

REMAP-CAP Amendment Tracker

<u>Amendment</u>	<u>Approvals</u>	<u>Submission date</u>	<u>Approval date</u>	<u>Documents</u>	<u>Summary</u>
Original approvals	REC HRA MHRA	23.03.18	01.06.18		Initial application
AM01	REC HRA (linked to AM02)	18.06.18	19.07.18	REMAP-CAP European Region-Specific Appendix V2.1 20180524	1 Addition of a single recruiting site (Poole Hospital) 2 Amendment to the European Region Specific Appendix
AM02	REC HRA	13.06.18	07.08.18		1 Addition of 7 new recruiting sites (North Tees, Royal Berkshire, Sunderland Royal, Basingstoke, Royal Blackburn, QA Portsmouth, James Cook)
AM03	REC HRA	10.12.18	30.01.19	REMAP-CAP European Region specific Appendix v2.2 26.10.2018 Non pandemic Patient information sheet and consent form V2.1 29.11.2018 Retrospective patient information sheet and consent form V2.1 29.11.2018 Personal Legal representative information sheet and consent form V2.1 29.11.2018 Professional Legal Representative consent form V1.1 29.11.2018	1 Addition of 3 new recruiting sites (Stoke Mandeville, Peterborough City, Tunbridge Wells) 2 Change in PI at 1 site (St James' Hospital, Leeds – PI Dr E. Paramasivam) 3 Updated information sheets 4 Updated European Region Specific Appendix
NS01	REC HRA	21.06.2019	05.07.19 11.07.19	Updated document: UK REMAPCAP PerLR ICF v2.3 2019.06.20 Superseded document: UK REMAPCAP PerLR ICF v2.2 2019.06.20	Notification of a typographical error in the REMAP-CAP information sheet / consent form for Personal Legal representative. On page 8, it was incorrectly titled ' consent form for patients able to give consent'. I have amended it to ' consent form for patients unable to give consent
AM04	REC HRA	29.07.19	03.09.19		1 Addition of 5 new recruiting sites (Milton Keynes, Darlington Memorial, North Durham, Northampton General, Royal Surrey) 2 Change in PI at one site (Royal Cornwall, New PI – Dr Mike Spivey)

AM05	REC HRA MHRA	27.11.19	09.01.20	REMAP-CAP Core Protocol V3 - FINAL_CLEAN - 10 July 2019 REMAP-CAP Macrolide Duration Domain-Specific Appendix V3 - FINAL_CLEAN - 10 July 2019 REMAP-CAP Corticosteroid Domain-Specific Appendix V3 - FINAL_CLEAN - 12 July 2019 REMAP-CAP European Region-Specific Appendix V3 - FINAL_CLEAN - 23 August 2019 REMAP-CAP Statistical Analysis Appendix V3 - FINAL_CLEAN - 24 August 2019 REMAP-CAP Antibiotic Domain-Specific Appendix V3 - FINAL_CLEAN - 10 July 2019 REMAP-CAP - Antiviral Domain-Specific Appendix V1 - FINAL - 10 July 2019 REMAP-CAP Registry Appendix v1 - UK_FINAL - 11 Sep 2019 REMAP-CAP Protocol Summary V3 - FINAL_CLEAN - 11 Sep 2019 Non pandemic UK REMAP CAP PIS ICF V2.3 29.10.2019 UK REMAP CAP Retrospective PIS ICF V2.3 29.10.2019 UK REMAP CAP PerLRIS ICF V2.4 29.10.2019	1 Amendments to the core protocol 2 Addition of the New domain appendices 3 Addition of an intervention to the pre-existing Corticosteroid domain
AM06	REC HRA	13.02.20	09.03.20	REMAP-CAP - PatC - V1.1 - CLEAN - 20200212	1 Addition of Pandemic appendix to Core
AM07	REC HRA MHRA	16.03.20	27.03.20	European Region Specific Appendix v3.1 13.03.2020 REMAP-CAP - COVID-19 Antiviral Domain-Specific Appendix V1.0 - 11 March 2020 REMAP-CAP - COVID-19 Immune Modulation Domain-Specific Appendix V1.0 - 11 March 2020 Non pandemic UK REMAP CAP PIS ICF V2.4 2020.03.16 UK REMAP CAP Retro PIS ICF V2.4 2020.03.16 UK REMAPCAP PerLRIS ICF v2.5 2020.03.16 Pandemic UK REMAP CAP COVID19 PIS ICF V1.0 2020.03.16 Amended to UK REMAP CAP COVID19 PIS ICF V1.1 2020.03.19 UK REMAP CAP COVID19 Retro PIS ICF V1.0 2020.03.16	1 Addition of 10 new recruiting sites (Charing Cross Hospital, Hammersmith Hospital, St Mary's Hospital, Royal Free Hospital, John Radcliffe Hospital, Addenbrookes Hospital, York Hospital, Belfast City Hospital, Royal Victoria Belfast, Mater Hospital) 2 updated EU Region specific appendix 3 Addition of COVID-19 Antiviral domain 4 Addition of COVID-19 immune modulation domain 5 updated information sheets and consent forms 6 New COVID-19 specific information sheets and consent forms

