Amendment Tool

v1.5 25 Mar 2021

For office use

QC: No

Section 1: Project information

Short project title*:	PRINCIPLE
IRAS project ID* (or REC reference if no IRAS project ID is available):	281958
Sponsor amendment reference number*:	SA 15
Sponsor amendment date* (enter as DD/MM/YY):	26 April 2021
Briefly summarise in lay language the main changes proposed in this amendment. Explain the purpose of the changes and their significance for the study. If the amendment significantly alters the research design or methodology, or could otherwise affect the scientific value of the study, supporting scientific information should be given (or enclosed separately). Indicate whether or not additional scientific critique has been obtained (note: this field will adapt to the amount of text entered)*:	1. Addition of Ivermectin treatment arm 2. Trial name change 3. AE and SAE reporting 4. Study documents 5. Confirmation of the discontinuation of the Budesonide arm.

Project type (select):	◉ 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? (select):	◉ 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** (i.e. a substantial amendment previously given an unfavourable opinion)?	○ 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 clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	◉ Yes	○ No		
EudraCT number*:	2020-001209-22			
Was this clinical trial of an investigational medicinal product (CTIMP) processed under the Combined Ways of Working (CWoW) pilot?:	○ Yes	◉ No		
Did the study receive Pharmacy Assurance?:	○ 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 outside the direct care team 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 children 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?	☑	☑	☑	☑
Which nations had participating non-NHS/HSC organisations prior to this amendment?	☑	☐	☐	☐
Which nations will have participating non-NHS/HSC organisations after this amendment?	☑	☐	☐	☐

Section 2: Summary of change(s)

What do you want to update?:	◉ Project information ○ New site/PI only

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 Amendment Options" tab. To add another change, tick the "Add another change" box.

Change 1				
Area of change (select)*:	CTIMP IMP			
Specific change (select - only available when area of change is selected first)*:	IMP being added to the study for the first time			
Further information (free text - note that this field will adapt to the amount of text entered):	Addition of Ivermectin treatment arm. IMP specific documents have been created: Intervention Specific Appendix, PIS appendix, Medication card, IMP label. Ivermectin has in vitro activity against SARS-CoV-2, and emerging clinical evidence from multiple small trials suggest it may effectively reduce SARS-CoV-2 viral loads, reduce time to recovery, and reduce mortality among people with COVID-19. However, data from large, robust clinical trials is lacking.			
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? (**please note** that this answer may affect the categorisation for the change):	◉ All		○ Some	
Where are the participating non-NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐

Add another change: ☑

Change 2				
Area of change (select)*:	Administrative details for the project			
Specific change (select - only available when area of change is selected first)*:	Project identification (e.g. change of title, reference numbers)			
Further information (free text - note that this field will adapt to the amount of text entered):	Updated to: Platform Randomised trIal of treatmeNts in the Community for epIdemic and Pandemic iLInEsses (PRINCIPLE). All other douments not submitted with this amendment will be updated with the new trial logo and trial title. The current trial title includes the phrase 'older people', but following a previous amendment, some people aged 18 and over will now be eligible. Together with the possibility of developing PRINCIPLE into a sustainable, long term platform for respiratory tract infection research beyond this pandemic, the trial title has been updated.			
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? (**please note** that this answer may affect the categorisation for the change):	◉ All		○ Some	
Where are the participating non-NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐

Add another change: ☑

Change 3				
Area of change (select)*:	CTIMP safety			
Specific change (select - only available when area of change is selected first)*:	Study oversight - Additional monitoring, not part of an urgent safety measure, but taken on a precautionary basis			
Further information (free text - note that this field will adapt to the amount of text entered):	i) Pregnancy in female participants taking ivermectin, favipiravir and colchicine will be reported after treatment and follow-up information regarding the outcome of the pregnancy and any postnatal sequelae in the infant will be required. ii) For colchicine, the protocol states that events rated as a 'major problem' will be assessed by a clinician for potential reporting as an SAE. This wording has been updated to clarify that this safety oversight will be for the duration of IMP administration (14 days). iii) Clarification that some SAEs may be identified restrospectively from data extracts, these will be reported within 24 hours of becoming aware of the event			
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? (**please note** that this answer may affect the categorisation for the change):	◉ All		○ Some	
Where are the participating non-NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐

Add another change: ☑

Change 4				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other minor change to study documents (e.g. information sheets, consent forms, questionnaires, letters) that can be implemented within existing resource in place at participating organisations - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	Protocol, PIS with changes described above			
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? (**please note** that this answer may affect the categorisation for the change):	◉ All		○ Some	
Where are the participating non-NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐

Add another change: ☑

Change 5				
Area of change (select)*:	CTIMP IMP			
Specific change (select - only available when area of change is selected first)*:	Other - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	Confirmation that the Budesonide arm was discontinued on 31st March 2021.			
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? (**please note** that this answer may affect the categorisation for the change):	◉ All		○ Some	
Where are the participating non-NHS/HSC organisations located that will be affected by this change?*:	☑	☐	☐	☐

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

Applicant identification:	◉ Sponsor ○ Legal representative of the sponsor ○ Person or organisation authorised by the sponsor
Organisation:	University of Oxford
Name [first name and surname]:*	Elaine Chick
Address:	CTRG, Boundary Brook House, Oxford, OX3 7GB
Telephone number:	0000 000000
Fax number:	0000 000000
Purchase Order (PO) number for MHRA invoicing:	TBC - Finance Dept currently raising the PO for payment
Email address:*	principle@phc.ox.ac.uk; ctrg@admin.ox.ac.uk

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 locked PDF copy of the completed amendment tool which must be included in the amendment submission. Please ensure that the amendment tool is completed correctly before locking it for submission.

Lock for submission

After locking the tool, proceed to submit the amendment online. The "Submission Guidance" tab provides further information about the next steps for the amendment.

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				Y				Y				Y	A
Change 2:	(Y)	N				Y				(Y)				(Y)				(Y)	C
Change 3:	N	N				(Y)				(Y)				(Y)				(Y)	A
Change 4:	N	N				(Y)				(Y)				(Y)				(Y)	C
Change 5:	Y	Y				Y				Y				Y				Y	A
Overall reviews for the amendment:																			
Full review:	Y	Y				Y				Y				Y				Y	
Notification only:	N	N				N				N				N				N	
Overall amendment type:	Substantial for review																		
Overall Category:	A																		

For national coordinating function office use:	
Update HARP:	This amendment may involve an update to contact details, project end date, or other project details. Ensure that HARP is updated with the current details. If this is the only change, no further study-wide review is required.