ID: 130852.

Study: COVID-19: Healthcare Worker Bioresource: Immune Protection and Pathogenesis in SARS-CoV-2.

NCT Number: 04318314.

Document Date: 21/09/2020.

Title of document: Notice of Substantial Amendment Number 4.

South Central / Oxford A Research Ethics Committee
Bristol Research Ethics Committee Centre
Whitefriars Level 3 Block B Lewins Mead Bristol BS1 2NT

21st Sept 2020

Dear Research Ethics Committee, Dear Dr Davies

RE: IRAS 281844 "COVID-19 consortium (COVIDsortium): Healthcare worker Bioresource and preliminary analysis: Immune Protection and Pathogenesis in SARS-CoV-2 (COVID-HCW Study)"
Chief Investigator: Professor James Moon; Principal Investigator (Barts Health): Dr Thomas Treibel, Principal Investigator (Royal Free Hospital): Dr Marianna Fontana.

Notice of Substantial Amendment - Number 4

We would like to start by thanking the Committee for their continued support in enabling us to both expedite and continue the COVID-HCW Study (NCT04318314) under the extraordinary circumstance of the COVID-19 pandemic. With permissions in place, we were able to recruit the entire initial cohort of 400 participants within 7 working days - completed on the 1st of April 2020. Since then we have expanded the study to a total of 731 participants across St. Bartholomew Hospital, NHS Nightingale and the Royal Free Hospital. These participants returned on a weekly basis at a high follow-up rate for 16 weeks until early August. We also performed a "repeat bleed" of participants with symptoms and serology of interest (Amendment 3). Samples have been analysed by Public Health England (PHE) and internationally leading immunology and virology labs at UCL (Maine/Noursadeghi), Imperial (Boyton/Altman) and QMUL (McKnight). Since the arrival of the 1st wave of SARS-CoV-2, our understanding of this new disease has exponentially increased. In order to adapt to the rapidly changing research and clinical environments as well as the accumulating scientific body, we would like to amend our protocol to adapt to the changing landscape and impending second 2nd wave of SARS-CoV-2:

1	Increase in blood sampling volume at 6 and 12 months
2	Simplification of the cardiovascular substudy

Main changes: We would be grateful if you considered the following amendments of our study:

1) **Increase in blood sampling volume at 6 and 12 months:** The host response to SARS-CoV-2 is both mediated by neutralising antibodies and the T cell response. Whereas serological analysis can be performed on relatively small blood volumes, work on neutralising antibodies and the T cell response require larger volumes. We investigated this in a sub-cohort of 120 participants in a targeted rebleed in early August (amendment 3). Findings of this analysis are currently prepared for publication and are highly significant. In order to understand the significance of neutralisation and T cell response across the whole cohort, we would like the permission to increase the blood sampling at the 6 and 12 months follow-up to increase up to a total of 50mL: Serum (6mL), plasma (6mL), RNA pax (2.5mL), peripheral blood mononuclear cells (PBMC) for T cell response and neutralisation (35mL). The additional blood volume requested will not inconvenience participants as provisions and request for phlebotomy at 6 months has been requested previously as per "Notice of substantial amendment - number 3".

2) **Simplification of the cardiovascular substudy:** We have simplified this study and removed the 24h blood pressure monitoring as this will be too burdensome for the participants.

Thank you for considering our application for further amendment. If you have questions/queries about any aspects of the study, please contact us immediately.

Prof James Moon, Chief Investigator,
Dr Thomas Treibel, Principal Investigator Barts Health,
Dr Charlotte Manisty, Principal Investigator Barts Health,
Dr Marianna Fontana, Principal Investigator Royal Free Hospital.

Amendment Tool

v1.1 22 May 2020

For office use

QC: No

Section 1: Project information

Short project title*:	COVID-19: Healthcare worker Bioresource: Immune and Pathogenesis
IRAS project ID* (or REC reference if no IRAS project ID is available):	281844
Sponsor amendment reference number*:	Non Substantial Amendment 4
Sponsor amendment date* (enter as DD/MM/YY):	17 September 2020
Summary of amendment including justification*:	1. Increase in blood sampling volume at 6 and 12 months 2. Simplification of the cardiovascular substudy