				UK REMAPCAP COVID19 PerLRIS ICF v1.0 2020.03.16	
AM08	REC HRA	25.03.20	30.03.20		1 Addition of co-PI at Belfast City Hospital, Royal Victoria Hospital and Mater Hospital: 2. Addition of 21 new recruiting sites (Guy's & St Thomas' Hospital, Bolton Hospital, Wythenshawe Hospital, The Cumberland Infirmary, West Cumberland Hospital, South Tyneside Hospital, Royal United Bath, City Hospital Birmingham, Royal Brompton Hospital, Royal Marsden Hospital, Northwick Park Hospital, Ealing Hospital, Central Middlesex Hospital, Frimley Park Hospital, Wexham Hospital, Southend Hospital, Royal Gwent Hospital, King's Mill Hospital, Southampton Hospital, Salford Royal Hospital, Royal Liverpool Hospital).
AM09	REC HRA	30.03.20	09.04.20	Pandemic – Scotland UK REMAP CAP COVID19 PIS ICF V1.0 2020.03.28 - Scotland UK REMAP CAP COVID19 Retro PIS ICF V1.0 2020.03.28 Recovered Capacity - Scotland UK REMAPCAP COVID19 PerLRIS ICF v1.0 2020.03.28 Attorney Guardian Relative - Scotland UK REMAP-CAP ProLR ICF V1.0 2020.03.28 clean Scotland	1 Addition of 13 new recruiting sites (Bristol Royal, The Royal London, City Hospital Nottingham, Craigavon Area Hospital, Altnagelvin Hospital, NHS Nightingale Hospital, Antrim Area Hospital, Freeman Hospital, Northern General Hospital) including addition of 4 New Scottish Sites (Glasgow Royal Infirmary, Edinburgh Royal Infirmary, Queen Elizabeth Glasgow, Western General Edinburgh) 2 Change of PIs at 2 sites 3 addition of information sheets and consent forms for Scottish sites

AM10	REC HRA MHRA	06.04.20	09.04.20 expedited	REMAP-CAP - COVID-19 Antiviral Domain-Specific Appendix V2.0 - 01 April 2020_CLEAN Pandemic – England, Wales & NI UK REMAP CAP COVID19 PIS ICF V1.2 2020.04.06 UK REMAP CAP COVID19 Retro PIS ICF V1.2 2020.04.06 UK REMAPCAP COVID19 PerLRIS ICF v1.2 2020.04.06	1 Addition of an additional antiviral agent, hydroxychloroquine to the COVID anti-viral domain We will evaluate this agent on its own and also in combination with kalettra. 2 We added this intervention into the information sheets and made a few minor semantic changes to make some of the terminology more lay friendly.
AM11	REC HRA MHRA	09.04.2020	17.04.2020 Expedited + additional approval re clarification in dosing on 27.04.2020	REMAP-CAP - COVID-19 Immune Modulation Domain-Specific Appendix V2.0 - 07 April 2020_CLEAN REMAP-CAP - COVID-19 Immune Modulation Domain-Specific Appendix V2.0 - 07 April 2020_TC SmPC Sarilumab (Kevzara) SmPC Tocilizumab (RoActemra) Summary of changes to COVID19 Immune Modulation Therapy Domain Specific Appendix V1.0 - 08 April 2020 Pandemic UK REMAP CAP COVID19 PIS ICF V1.3 2020.04.09 TC E&W UK REMAP CAP COVID19 Retro PIS ICF V1.3 2020.04.09 TC E&W UK REMAPCAP COVID19 PerLRIS ICF v1.3 2020.04.09 TC E&W UK REMAP CAP COVID19 PIS ICF V1.1 2020.04.09 – Scotland TC UK REMAP CAP COVID19 Retro PIS ICF V1.1 2020.04.09 Recovered Capacity – Scotland TC UK REMAPCAP COVID19 PerLRIS ICF v1.1 2020.04.09 Attorney Guardian Relative – Scotland TC UK REMAP CAP COVID19 PerLRIS ICF v1.2 2020.04.09_NI TC UK REMAP CAP COVID19 PIS ICF V1.2 2020.04.09_NI TC	Addition of 2 additional immune modulatory agent, Tocilizumab and Sarilumab to the COVID immune modulation domain. Other minor changes to this DSA include a change to statistical methods to facilitate more rapid evaluation of interventions. added these interventions into the information sheets and made a few minor changes to make some of the terminology more lay friendly.

				UK REMAP CAP COVID19 Retro PIS ICF V1.2 2020.04.09_NI TC	
NS02	REC HRA	10.04.2020	n/a	<i>HRA stated: As of 8th april, for CTIMP COVID-19 studies the HRA no longer require the submission of a substantial or non-substantial amendment each time a site and PI is added</i>	Addition of 12 new recruiting sites (HRA and REC had confirmed that new sites should be added as part of non substantial amendment to fast track approvals during the pandemic)
AM12	HRA	15.04.20	15.04.20 expedited	Substantial amendment letter generated and submitted by the HRA	All UK NHS organisations that have ICU's / Critical care facilities. This includes all NHS ICU units in England and in the devolved states so that they may enrol and randomise patients with acute COVID-19 infection into the REMAP-CAP study. All Principal Investigators at these organisations, as deemed appropriate by the sponsor. This should be taken to include cases where the PI is changed at a previously approved NHS site.
AM13	REC HRA	19.04.20	22.04.20 Expedited review	REMAP-CAP COVID-19 Immunoglobulin Therapy Domain-Specific Appendix V1- 19 April 2020 Pandemic - E&W UK REMAP CAP COVID19 PIS ICF V1.4 2020.04.19 UK REMAP CAP COVID19 Retro PIS ICF V1.4 2020.04.19 UK REMAPCAP COVID19 PerLRIS ICF v1.4 2020.04.19 Pandemic NI UK REMAP CAP COVID19 PerLRIS ICF v1.3 2020.04.19_NI UK REMAP CAP COVID19 PIS ICF V1.3 2020.04.19_NI UK REMAP CAP COVID19 Retro PIS ICF V1.3 2020.04.19_NI Pandemic Scotland UK REMAP CAP COVID19 PIS ICF V1.2 2020.04.19 - Scotland UK REMAPCAP COVID19 PerLRIS ICF v1.2 2020.04.19 Attorney Guardian Relative - Scotland UK REMAP CAP COVID19 Retro PIS ICF V1.2 2020.04.19 Recovered Capacity - Scotland	1 Addition of the COVID-19 Immunoglobulin Domain specific appendix v1 19.04.20. 2 We added these interventions into the information sheets and made a few minor semantic changes to make some of the terminology more lay friendly.

