

Amendment Tool

v1.5 25 Mar 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 20			
Sponsor amendment date* (enter as DD/MM/YY):	15 October 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)*:	We wish to amend the section on consent obtained by legal representative. This replaces the current requirement to obtain personal consent with the requirement to inform the participant of their involvement and their rights and how to exercise them. We have also added clarification about who can act as an independent legal representative and seek approval for a newsletter to send to all surviving participants. We also wish to re-order the outcomes for the early phase assessment of dimethyl fumarate and increase the sample size from 400 to 700 to maintain statistical power with the new primary outcome.			
Project type (select):	<input checked="" type="radio"/> Specific study <input type="radio"/> Research tissue bank <input type="radio"/> Research database			
Has the study been reviewed by a UKECA-recognised Research Ethics Committee (REC) prior to this amendment?:	<input checked="" type="radio"/> Yes <input type="radio"/> No			
What type of UKECA-recognised Research Ethics Committee (REC) review is applicable? (select):	<input checked="" type="radio"/> NHS/HSC REC <input type="radio"/> 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)?	<input type="radio"/> Yes <input checked="" type="radio"/> No			
Where is the NHS/HSC Research Ethics Committee (REC) that reviewed the study based?:	England	Wales	Scotland	Northern Ireland
	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Was the study a clinical trial of an investigational medicinal product (CTIMP) OR does the amendment make it one?:	<input checked="" type="radio"/> Yes <input type="radio"/> No			
EudraCT number*:	2020-001113-21			
Was this clinical trial of an investigational medicinal product (CTIMP) processed under the Combined Ways of Working (CWoW) pilot?:	<input type="radio"/> Yes <input checked="" type="radio"/> No			
Did the study receive Pharmacy Assurance?:	<input checked="" type="radio"/> Yes <input type="radio"/> No			
Was the study a clinical investigation or other study of a medical device OR does the amendment make it one?:	<input type="radio"/> Yes <input checked="" type="radio"/> No			
Did the study involve the administration of radioactive substances, therefore requiring ARSAC review, OR does the amendment introduce this?:	<input type="radio"/> Yes <input checked="" type="radio"/> 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?:	<input type="radio"/> Yes <input checked="" type="radio"/> No			
Did the study involve adults lacking capacity OR does the amendment introduce this?:	<input checked="" type="radio"/> Yes <input type="radio"/> No			
Did the study involve access to confidential patient information outside the direct care team without consent OR does the amendment introduce this?:	<input type="radio"/> Yes <input checked="" type="radio"/> No			
Did the study involve prisoners OR does the amendment introduce this?:	<input type="radio"/> Yes <input checked="" type="radio"/> No			
Did the study involve children OR does the amendment introduce this?:	<input checked="" type="radio"/> Yes <input type="radio"/> No			
Did the study involve NHS/HSC organisations prior to this amendment?:	<input checked="" type="radio"/> Yes <input type="radio"/> No			
Did the study involve non-NHS/HSC organisations OR does the amendment introduce them?:	<input type="radio"/> Yes <input checked="" type="radio"/> No			
	England	Wales	Scotland	Northern Ireland
Lead nation for the study:	<input checked="" type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
Which nations had participating NHS/HSC organisations prior to this amendment?	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
Which nations will have participating NHS/HSC organisations after this amendment?	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

Section 2: Summary of change(s)

What do you want to update?:	<input checked="" type="radio"/> Project information
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What do you want to update:

☐ 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)*:	Participant Procedures			
Specific change (select - only available when area of change is selected first)*:	Recruitment - Change in identification, approach, recruitment or consent of participants			
Further information (free text - note that this field will adapt to the amount of text entered):	Following a meeting with MHRA, HRA and REC chair/vice-chair, we wish to amend the section on consent obtained by legal representative. This replaces the current requirement to obtain personal consent with the requirement to inform the participant of their involvement and their rights and how to exercise them. We have also added clarification about who can act as an independent legal representative.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 2				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Other significant 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):	We seek approval of a newsletter to send to all surviving participants to update them on trial progress and results. This also includes text for participants whose consent was obtained from a legal representative and who may not have been informed of their participation before they left hospital. This includes information about their rights and how to exercise them.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

Add another change: ☒

Change 3				
Area of change (select)*:	Study Design			
Specific change (select - only available when area of change is selected first)*:	Other significant change to study design 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):	Change in order of outcomes for early phase assessment of dimethyl fumarate arm, such that the primary objective is the WHO ordinal scale. This is because the duration of admission (in blinded data) is shorter than before meaning a measurement of S/F94 at 5 days has missing data due to prior discharge.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	

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):	Removal of 3 month follow-up outside UK. This was defined initially when it was necessary to screen for tuberculosis recurrence after infliximab administration. Now this arm has been removed we only need to collect data at a single time point.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>

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):	<input type="radio"/> All	<input checked="" type="radio"/> Some
Add another change: <input checked="" type="checkbox"/>		

Change 5				
Area of change (select)*:	Study Design			
Specific change (select - only available when area of change is selected first)*:	Inclusion/exclusion criteria - Minor change unlikely to affect safety or scientific value of study			
Further information (free text - note that this field will adapt to the amount of text entered):	Because children with PIMS-TS no longer have comparisons in the main randomisation, their randomisation between tocilizumab, anakinra or usual care is no longer best described as a 'second' randomisation. Consequently, the requirement to have been recruited in the previous 21 days is no longer required.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	
Add another change: <input checked="" type="checkbox"/>				

Change 6				
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):	Stylistic changes to PIS/ICF (requested by the public advisory group).			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	
Add another change: <input checked="" type="checkbox"/>				

Change 7				
Area of change (select)*:	Study Documents			
Specific change (select - only available when area of change is selected first)*:	Correction of typographical errors			
Further information (free text - note that this field will adapt to the amount of text entered):	Ketone monitoring is only required for patients with diabetes in the empagliflozin-treated group (as specified in justification for change of previous amendment and appendix). We have also removed some other duplication from the protocol to simplify it.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	
Add another change: <input checked="" type="checkbox"/>				

Change 8				
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):	Information on use of live vaccines added to child PIS; additional clause in ICF regarding GP contact (to align with adult ICF and allow for provision of discharge summary to GP per protocol); adult & child PIS updated to clarify possible audits from sponsor/host site.			
Applicability:	England	Wales	Scotland	Northern Ireland
Where are the participating NHS/HSC organisations located that will be affected by this change?*	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>
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):	<input checked="" type="radio"/> All		<input type="radio"/> Some	
Add another change: <input type="checkbox"/>				

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:	<input checked="" type="radio"/> Sponsor <input type="radio"/> Legal representative of the sponsor <input type="radio"/> Person or organisation authorised by the sponsor
Organisation:	University of Oxford
Name [first name and surname]*:	Elaine Chick
Address:	RGEA, Boundary Brook House, Churchill Drive, Headington, Oxford OX3 7GB
Telephone number:	
Fax number:	
Purchase Order (PO) number for MHRA invoicing:	H62017838
Email address*:	ctr@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	N				Y				Y				Y				Y	A
Change 2:	Y	N				Y				Y				Y				Y	C
Change 3:	Y	Y				Y				Y				Y				Y	C
Change 4:	N	N				(Y)				(Y)				(Y)				(Y)	C
Change 5:	N	N				(Y)				(Y)				(Y)				(Y)	A
Change 6:	N	N				(Y)				(Y)				(Y)				(Y)	C
Change 7:	N	N				N				N				N				N	N/A
Change 8:	N	N				(Y)				(Y)				(Y)				(Y)	C
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																		