychloroquine, Azithromycin, Doxycycline, Pulmicort Turbohaler 400, Colchicine, Favipiravir (Avigan) |
| Protocol number: | PRINCIPLE |
| Substantial Amendment Code Number: | SA 13, 22 February 2021 |

**NOTICE OF ACCEPTANCE OF AMENDMENT**

I am writing to inform you that the Licensing Authority accepts the proposed amendment to your clinical trial authorisation (CTA), received on 09/03/2021.

MEDICAL
TOXICOLOGY - Remarks: Nonclinical remark (no response required) - it is noted that the Investigator's brochure is dated 20 March 2020 and, therefore, a revision will be expected soon.
PHARMACEUTICAL

This amendment may therefore be made.

If applicable, you should ensure your trial details have been updated on the database where you have registered your trial.

You are reminded that where it is appropriate, the Ethics Committee should also be notified of amendments.

Yours sincerely,

**Clinical Trials Unit**
**MHRA**

Medicines and Healthcare Products Regulatory Agency

Health Research Authority

**South Central - Berkshire Research Ethics Committee**

Bristol REC Centre
Whitefriars
Level 3, Block B
Lewins Mead
Bristol
BS1 2NT

15 March 2021

Christopher Butler
University of Oxford
Radcliffe Observatory Quarter, Woodstock Road
Oxford
OX2 6GG

Dear Professor Butler

| | |
|---|---|
| **Study title:** | **Platform Randomised trial of INterventions against COVID-19 In older peoPLE** |
| **REC reference:** | **20/SC/0158** |
| **Protocol number:** | **PRINCIPLE** |
| **EudraCT number:** | **2020-001209-22** |
| **Amendment number:** | **SA 13** |
| **Amendment date:** | **22 February 2021** |
| **IRAS project ID:** | **281958** |

The above amendment was reviewed by the Sub-Committee in correspondence.

**Ethical opinion**

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

**Approved documents**

The documents reviewed and approved at the meeting were:

| *Document* | *Version* | *Date* |
|---|---|---|
| Annex 2: Notification of Amendment [Annex 2] | N/A | 09 March 2021 |
| Completed Amendment Tool [SA13 Locked Amendment Tool] | N/A | 22 February 2021 |
| Cover Letter [REC Cover Letter] | N/A | 09 March 2021 |
| Investigator Brochure/SmPC [Favipiravir Investigator's Brochure] | 12 | 20 March 2020 |
| Letter from sponsor [SA13 Sponsor Approval] | N/A | 09 March 2021 |
| Other [SA13 UPH Approval] | N/A | 04 February 2021 |
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| Participant information sheet (PIS) [PIS Appendices (tracked)] | 2.1 | 22 February 2021 |
| Participant information sheet (PIS) [PIS] | 4.0 | 22 February 2021 |
| Participant information sheet (PIS) [PIS (tracked)] | 4.0 | 22 February 2021 |
| Participant information sheet (PIS) [PRINCIPLE_Pictorial PIS v2.5_13.03.2021_tracked] | 2.5 | 13 March 2021 |
| Research protocol or project proposal [Protocol (tracked)] | 7.1 | 22 February 2021 |
| Research protocol or project proposal [Protocol] | 7.1 | 22 February 2021 |

**Membership of the Committee**

The members of the Committee who took part in the review are listed on the attached sheet.

**Working with NHS Care Organisations**

Sponsors should ensure that they notify the R&D office for the relevant NHS care organisation of this amendment in line with the terms detailed in the categorisation email issued by the lead nation for the study.

**Amendments related to COVID-19**

We will update your research summary for the above study on the research summaries section of our website. 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 have not 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.