NS03	REC HRA MHRA			Old document UK REMAP-CAP ProLR ICF V1.1 2018.11.30 Updated document UK REMAP-CAP ProLR ICF V1.2 2020.04.20	Typographical error on ProLR V1.1 Header indicated Protocol version 2 rather than version 3
AM14	REC HRA MHRA	22.04.20	27.04.20 Expedited review	REMAP-CAP COVID-19 Therapeutic Anticoagulation Domain-Specific Appendix V1- 20 April 2020 Pandemic E&W UK REMAP-CAP ProLR ICF V1.2 2020.04.20 UK REMAP CAP COVID19 PIS ICF V1.5 2020.04.22 UK REMAP CAP COVID19 Retro PIS ICF V1.5 2020.04.22 UK REMAPCAP COVID19 PerLRIS ICF v1.5 2020.04.22 Pandemic NI UK REMAP CAP COVID19 PerLRIS ICF v1.4 2020.04.22_NI UK REMAP CAP COVID19 PIS ICF V1.4 2020.04.22_NI UK REMAP CAP COVID19 Retro PIS ICF V1.4 2020.04.22_NI Pandemic Scotland UK REMAP CAP COVID19 PIS ICF V1.3 2020.04.22 - Scotland UK REMAPCAP COVID19 PerLRIS ICF v1.3 2020.04.22 Attorney Guardian Relative – Scotland UK REMAP CAP COVID19 Retro PIS ICF V1.3 2020.04.22 Recovered Capacity - Scotland	1 Addition of the Therapeutic Anticoagulation Domain specific appendix v1 20.04.20. 2 We added this intervention into the information sheets and made a few minor semantic changes to make some of the terminology more lay friendly.
AM15	REC HRA MHRA	06.05.20	12.05.20 Expedited review		Doses of Anakinra approved as per AM011, but not updated on the CTA. New dosing from Immune modulation domain v2: Anakinra will be administered as an intravenous bolus injection via a central or peripheral line. A loading dose of 300 mg will be administered, followed by maintenance doses of 100 mg of anakinra administered every 6 hours. In patients with creatinine clearance of less than 30 ml/min or receiving renal replacement therapy, anakinra will be dosed every 12 hours. Duration of therapy

					Anakinra will be administered four times daily until the patient has been breathing without receiving invasive mechanical ventilation for more than 24 hours or for 14 days in patients who continue to receive invasive mechanical ventilation. For patients not receiving invasive mechanical ventilation, the drug will stop on ICU discharge or after 14 days, whichever occurs first. Correction to an error in our original MHRA CTA application regarding specific populations of patient included in this study. We had ticked excluding women of child bearing age (using and not using contraception) , but as discussed with the MHRA at that time, these patients would be included for some IMPs but not others. In light of the pandemic we feel this population of patients as well as pregnant women and breastfeeding women, would benefit from this study and would like to ensure they are able to be included. Pregnant and breastfeeding women are excluded from certain domains and if treating clinicians feel it would not be in their best interest to enter the study, they can be excluded on an individual basis
AM016	MHRA	20.05.20	22.05.20 Expedited review		Addition of 2 IMP products to the CTA 1. The addition of unlicensed Sarilumab. The manufacturer (Sanofi Montpellier) will be providing the

					study with both licenced and unlicensed product for use in REMAP-CAP. The unlicensed product will be provided with clinical trial labels (submitted to MHRA), GMP certification and QP declaration. Sarilumab will be supplied to trial sites through PHE authorised distribution sites 2. The addition of Kaletra 80mg/20mg Oral Solution.
AM017	REC HRA	23.05.20	26.05.20 Expedited review		MHRA requested a pause to hydroxychloroquine allocation within the REMAP-CAP study. The pause to this intervention was part of an urgent safety measure. For patients who are currently being treated with hydroxychloroquine, an individual risk assessment by the treating clinician should be made as to whether to continue or stop the treatment as per protocol.
AM018	MHRA	01.06.20	03.06.20 Expedited review	MHRA CTA	Addition of releasing site information to section D9 of the MHRA CTA for unlicensed Sarilumab and the Kaletra oral solution
AM019	REC HRA MHRA	05.06.20	11.06.20 Expedited review	REMAP-CAP COVID-19 Immunoglobulin Therapy Domain-Specific Appendix V1.1- 01 June 2020 Summary of changes to Pandemic Appendix to Core Protocol V1.0 - 24 May 2020 REMAP-CAP - PATC - V2.0 - 18 May 2020_CLEAN	Changes to Pandemic Appendix to Core – Alignment of REMAP-CAP and REMAP-COVID in readiness for pre-ICU randomisation for certain domains, and the introduction of moderate and severe patients. Changes to Immunoglobulin domain.

AM020	Rec HRA MHRA	10.07.20	15.07.20 Expedited review	Updates to the Therapeutic Anticoagulation Domain Specific Appendix: REMAP-CAP - Therapeutic Anticoagulation - V2 - 24 June 2020_TC REMAP-CAP - Therapeutic Anticoagulation - V2 - 24 June 2020_CLEAN Summary of changes to Therapeutic Anticoagulation Domain-Specific Appendix V1.0 - 24 June 2020_FINAL The main change to this domain is to include patients with COVID-19 before they are admitted to ICU. We have therefore made changes to the participant information sheets to include these patients. We have reformatted the documentation to be more modular (for use in the general hospital ward and in the intensive care) and simplified and clarified the wording in various places. This reformatting has also been completed for the non-pandemic IS_CF documentation. The addition of 2 new Domain specific Appendices: REMAP-CAP Vitamin C Domain Specific Appendix V2 - 08 June 2020 for patients with COVID-19 and community acquired pneumonia (not yet active) REMAP-CAP Simvastatin Domain-Specific Appendix - V1.0 - 07 July 2020 for patients with COVID-19 (not yet active) Updated information sheets : Pandemic Patients: England/Wales UK REMAP CAP COVID19 PIS ICF V1.6 2020.10.07 UK REMAP CAP COVID19 Retro PIS ICF V1.6 2020.07.10 UK REMAPCAP COVID19 PerLRIS ICF v1.6 2020.07.10 UK REMAP-CAP ProLR ICF V1.3 2020.07.10 TC Northern Ireland UK REMAP CAP COVID19 PerLRIS ICF v1.5 2020.07.10_NI UK REMAP CAP COVID19 PIS ICF V1.5 2020.07.10_NI UK REMAP CAP COVID19 Retro PIS ICF V1.5 2020.07.10_NI UK REMAP-CAP ProLR ICF V1.3 2020.07.10 TC Scotland UK REMAP CAP COVID19 PIS ICF V1.4 2020.07.10 – Scotland UK REMAP CAP COVID19 Retro PIS ICF V1.4 2020.07.10 Recovered Capacity – Scotland	
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AM021	REC HRA MHRA	23.07.20	03.08.20 Expedited review	REMAP-CAP Simvastatin domain specific appendix v1.1 23.07.2020	Update to Simvastatin DSA to add an exclusion criteria - <i>“Women who are known or suspected to be pregnant or</i>

