

Amendment Tool

v1.6 06 December 2021

For office use

QC: No

Section 1: Project information

Short project title*:	The RECOVERY Trial			
IRAS project ID* (or REC reference if no IRAS project ID is available):	281712			
Sponsor amendment reference number*:	Substantial Amendment 31			
Sponsor amendment date* (enter as DD/MM/YY):	22 June 2023			
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) Removal of three COVID-19 treatment comparisons that have now closed: empagliflozin, Paxlovid and molnupiravir. Participant materials are updated to reflect this. 2) Inclusion of non-UK RECOVERY sites in influenza comparisons 3) Removal of the Gambia, Sri Lanka and Pakistan as a collaborating sites 4) Update protocol text to ensure it is consistent throughout with previous amendments, reflects the current post-pandemic situation, and gives equal importance to the influenza and COVID-19 aspects of the trial. 5) Collection of some additional baseline information from routinely collected records 6) Allowance on-site monitoring if necessary, now that pandemic restrictions have been relaxed 7) Approval for additional testing of baseline blood samples			
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
	Yes	No	No	No
Was the study a clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	Yes		No	
EudraCT number*:	2020-001113-21			
Was this clinical trial of an investigational medicinal product (CTIMP) processed under the CTIMP combined review service (formerly known as 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 young offenders who are in custody or supervised by the probation service 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	
Lead nation for the study:	England	Wales	Scotland	Northern Ireland
	Yes	No	No	No

Which nations had participating NHS/HSC organisations prior to this amendment?	Yes	Yes	Yes	Yes
Which nations will have participating NHS/HSC organisations after this amendment?	Yes	Yes	Yes	Yes

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, click 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)*:	Change of IMPs			
Further information (free text - note that this field will adapt to the amount of text entered):	Removal of three COVID-19 treatment comparisons that have now closed from the protocol and participant documents: empagliflozin, Paxlovid and molnupiravir.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	Yes	Yes	Yes	Yes
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	
Remove all changes below				

Change 2				
Area of change (select)*:	Study Management			
Specific change (select - only available when area of change is selected first)*:	Non-UK countries - Inclusion or withdrawal of an EU Member State or third country			
Further information (free text - note that this field will adapt to the amount of text entered):	Removal of the limitation of influenza comparisons to the UK, as we wish non-UK RECOVERY sites to participate in these comparisons. We are removing some countries from our collaborator list: Sri Lanka and Pakistan (where we were never able to open to recruitment), and The Gambia (which was open to recruitment, but has closed because of capacity issues without having recruited any participants).			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	Yes	No	No	No
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	
Remove all changes below				

Change 3	
Area of change (select)*:	Study Documents
Specific change (select - only available when area of change is selected first)*:	Protocol - Non-substantial changes (e.g. not affecting safety or the scientific value of the trial)
	<p>Update of protocol text in several places:</p> <p>i) To ensure it is consistent throughout with previous amendments & remove reference to completed comparisons</p> <p>ii) To reflect the fact that this ongoing platform trial is now investigating treatments of two endemic viral infections (SARS-CoV-2 and influenza) rather than responding to the evolving SARS-CoV-2 pandemic. To avoid confusion for patients with influenza and for collaborators at sites participating only in influenza comparisons, we would like to change the layout of the headings in the protocol and ICFs to emphasise the short trial title (as the full title mentions COVID-19 but not influenza). We have removed the full trial title from the logo for the same reason. Actually changing the full trial title at this stage would not be appropriate, as it would cause confusion among collaborators and the public. and would require many documents and</p>

Further information (free text - note that this field will adapt to the amount of text entered):

approvals to be updated across seven countries (including at sites participating only in COVID-19 comparisons).

iii) To reintroduce text that was lost from a previous amendment, which clarified that patients are eligible for the trial if they lack capacity because of a prior condition (the explicit statement of this was accidentally removed in version 18 (SA20) although remained in the ICF) - section 2.2

iv) Addition of details of routinely collected safety outcomes that have been introduced since the first protocol - section 3.1.3

v) Update to allow licensed IMPs to be labelled according to the requirements for unlicensed treatments (as doing so may facilitate supply of the IMP) - section 6.5

vi) Collection of some additional clinical data at trial entry, to categorise severity of disease. These routinely collected clinical observations, blood tests and radiology results will already be in participants' medical records. None will require any tests to be done for the purposes of research. Details are in protocol section 2.3

vii) Section 5.2 of the protocol has been updated to reflect the fact that on-site monitoring is possible now that pandemic infection control measures have been relaxed. Monitoring will continue to use remote checks where practical (for example, where data can be checked via national NHS databases), and will focus on data items that are critical to quality.

viii) Appendix 6 has been added to clarify which comparisons are active in different countries, and any country-specific variations in eligibility

Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	Yes	Yes	Yes	Yes
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	
			Remove all changes below	

Change 4					
Area of change (select)*:	Participant Procedures				
Specific change (select - only available when area of change is selected first)*:	Participant procedures - minor change that can be implemented within existing resource at participating organisations - Please specify in the free text below				
Further information In particular, please describe why this change can be implemented within the existing resource in place at the participating organisations (free text - note that this field will adapt to the amount of text entered)*	Additional testing of blood samples collected from participants in two comparisons that have now closed (convalescent plasma and the Regeneron monoclonal antibodies casirivimab/imdevimab). The rationale for this testing is detailed in the attached document.				
Applicability:	England	Wales	Scotland	Northern Ireland	
Where are the participating NHS/HSC organisations located that will be affected by this change?*	Yes	Yes	Yes	Yes	
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		
			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

Sponsor	
Applicant identification:	Legal representative of the sponsor Person or organisation authorised by the sponsor
Organisation:	University of Oxford
Name [first name and surname]*:	Heather House
Address:	RGEA, Boundary Brook House, Headington, Oxford, OX37GB
Telephone number:	
Fax number:	
Purchase Order (PO) number for MHRA invoicing:	H62017838
Email address*:	rgea.amend@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																	Category:	
	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
Change 1:	Y	Y				(Y)				(Y)				(Y)				(Y)	A
Change 2:	N	N				(Y)				(Y)				N				N	C
Change 3:	N	N				(Y)				(Y)				(Y)				(Y)	A
Change 4:	N	N				(Y)				(Y)				(Y)				(Y)	C
Overall reviews for the amendment:																			
Full review:	Y	Y				N				N				N				N	
Notification only:	N	N				Y				Y				Y				Y	
Overall amendment type:	Substantial for review																		
Overall Category:	A																		