**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.

**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 - 281958:** | **Please quote this number on all correspondence** |
|---|---|

Yours sincerely
PP

**Mr David Carpenter**
**Chair**

E-mail: berkshire.rec@hra.nhs.uk

*Enclosures:* *List of names and professions of members who took part in the review*

*Copy to:* *N/A N/A CTRG*

**South Central - Berkshire Research Ethics Committee**

**Attendance at Sub-Committee of the REC meeting in correspondence**

**Committee Members:**

| *Name* | *Profession* | *Present* | *Notes* |
|---|---|---|---|
| Mr David Carpenter | Retired Social Scientist | Yes | |
| Dr Mike Proven | University Research Governance Officer | Yes | |

**Also in attendance:**

| *Name* | *Position (or reason for attending)* |
|---|---|
| Miss Alison Doherty | Approvals Administrator |

# PRINCIPLE Trial - substantial Amendment 13

Elaine Chick <elaine.chick@admin.ox.ac.uk>

Tue 3/9/2021 10:11

**To:** Hannah Swayze <hannah.swayze@phc.ox.ac.uk>; PRINCIPLE Study <principle@phc.ox.ac.uk>
**Cc:** oxfordjro@mail.studyline.uk.com <oxfordjro@mail.studyline.uk.com>

2 attachments (814 KB)

281958_SA 13_.pdf; 281958_SA 13__A2.pdf;

Dear Hannah

I can confirm that the above referenced substantial amendment has been reviewed in CTRG and we are happy for it to be submitted to the relevant organisations for approval. This email can be forwarded as confirmation of sponsor approval for the amendment as required.

Please find attached the PDF version of the signed and locked amendment tool and annex 2.

Please submit this signed amendment tool, together with the tracked and clean copies of all amended documents, to the REC via the online amendment submission portal (for further guidance please refer to the HRA training video: how to complete online submission of amendments). Please make your MHRA submission, through the MHRA submission platform.

When you have received the submission confirmation, please email this, with the final documents you submitted, to the CTRG generic email address (ctrg@admin.ox.ac.uk).

Please send a copy of the approval letter(s) to the CTRG generic email address (ctrg@admin.ox.ac.uk) once you have received it/them. Please do not implement your amendment until all approval(s) are in place.

Kind regards,

Elaine

**Elaine Chick**

Deputy Head | Clinical Trials and Research Governance (CTRG)

Research Services, University of Oxford

Joint Research Office

Boundary Brook House, Churchill Drive Oxford OX3 7GB

Please note I usually work Monday-Thursday only

☎ 01865 616481

✉ elaine.chick@admin.ox.ac.uk

researchsupport.admin.ox.ac.uk

*Guidance (FAQs) for Clinical Research during the COVID-19 national emergency can be found on: https://researchsupport.admin.ox.ac.uk/ctrg*

PID14903-A019-SP001-AC001

NIHR | National Institute for Health Research

**CLINICAL RESEARCH NETWORK**
**COORDINATING CENTRE**
Minerva House
5 Montague Close
London
SE1 9BB

Tel: 020 3328 6700
Fax: 020 7636 5138
Email: crn@nihr.ac.uk
www.nihr.ac.uk

4th February 2021

Dear Chris

**RE: PRINCIPLE: Platform Randomised trial of INterventions against COVID-19 In older peoPLE**

Thank you for submitting the amendment of the above study to the NIHR Urgent Public Health Group for review. It was agreed to support the amendment, and (if you have not already done so) it is recommended that you seek urgent regulatory approval for the amendment to your study as a National Priority UPH study.

As you are no doubt aware, resources for supporting National Priority UPH studies are limited and therefore it is helpful for the UPH Group to have sight of amendments to studies. This will assist the UPH Group to review other studies submitted for UPH badging, and help to avoid the risk of conflict or duplication with UPH-badged studies. Therefore we would be grateful if you could inform the UPH Group of any future amendments to the study.

The NIHR CRN Research Delivery team will be updated on this amendment to the study, and a member of the team will be in touch with you shortly to discuss the support required. However, if there is something that you would like to discuss as a matter of urgency please get in touch with us through the urgentpublichealthcrn@nihr.ac.uk email address.