					<i>breastfeeding will be excluded from the simvastatin intervention"</i>
AM022	REC HRA MHRA	1.10.201	12.10.20	Antiplatelet Domain specific Appendix: REMAP-CAP – Antiplatelet Domain v1.0 24/08/2020 CLEAN Pandemic: NI UK REMAP CAP COVID19 PerLRIS ICF v1.6 2020.10.01 NI UK REMAP CAP COVID19 PIS ICF V1.6 2020.10.01 NI UK REMAP CAP COVID19 Retro PIS ICF V1.6 2020.10.01 NI England/wales UK REMAP CAP COVID19 PIS ICF V1.7 2020.10.01 UK REMAPCAP COVID19 PerLRIS ICF v1.7 2020.10.01 UK REMAPCAP COVID19 Retro PIS ICF v1.7 2020.10 Scotland UK REMAP CAP COVID19 PerLR ICF V1.5 2020.10.01 Scotland UK REMAP CAP COVID19 PIS ICF V1.5 2020.10.01 Scotland UK REMAP CAP COVID19 Retro PIS ICF V1.5 2020.10.01 Scotland We have also listed the new IMPs for the Antiplatelet Domain (SmPCs attached) : Aspirin Prasugrel Clopidogrel Ticagrelor	This involves the addition of an Antiplatelet Domain specific Appendix: REMAP-CAP – Antiplatelet Domain v1.0 24/08/2020 CLEAN Changes to IS_CF for COVID-19 suspected /confirmed patients now includes a section for randomising to the antiplatelet domain for pre-ICU and ICU patients. We have also added space for witness consent in the event that the patient or the Personal Legal representative is not able to physically sign the consent form. I have attached and submitted both the TC and clean versions of the documents
AM023	HRA REC	13.11.20	17.11.20	Brief REMAP-CAP Patient information summary v1 13.11.20 Brief REMAP-CAP ProLR information summary v2 13.11.20 Corrected to Brief REMAP-CAP ProLR information summary v2 13.11.20 REMAP-CAP COVID poster v1 10.11.20	This amendment includes the addition of: A simple one page lay summary of the REMAP-CAP study for patients with COVID who have capacity but are unable to read /understand the full patient information sheets at the time of randomisation. Recruiting sites have indicated this would be an

					invaluable addition in the recruitment process, as some patients have sufficient capacity to say they wish to take part in the study but are unable to absorb all the information provided in the participant information sheets when they are acutely unwell in an emergency setting. This document will also allow patients to better understand the key principles of the study in advance of recruitment and confirm that they will review and sign the full information sheet and consent form at a later stage when they have sufficient capacity. A simple one page REMAP-CAP study summary as supportive information for Professional Legal Representatives in the event they require some simple information prior to signing the ProLR consent form. A simple REMAP-CAP COVID-19 waiting room poster that can be made available to patients and Personal Legal Representatives to increase awareness of the study for ICU and ward based recruitment. Addition of clinical trial stock of Vitamin C
AM024	MHRA	16.02.21	04.03.21	MHRA CTA	
AM025	REC HRA MHRA	09.03.21	17.03.21	Brief REMAP-CAP Patient information summary v2 04.03.21 Brief REMAP-CAP ProLR information summary v3 04.03.21 Pandemic UK REMAP CAP COVID19 PerLRIS ICF v1.7 02.03.21 NI UK REMAP CAP COVID19 PIS ICF V1.7 02.03.21 NI UK REMAP CAP COVID19 Retro PIS ICF V1.7 02.03.21 NI	Addition of ACE2 RAS domain Addition of new interventions for anticoagulation domain Increase of patient recruitment number from 1000 to 6000 Update all full information sheets and consent forms

