Amendment Tool

v1.5 25 Mar 2021

For office use

QC: No

Section 1: Project information

Short project title*:	REMAP-CAP			
IRAS project ID* (or REC reference if no IRAS project ID is available):	237150			
Sponsor amendment reference number*:	AM027			
Sponsor amendment date* (enter as DD/MM/YY):	29 June 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)*:	AM027 involves: The addition of the DMX-200 intervention (ACE2/RAS domain) to the Participant information sheets as well as the addition of DMX-200 documentation. We added 1 IMP product to the MHRA CTA: DMX-200. As requested an RSI section has been added to the IB. I would also like to inform you of the closure of the REMAP-CAP Antiplatelet domain.			
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*:	2015-002340-14			
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?	☑	☑	☑	☑

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):	DMX-200 is a novel drug, an intervention within the ACE2/RAS domain that will be supplied as a clinical trial IMP with clinical trial labelling.			
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	

Add another change: ☑

Change 2				
Area of change (select)*:	Study Management			
Specific change (select - only available when area of change is selected first)*:	Funding arrangements - Changes that do not affect payments to participants/researchers/sites			
Further information (free text - note that this field will adapt to the amount of text entered):	Submission of the RECOVER fundIng agreement that has been agreed now that the PREPARE agreement has come to an end.			
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	

Add another change: ☑

Change 3				
Area of change (select)*:	Study Management			
Specific change (select - only available when area of change is selected first)*:	Other significant change - Please specify in the free text below			
Further information (free text - note that this field will adapt to the amount of text entered):	closure of the REMAP-CAP Antiplatelet domain.On the 22nd of June 2021 the REMAP-CAP International Trial Steering Committee (ITSC) received correspondence from the REMAP-CAP DSMB notifying us of Platform Conclusions arising from an adaptive analysis. This adaptive analysis revealed that for patients with COVID-19 who are receiving organ support in an ICU, antiplatelet therapy, either with aspirin or P2Y12 inhibitor (which were found to be equivalent), was ineffective when compared to no antiplatelet therapy (OR = 0.99 [95% CrI 0.82 – 1.19], probability of OR < 1.2 = 98%). The unanimous recommendation of the DSMB was that this domain be closed for patients with severe COVID-19 (i.e. patients receiving organ support in an ICU). This recommendation has been accepted by the ITSC. In addition, in light of the recent publication of results from the RECOVERY trial, which found that treatment with aspirin did not improve 28-day mortality, the REMAP-CAP ITSC have decided to also close the Antiplatelet Domain to patients with moderate COVID-19 (i.e. hospitalised patients not receiving organ support in an ICU). These data are reflective of high-quality evidence from a large randomised trial, which further suggest that antiplatelet therapy is not associated with improved outcomes for patients with COVID-19.			
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	

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 Medical Center Utrecht
Name [first name and surname]:*	Erika Groeneveld
Address:	Heidelberglaan 100, Utrecht, The Netherlands
Telephone number:	+31 (0)8875 55196
Fax number:	N/A
Purchase Order (PO) number for MHRA invoicing:	R5418.70
Email address:*	eu.remapcap@utrecht.nl

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:	N	N				(Y)				(Y)				(Y)				(Y)	C
Change 3:	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																		