Finally, you may find the following information helpful:

## Core datasets

To ensure key information needed by decision makers about the effects of interventions is included in your study, please consider the use of core outcome sets such as the COMET initiative http://www.comet-initiative.org/Studies/Details/1538

As outlined in the application form, a small dataset of information about your study will be uploaded to the NIHR website and linked to the Health Research Agency website. If you have any queries regarding sharing these data publicly, please contact covid19application@nihr.ac.uk

## Media activity

If you wish to publicise this research in UK media (including social media), please notify pressoffice@nihr.ac.uk 24 hours in advance. The NIHR press office team is maintaining a centrally-held media grid for COVID-19 research. In the event that journalists contact you after information about your study is uploaded to the NIHR website and prior to any planned publicity, please contact the NIHR press office regarding an expedited approach.

## ISRCTN registration

It is compulsory for **all** Urgent Public Health (UPH) badged studies to be entered on the ISRCTN registry. ISRCTN is able to offer same-day registration for UPH badged studies. To access this please contact info@ISRCTN.com before creating or logging into your ISRCTN account and making your ISRCTN application through the ISRCTN online submission portal. Alternatively, you can apply for your ISRCTN registration through our Central Portfolio Management System (CPMS) on receipt of your CPMS ID. Instructions on how to do this will be provided. All non-commercial studies badged as UPH are able to have their registration fee paid by the Department of Health and Social Care. Reimbursement is not possible if you have already applied and received an ISRCTN before confirmation of your UPH badging and inclusion on the NIHR CRN Portfolio.

## Demographic data collection

Following NICE guidelines (https://www.nice.org.uk/covid-19/support-for-developers-of-medicinal-products-for-covid-19) a full range of baseline patient characteristics should be collected so that the relevance of the patient population to the NHS patient population can be evaluated. This includes sex, age, ethnicity, comorbidities, smoking status, residence in care home, functional status, and confinement status.

**Patient Information Leaflets (PILs) translation**

For UPH studies, the NIHR CRN is offering a PILs translation service which provides full and certified translation of PIL into languages specified. The aim of this service is to enable increased opportunity and equity for participation, increase the speed of trial delivery and reduce burden on sites and LCRNs. The following six languages are offered: Polish, Bengali, Urdu, Punjabi, French, Portuguese. Study teams can access this service through the Research Delivery Directorate.

**PPIE and participation support for UPH studies**

The CRN has a Public Advisory Forum to provide PPIE support to UPH studies. The forum consists of lay Research Champions who have been trained around health research and have received an induction around coronavirus research specifically. UPH study teams can seek involvement from the Public Advisory Group around any specific issues related to the design and delivery of UPH studies, by contacting crncc.ppie@leeds.ac.uk

To support UPH studies with any specific challenges around the participation of BAME communities in COVID-19 studies, the University of Leicester (NIHR ARC East Midlands) Centre for BME Health (https://centreforbmehealth.org.uk/) is offering expert guidance for study teams and research delivery teams. If you have specific enquiries about engaging BAME communities with your UPH study please contact ppie.crncc@leeds.ac.uk who will connect you with the Centre.

**Future Study Amendments**

If you plan to make an amendment to your research project, these should be submitted for NIHR Urgent Public Health Group review via the online submission form.