				UK REMAP CAP COVID19 PIS ICF V1.8 02.03.21 E&W UK REMAPCAP COVID19 PerLRIS ICF v1.8 02.03.21 E&W UK REMAPCAP COVID19 Retro PIS ICF v1.8 02.03.21 E&W UK REMAP CAP COVID19 PerLR ICF V1.6 02.03.21 Scotland UK REMAP CAP COVID19 PIS ICF V1.6 02.03.21 Scotland UK REMAP CAP COVID19 Retro PIS ICF V1.6 02.03.21 Scotland	Update lay summary information sheets
AM026	REC HRA MHRA	03.06.21	REC and HRA approval 29.07.21 (AM026 and AM027 approved together) MHRA rejected this amendment and the IMP specific documentation was resubmitted as part of AM027	RECOVER funding agreement Pandemic: UK REMAP CAP COVID19 PerLRIS ICF v1.8 01.06.21 NI UK REMAP CAP COVID19 PIS ICF v1.8 01.06.21 NI UK REMAP CAP COVID19 Retro PIS ICF v1.8 01.06.21 NI UK REMAP CAP COVID19 PIS ICF v1.9 01.06.21 E&W UK REMAPCAP COVID19 PerLRIS ICF ICF v1.9 01.06.21 E&W UK REMAPCAP COVID19 Retro PIS ICF v1.9 01.06.21 E&W UK REMAP CAP COVID19 PerLR ICF ICF v1.7 01.06.21 Scotland UK REMAP CAP COVID19 PIS ICF v1.7 01.06.21 Scotland UK REMAP CAP COVID19 Retro PIS ICF v1.7 01.06.21 Scotland	Addition of the RECOVER funding agreement (since the PREPARE agreement funding ended); extension in recruitment period till 13.02.22 Closure of the antiplatelet domain. The addition of the DMX-200 intervention (ACE2/RAS domain) and their addition to the Participant information sheets
AM027	REC HRA MHRA	30.06.21	29.07.21	Addition of the DMX-200 intervention to the ACE2/RAS Domain DIL2501 REMAP CAP label Proof english & dutch 20210505 DMX-200 ARDS IB v4 SIGNED DMX-200 ARDS IB v4.0 track changes DMX-200 COVID-19 IMPD v2.0 April 2021 DMX-200_REMAP_CAP_label_proof_Part_2_sign_of 20210506 Grant Agreement-101003589-RECoVER_FE IRASEudractExport MhraProductsForm (AM026) MIA_Fisher_DE_BW_01_MIA_2021_0022_DE+ EN QP Declaration REMAP CAP_27May2021 Site GMP Certificate FDA EU and Registration Database Reference 2020 Signed	

AM028	REC HRA MHRA	21.08.21	06.10.21	Cysteamine_Nylexa IMPD_V1.0_18 Aug 2021 Nylexa clinical label_Version4.0_13 Jul 2021 REMAP-CAP - Domain Specific Appendix - Cysteamine - V1.0 - 21 June 2021 REMAP-CAP pharmacy guide - Version 3 - 18 August 2021_CLEAN IRASEudractExport MhraProductsForm AM028 Updated COVID-19 participant information sheets Brief REMAP-CAP Patient information summary v3 16.08.21 Brief REMAP-CAP ProLR information summary v4 16.08.21 Pandemic UK REMAP CAP COVID19 PerLRIS ICF v1.9 16.08.21 NI UK REMAP CAP COVID19 PIS ICF v1.9 16.08.21 NI UK REMAP CAP COVID19 Retro PIS ICF v1.9 16.08.21 NI UK REMAP CAP COVID19 PIS ICF v1.10 16.08.21 E&W UK REMAPCAP COVID19 PerLRIS ICF ICF v1.10 16.08.21 E&W UK REMAPCAP COVID19 Retro PIS ICF v1.10 16.08.21 E&W UK REMAP CAP COVID19 PerLR ICF ICF v1.8 16.08.21 Scotland UK REMAP CAP COVID19 PIS ICF v1.8 16.08.21 Scotland UK REMAP CAP COVID19 Retro PIS ICF v1.8 16.08.21 Scotland Updated Non-pandemic: UK REMAP CAP PIS ICF V2.6 16.08.21 UK REMAP CAP Retro PIS ICF V2.6 16.08.21 UK REMAPCAP PerLR IS ICF v2.7 16.08.21 UK REMAP CAP PerLR IS ICF v2.7 16.08.21_NI UK REMAP CAP PIS ICF V2.6 16.08.21_NI UK REMAP CAP Retro PIS ICF V2.6 16.08.21_NI UK REMAP CAP PerLR IS ICF v2.7 16.08.21_ Attorney Guardian Relative – Scotland	
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				UK REMAP CAP PIS ICF V2.6 16.08.21_Scotland UK REMAP CAP Retro PIS ICF V2.6 16.08.21_ Recovered Capacity – Scotland	
NS04	REC HRA	20.09.21	20.09.21	NIHR funding extension agreement	This involves clarification that the current funding allows for continued REMAP-CAP recruitment till the 30 th June 2022. Updated end date for patient recruitment. REMAP-CAP is designed as a perpetual study but additional funding extensions (provided by the RECOVER agreement and the NIHR) are now in place to continue recruitment of REMAP-CAP patients till 30.06.22
AM029	HRA MHRA	22.09.21	06.10.21	We added 1 IMP product to the MHRA CTA Cysteamine Bitartrate For AM029 I have submitted the below documents to both the MHRA and the HRA Portals: Amendment_Tool_v1_5_25Mar21 REMAP-CAP AM029 22.09.21 Locked Cysteamine_Nylexa IMPD_V1.0_18 Aug 2021 Nylexa clincial label_Version4.0_13 Jul 2021 REMAP-CAP - Domain Specific Appendix - Cysteamine - V1.0 - 21 June 2021 REMAP-CAP pharmacy guide - Version 3 - 18 August 2021_CLEAN MhraProductsForm_AM028 200821 IRASEudractExport Cysteamine_Nylexa IB_Version1.1_22 Sep 2021_Track changed Cysteamine_Nylexa IB_Version1.1_22 Sep 2021	Much of this documentation was submitted as part of AM028, however the MHRA required additional information be provided within the IB and so provided a notice of non-acceptance for AM028. The IMP documentation, supplied as part of AM028, plus the updated IB (track changed and clean) is now being resubmitted as AM029 for review and approval by the MHRA and HRA. All patient facing documentation remains as part of AM028 for review and approval by the REC / HRA.
NS05	REC HRA	13.10.21	N/A	UK REMAP CAP Retro PIS ICF V2.6 2021.08.16 CLEAN (adult)	As part of AM028 all pandemic and non-pandemic participant information sheets and consent forms were updated, reviewed and approved, as well as the summary information