Project type:	◉ Specific study ○ Research tissue bank ○ Research database			
Has the study been reviewed by a UKECA-recognised Research Ethics Committee (REC) prior to this amendment?:	◉ Yes	○ No		
What type of UKECA-recognised Research Ethics Committee (REC) review is applicable?:	○ ◉ NHS/HSC REC ○ ○ Ministry of Defence (MoDREC)			
Is all or part of this amendment being resubmitted to the Research Ethics Committee (REC) as a modified amendment?	○ Yes	○ No		
Where is the NHS/HSC Research Ethics Committee (REC) that reviewed the study based?:	England: ◉	Wales: ○	Scotland: ○	Northern Ireland: ○
Was the study a clinicial trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	○ Yes	◉ No		
Was the study a clinical investigation or other study of a medical device OR does the amendment make it one?:	○ ○ Yes	◉ ○ No		
Did the study involve the administration of radioactive substances, therefore requiring ARSAC review, OR does the amendment introduce this?:	○ ○ Yes	◉ ○ No		
Did the study involve the use of research exposures to ionising radiation (not involving the administration of radioactive substances) OR does the amendment introduce this?:	○ Yes	◉ No		
Did the study involve adults lacking capacity OR does the amendment introduce this?:	○ ○ Yes	◉ ○ No		
Did the study involve access to confidential patient information without consent OR does the amendment introduce this?:	○ Yes	◉ No		
Did the study involve prisoners OR does the amendment introduce this?:	○ Yes	◉ No		
Did the study involve NHS/HSC organisations prior to this amendment?:	◉ Yes	○ No		
Did the study involve non-NHS/HSC organisations OR does the amendment introduce them?:	○ ○ Yes	◉ ○ No		
	England	Wales	Scotland	Northern Ireland
Lead nation for the study:	◉	○	○	○
Which nations had participating NHS/HSC organisations prior to this amendment?	☑	☐	☐	☐
Which nations will have participating NHS/HSC organisations after this amendment?	☑	☐	☐	☐
	☐ ○	☐	☐ ○	☐

Section 2: Summary of change(s)

Please note: Each change being made as part of the amendment must be entered separately. For example, if an amendment to a clinical trial of an investigational medicinal product (CTIMP) involves an update to the Investigator's Brochure (IB), affecting the Reference Safety Information (RSI) and so the information documents to be given to participants, these should be entered into the amendment tool as three separate changes. A list of all possible changes is available on the "Glossary of Changes" tab. To add another change, tick the "Add another change" box.

Change 1	
Area of change (select)*:	Participant Procedures
Specific change (select - only available when area of change is selected first)*:	Amendment following urgent safety measure(s) taken to protect participants
Further information (free text):	08/06/2020), we will request: a) 50mls of blood total at each sampling interval of 6 and 12months. b) 50mls of blood to be made up of: Serum (6mL), plasma (6mL), RNA pax (2.5mL), peripheral blood mononuclear cells (PBMC) for T cell response and neutralisation (35mL).

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐
Will all participating NHS/HSC organisations be affected by this change, or only some?:	◉ All		○ Some	
	☐	☐	Add another change:	☑

Change 2	
Area of change (select)*:	Study Design
Specific change (select - only available when area of change is selected first)*:	Data collection, transfer or processing of identifiable participant information - Changes in arrangements or organisations involved (other than the addition of new participating organisations)
Further information (free text):	Simplification of the cardiovascular substudy: We have simplified this study and removed the 24h blood pressure monitoring as this will be too burdensome for the participants.

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐
Will all participating NHS/HSC organisations be affected by this change, or only some?:	◉ All		○ Some	
	☐	☐	Add another change:	☐

☐ ○ ☐ ☐ ○ ☐

Section 3: Declaration(s) and lock for submission

Declaration by the Sponsor or authorised delegate

- I confirm that the Sponsor takes responsibility for the completed amendment tool
- I confirm that I have been formally authorised by the Sponsor to complete the amendment tool on their behalf

Name [first name and surname]:*	Pushpsen Joshi
Email address:*	pushpsen.joshi1@nhs.net

Lock for submission

Please note: This button will only become available when all mandatory (*) fields have been completed. When the button is available, clicking it will generate a PDF copy of the completed amendment tool that can be included in the amendment submission. Please ensure that the amendment tool is completed correctly before locking it for submission.

Lock for submission

Section 4: Review bodies for the amendment

Please note: This section is for **information only**. Details in this section will complete automatically based on the options selected in Sections 1 and 2.

	Review bodies																	
	UK wide:						England and Wales:				Scotland:				Northern Ireland:			
	REC	Competent Authority MHRA - Medicines	Competent Authority MHRA - Devices	ARSAC	Radiation Assurance	UKSW Governance	REC (MCA)	CAG	HMPPS	HRA and HCRW Approval	REC (AWIA)	PBPP	SPS (RAEC)	National coordinating function	HSC REC	HSC Data Guardians	Prisons	National coordinating function	Category:
Change 1:	Y					Y				Y									A
Change 2:	N					Y				Y									A
Overall reviews for the amendment:																			
Full review:	Y					Y				Y									
Notification only:	N					N				N									
Overall amendment type:	Substantial for review																		
Overall Category:	A																		