With best wishes

Nick Lemoine
Medical Director, NIHR Clinical Research Network

cc. Chelsea Drake NIHR CRN Head of Communications
Lead LCRN: Thames Valley and South Midlands
Research Delivery Directorate
Business Development and Marketing Directorate
Devolved Nations Representatives

**NHS Highland**

| | |
|---|---|
| R&D Ref No: | **H1629** |
| REC Ref No: | **20/SC/0158** |
| NRS Ref No: | **NRS20/281958** |
| EudraCT Ref No: | **2020-001209-22** |
| MHRA Ref No: | **21584/0426/001** |
| **Today's Date**: | **06/04/2021** |

**Frances Hines**
Research, Development & Innovation Manager
NHS Highland Research, Development & Innovation Department
Centre for Health Science
Old Perth Road
Inverness
IV2 3JH

Tel: 01463 255821
E-mail: frances.hines@nhs.scot
www. nhshighland.scot.nhs.uk

Dr Clare Bradley
Speciality Research Doctor
CRF, RD&I Division
NHS Highland
Centre for Health Science
Old Perth Road
Inverness IV2 3UH
By email: clare.bradley1@nhs.scot

Dear Clare,

**LETTER OF APPROVAL OF YOUR RESEARCH PROJECT AMENDMENT**

**PROJECT TITLE: PRINCIPLE: Platform Randomised trial of INterventions against COVID-19 In older peoPLE**
**REC: 20/SC/0158**
**NHS Highland R&D Ref Number: H1629**

| | | |
|---|---|---|
| **Amendment Type:** | **Substantial (SA)** | ✓ |
| | **Modified SA** | |
| | **Non-substantial (NSA)** | |
| **Amendment No:** | **SA13** | |
| **Amendment Date:** | **22.02.21** | |
| **Current Protocol Version No:** | **V7.1 Dated 22.02.21** | |

We have been notified of the above amendment to your research project and have received the following documents:

- Completed Amendment Tool.
- Amended documents corresponding with those approved in the REC amendment approval letter (South Central - Berkshire Research Ethics Committee) dated 15.03.21.
- MHRA approval letter dated 09.03.21.

The **RD&I Division**, NHS Highland, is happy to **approve** this amendment as it is within the scope of the original Management Approval Letter (09.06.20).

Yours sincerely,

Frances Hines

Frances Hines
NHS Highland Research, Development & Innovation Manager

cc Avril Donaldson, Clinical Research Nurse
NHS Highland Research, Development & Innovation Division, The Centre for Health Science, Old Perth Road, Inverness IV2 3JH
By email: avril.donaldson@nhs.scot

Mary Mckenzie, Senior Pharmacy Technician,
Research Pharmacy, The Centre for Health Science, Old Perth Road, Inverness IV2 3JH
By email: mary.mckenzie2@nhs.scot

Samantha Holden, NHS Highland Research Co-ordinator (Primary Care)
By email: samantha.holden@nhs.scot

Dr Hannah Swayze, PRINCIPLE Study
By email: hannah.swayze@phc.ox.ac.uk

**NHS Forth Valley**

Carseview House
Castle Business Park
Stirling
FK9 4SW

Telephone:
Fax:

Christopher Butler
University of Oxford
Radcliffe Observatory Quarter, Woodstock Road
Oxford
OX2 6GG

| | |
|---|---|
| Date | 31 March 2021 |
| Your Ref | |
| R&D Ref | FV1215 |
| | |
| Enquiries to | Fv.randd-depart@nhs.scot |
| Extension | |
| Direct Line: | 01324 614690 |

Dear Professor Butler

**Study title: Platform Randomised trial of INterventions against COVID-19 In older peoPLE**
**REC reference: 20/SC/0158**
**Amendment number: SA 13**
**Amendment date: 22 February 2021**

I am writing to confirm that NHS Forth Valley will accept the Amendment(s) detailed above, as given a Favourable Opinion by the South Central - Berkshire Research Ethics Committee on 15 March 2021.

Please note that NHS Forth Valley did not give formal R&D approval of this study due to the remote nature of the activity.

Yours sincerely

Pp

**MR. ANDREW MURRAY**
**Medical Director**

CC: principle@phc.ox.ac.uk
jacqueline.laird3@nhs.scot

List of Documents received:

| *Document* | *Version* | *Date* |
|---|---|---|
| Annex 2: Notification of Amendment [Annex 2] | N/A | 09 March 2021 |
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