					sheets. Unfortunately due to the volume of participant information sheets submitted during the upload process the UK REMAP-CAP Retrospective Information for participants and Consent Form, V2.6 (track changed and clean version) dated 16th August 2021 was missed. The changes were exactly the same as those submitted, reviewed and approved for the other documentation submitted for English Sites, Northern Irish sites and Scottish sites. For this reason this missed document is being submitted as part of a non substantial amendment
AM030	REC HRA (Not approved) MHRA (Not approved)	30.11.21	Not approved, Amended and Resubmitted as AM032	<u>Documents submitted as part of Substantial amendment AM030:</u> REMAP-CAP - ACE2 RAS DSA - V2 - 14 Oct 2021 REMAP-CAP - ACE2 RAS DSA - V2 - 14 Oct 2021_TC Summary of changes to ACE2 RAS Domain-Specific Appendix V1.0 - 16 Nov 2021 REMAP-CAP - Monoclonal Antibody DSA V1 22 November 2021 REMAP-CAP COVID-19 Immunoglobulin Therapy Domain-Specific Appendix V3 - 24 November 2021 REMAP-CAP COVID-19 Immunoglobulin Therapy Domain-Specific Appendix V3 - 24 November 2021_TC from V1.01 Amendment_Tool_AM30_20211201 revised-gb-spc-ronapreve-clean-120mg-ml12aug2021docx TRV027 Vial Carton Label version3 REMAP-CAP 19Jul21 TRV027 IMPD V4.0 26August2021 TRV027 IMPD V4 Signature page TRV027 IB Ed 7 30Nov2021 Brief REMAPCAP ProLR_IS summary v5 261121 TC Brief REMAPCAP ProLR_IS summary v5 261121 CLEAN Pandemic UK REMAP CAP COVID19 PerLR ICF V1.9 2021.11.26 Scotland TC	This involves: The addition of a new intervention, TRV027 into the ACE2 RAS domain The reopening of the immunoglobulin domain with new interventions The addition of the Monoclonal Antibody Domain I also made the below changes to the MHRA CTA. TRV027 casirivimab / imdevimab (Ronapreve)

				UK REMAP CAP COVID19 PerLR ICF V1.9 2021.11.26 Scotland CLEAN UK REMAP CAP COVID19 PIS ICF V1.9 2021.11.26 Scotland TC UK REMAP CAP COVID19 PIS ICF V1.9 2021.11.26 Scotland CLEA UK REMAP CAP COVID19 Retro PIS ICF V1.9 2021.11.26 Scotland TC UK REMAP CAP COVID19 Retro PIS ICF V1.9 2021.11.26 Scotland CLEAN UK REMAP CAP COVID19 PerLRIS ICF v1.10 2021.11.26 NI TC UK REMAP CAP COVID19 PerLRIS ICF v1.10 2021.11.26 NI CLEAN UK REMAP CAP COVID19 PIS ICF V1.10 2021.11.26 NI TC UK REMAP CAP COVID19 PIS ICF V1.10 2021.11.26 NI CLEAN UK REMAP CAP COVID19 Retro PIS ICF V1.10 2021.11.26 NI TC UK REMAP CAP COVID19 Retro PIS ICF V1.10 2021.11.26 NI CLEAN UK REMAP CAP COVID19 PerLRIS ICF v1.11 2021.11.26 TC (E&W) UK REMAP CAP COVID19 PerLRIS ICF v1.11 2021.11.26 CLEAN (E&W) UK REMAP CAP COVID19 PIS v1.11 TC (E&W) UK REMAP CAP COVID19 PIS v1.11 CLEAN (E&W) UK REMAP CAP COVID19 Retro PIS ICF v1.11 2021.11.26 TC (E&W) UK REMAP CAP COVID19 Retro PIS ICF v1.11 2021.11.26 CLEAN (E&W)	
AM031	MHRA	17.12.21	20.12.21 Note: (categorised as 'substantial, for information' so did not require review/ approval by sites)	1. IMPD v2.0 dated 13 Dec 2021_track changed 2. IMPD v2.0 dated 13 Dec 2021_Final 3. Cysteamine label v5.0 dated 20 Aug 2021 – Expiry date extended up to Jun 2022	The main changes in the revised IMPD include: 1. Change of AMRI name to Curia (Scotland) Limited – page 101 2. Inclusion of 18m stability report for non-GMP batch and 6month stability report for GMP batch : Section 2.1.P.& Stability – p 171 onwards. This data supports extension of expiry date to Jun 2022 3. Shelf-life extension plan – page 177-178
AM032	REC HRA	17.12.21	11.01.22	Documents submitted as part of Substantial amendment AM030: REMAP-CAP - Monoclonal Antibody DSA V1 22 November 2021	The reopening of the immunoglobulin domain with new interventions

	MHRA			REMAP-CAP COVID-19 Immunoglobulin Therapy Domain-Specific Appendix V3 - 29 November 2021 CLEAN REMAP-CAP COVID-19 Immunoglobulin Therapy Domain-Specific Appendix V3 - 24 November 2021_TC from V1.01 REMAP-CAP Amendment_Tool_AM32_20211217 revised-gb-spc-ronapreve-clean-120mg-ml12aug2021docx Brief REMAPCAP ProLR_IS summary v5 261121 TC (E&W) Brief REMAPCAP ProLR_IS summary v5 261121 CLEAN (E&W) Pandemic UK REMAP CAP COVID19 PerLR ICF V1.9 2021.11.26 Scotland TC UK REMAP CAP COVID19 PerLR ICF V1.9 2021.11.26 Scotland CLEAN UK REMAP CAP COVID19 PIS ICF V1.9 2021.11.26 Scotland TC UK REMAP CAP COVID19 PIS ICF V1.9 2021.11.26 Scotland CLEAN UK REMAP CAP COVID19 Retro PIS ICF V1.9 2021.11.26 Scotland TC UK REMAP CAP COVID19 Retro PIS ICF V1.9 2021.11.26 Scotland CLEAN UK REMAP CAP COVID19 PerLRIS ICF v1.10 2021.11.26 NI TC UK REMAP CAP COVID19 PerLRIS ICF v1.10 2021.11.26 NI CLEAN UK REMAP CAP COVID19 PIS ICF V1.10 2021.11.26 NI TC UK REMAP CAP COVID19 PIS ICF V1.10 2021.11.26 NI CLEAN UK REMAP CAP COVID19 Retro PIS ICF V1.10 2021.11.26 NI TC UK REMAP CAP COVID19 Retro PIS ICF V1.10 2021.11.26 NI CLEAN UK REMAP CAP COVID19 PerLRIS ICF v1.11 2021.11.26 TC (E&W) UK REMAP CAP COVID19 PerLRIS ICF v1.11 2021.11.26 CLEAN (E&W) UK REMAP CAP COVID19 PIS v1.11 TC (E&W) UK REMAP CAP COVID19 PIS v1.11 CLEAN (E&W) UK REMAP CAP COVID19 Retro PIS ICF v1.11 2021.11.26 TC (E&W) UK REMAP CAP COVID19 Retro PIS ICF v1.11 2021.11.26 CLEAN (E&W)	The addition of the Monoclonal Antibody Domain The below changes to the MHRA CTA. casirivimab / imdevimab (Ronapreve)
AM033	MHRA	17.02.22	01.03.22	MhraProductsForm_REMAP-CAP AM033 170222 MIA (IMP) 18693 v 41 REMAP-CAP DMX-200 MIA (IMP) Certificate of GMP Compliance 03Nov2021 REMAP-CAP AM033 Amendment_Tool_v1_6_LOCKED	Addition of UK QP oversight of DMX-200 by Fisher Clinical services UK LTD, Langhurstwood road, Horsham, RH12 4QD, UK. Submission of associated MIA IMP

					Submission of Certificate of GMP compliance for Fisher Clinical services, Horsham.
AM034	REC/HRA (Information) MHRA (Review)	03.03.22	13.04.22	MhraProductsForm_REMAP-CAP AM034 020322 Ascorbic Acid Smpc REMAP-CAP AM034 Amendment_Tool_v1_6_LOCKED	Addition of releasing site information to section D9 of the MHRA CTA for licensed ascorbic acid This involves changes to the MHRA CTA for the Ascorbic Acid stock for use within REMAP-CAP Stock: 50ml vials of concentrate for solution for injection/infusion contains: 7,5g ascorbic acid Addition of UK Releasing site: Alliance Healthcare; Unit 1, High View Road Ind Units, South Normanton, Derbyshire; DE55 2DT Marketing Authorisation holder: Pascoe pharmazeutische Präparate GmbH UK MA number: PL 14369/0009 Submission of associated SmPC We are also formally submitting an amendment for the Pause of the ACE2/RAS domain within REMAP-CAP
AM035	REC /HRA /MHRA	12.04.22	12.05.22	MhraProductsForm_REMAP-CAP AM035 110422 Cysteamine_Nylexa IMPD_V3.0_08 Apr 2022_Final Cysteamine_Nylexa IMPD_V3.0_08 Apr 2022_track changed REMAP-CAP AM035 Amendment_Tool_v1_6_LOCKED GB_REMAP-CAP_SubjectInsurance_Allianz_Endorsement 2_20210715 GB_REMAP-CAP_SubjectInsurance_Allianz_Endorsement 1_20210125 Subject Insurance Certificate	Addition of releasing site information to section D9 of the MHRA CTA for cysteamine. This involves changes to the MHRA CTA for the Cysteamine stock for use within REMAP-CAP Addition of UK Releasing site: Catalent CTS (Edinburgh) Limited ,Unit 1, Inchwood Park, Bathgate,West Lothian, EH48 2FY, United Kingdom Marketing Authorisation holder: Catalent CTS (Edinburgh) Limited ,

					MIA (IMP) number: 25274 Submission of associated IMPD V3 08.04.22 (tracked changes and final) Update in clinical trial insurance to cover till 01.06.2023
AM036	REC / HRA / MHRA	31.05.2022	26.06.22	REMAP-CAP AM036 Amendment_Tool_v1_6_LOCKED REMAP-CAP_Protocol_EuropeanRSA_V3.3_20200408_eng REMAP-CAP_Protocol_EuropeanRSA_V3.3_20200408_eng_TC REMAP-CAP_Protocol_EuropeanRSA_V3.4_20200420_eng REMAP-CAP_Protocol_EuropeanRSA_V3.4_20200420_eng_TC REMAP-CAP_Protocol_EuropeanRSA_V3.5_20200503_eng REMAP-CAP_Protocol_EuropeanRSA_V3.5_20200503_eng_TC REMAP-CAP_EuropeanRSA_ChangeHistory_20210910_eng_2 Cysteamine_Nylexa IMPD_V4.0_25 May 2022_Final Cysteamine_Nylexa IMPD_V4.0_25 May 2022_track changed RECOVER Amendment-Funding to 2023	Updates to the Region-Specific Appendix, Significant changes to the IMPD, Extension of funding for the study until December 2023 and pausing the anticoagulation domain.
AM037	REC HRA MHRA	14.11.2022	15.12.2022	REMAP-CAP AM037 Amendment_Tool_v1_6_LOCKED REMAP-CAP - SoC to CORE protocol V3.1 - 11Nov2022 REMAP-CAP Core Protocol V3.1 (UK) - 9 Nov 2022_TC REMAP-CAP Core Protocol V3.1 (UK) - 9 Nov 2022_CLEAN REMAP-CAP - SOC to Corticosteroid DSA V2 - 11Nov2022 REMAP-CAP Corticosteroid Domain-Specific Appendix V5 (UK)_20221109_TC from V3 REMAP-CAP Corticosteroid Domain-Specific Appendix V5 (UK)_20221109_CLEAN REMAP-CPA - SoC to Influenza Antiviral Domain-Specific Appendix - V1_11Nov22 REMAP-CAP - Influenza Antiviral Domain-Specific Appendix - V2 (UK) - 01 Nov 2022_TC REMAP-CAP - Influenza Antiviral Domain-Specific Appendix - V2 (UK) - 01 Nov 2022_CLEAN Dexamethasone 3.3 mg/ml Solution for Injection (vial) - Summary of Product Characteristics (SmPC) Xofluza 20 mg & 40 mg film coated tablets - Summary of Product Characteristics (SmPC) Tamiflu 30 mg Hard Capsules - Summary of Product Characteristics (SmPC) Adults	- Submission of the Core Protocol (V3.1 tracked changes and final) – study now includes adults and children on the wards and ICU - Submission of the Domain-Specific Appendix Antiviral domain (V2.0 tracked changes and final)- Addition of a new intervention, Baloxavir - Submission of the Domain-Specific Appendix corticosteroid domain (V5.0 tracked changes and final) - Addition of a new intervention, Dexamethasone - Changes to IS_CF for COVID-19, CAP and Influenza - Addition of IS_CF for children

				REMAP-CAP_Tel v1.0 25OCT22 REMAP-CAP_Privacy Notice v1.0 25OCT22 REMAP-CAP_PIS_ICF v1.12 2022.10.25_tracked REMAP-CAP_PIS_ICF v1.12 25OCT22 REMAP-CAP_PerLIS_ICF v1.12 2022.10.25_tracked REMAP-CAP_PerLIS_ICF v1.12 25OCT22 REMAP-CAP_PerLR Sum_ICF v1.12 25OCT22 REMAP-CAP_ProLR Sum_ICF v1.4 2022.10.25_tracked REMAP-CAP_ProLR Sum_ICF v1.4 25OCT22 REMAP-CAP_UK_leaflet_V2.0_TC_2022.11.10 REMAP-CAP_UK_leaflet_V2.0_2022.11.10 REMAP-CAP_UK_poster_V2.0_TC_2022.11.09 REMAP-CAP_UK_poster_V2.0_2022.11.09 Paed REMAP-CAP_YoungChild_PIS_ICF v1.0 25OCT22 REMAP-CAP_Child_10-15_PIS_ICF v1.0 25OCT22 REMAP-CAP_Child_16-17_PIS_ICF v1.0 25OCT22 REMAP-CAP_UK_poster_Child V1.0_2022.11.09 MhraProductsForm_AM037	• Submission of adult and paediatric recruitment advertisement • Closure of the ACE2 RAS domain • Closure of the continuous therapeutic anticoagulation intervention in the prior anticoagulation domain • Pause of the Vitamin C domain • Extension to wards/ICU
AM038	REC HRA MHRA	14.07.2023	10.08.2023	REMAP-CAP AM038 Amendment_Tool_v1_6_LOCKED Contract_Issue_Letter_-_NIHR155209.docx (1) REMAP-CAP - Influenza Antiviral Domain-Specific Appendix - V2.1 - 14 Feb 2023_CLEAN REMAP-CAP - Influenza Antiviral Domain-Specific Appendix - V2.1 - 14 Feb 2023_TC from V2 REMAP-CAP Text for ICU research video Adults REMAP-CAP_PerLIS_ICF v1.14 2023.05.24_tracked REMAP-CAP_PerLIS_ICF v1.14 2023.05.24_clean (v1.13 not active as ethics requested changes) REMAP-CAP_PerLR Sum_ICF v1.2 2023.05.24_tracked REMAP-CAP_PerLR Sum_ICF v1.2 2023.05.24_clean (v1.1 not active) REMAP-CAP_PerLR Video Consent v1.1 2023.05.24_tracked REMAP-CAP_PerLR Video Consent v1.1 2023.05.24_clean (v1.0 not active) REMAP-CAP_PIS_ICF v1.14 2023.05.24_tracked	• Change on DSA for antiviral '48hrs' not '96hrs' • Submission of a consent video • Submission of updated adult IS_CF (and resubmission following further info request from ethics) • Submission of the SmPC's for the antibiotic, macrolide, steroid, anticoagulation and antiviral domains • NIHR Grant agreement (extension of study end date)

				REMAP-CAP_PIS_ICF v1.14 2023.05.24_clean (v1.13 not active) REMAP-CAP_ProLR Sum_ICF v1.6 2023.05.24_tracked REMAP-CAP_ProLR Sum_ICF v1.6 2023.05.24_clean (v1.5 not active) REMAP-CAP_Video Consent v1.1 2023.05.24_tracked REMAP-CAP_Video Consent v1.1 2023.05.24_clean (v1.0 not active) REMAP-CAP_Privacy Notice v1.1 2023.04.18_tracked REMAP-CAP_Privacy Notice v1.1 2023.04.18_clean REMAP-CAP_SmPC_Amoxicillin-Clavulanate (Augmentin)_20200303 REMAP-CAP_SmPC_Azithromycin (Zedbac)_20180206 REMAP-CAP_SmPC_Azithromycin tablet_20220107 REMAP-CAP_SmPC_Ceftarolinefosamil (Zinforo)_20220215_stopped REMAP-CAP_SmPC_Ceftriaxone_20220119 REMAP-CAP_SmPC_Clarithromycin powder_20160914 REMAP-CAP_SmPC_Clarithromycin tablet_20171128 REMAP-CAP_SmPC_Erythromycin_20140425 REMAP-CAP_SmPC_Levofloxacin_20210106 REMAP-CAP_SmPC_Moxifloxacin (Avelox)_20201109 REMAP-CAP_SmPC_Piperacillin-Tazobactam (Tazocin)_20211223 REMAP-CAP_SmPC_Roxithromycin (RULID)_202005XX REMAP-CAP_SmPC_Hydrocortisone(Solu-Cortef)_20220107_eng REMAP-CAP_SmPC_DalteparinSodium(Fragmin)_20201009 REMAP-CAP_SmPC_Enoxaparin Sodium_20220427 REMAP-CAP_SmPC_Heparin Sodium_20180928 REMAP-CAP_SmPC_Tinzaparin Sodium_20210108 REMAP-CAP_SmPC_Dexamethasone Tablet_20220814_current REMAP-CAP_SmPC_Oseltamivir (Tamiflu)_20210525	
NS06	HRA	07.08.2023	10.08.2023	REMAP-CAP_Child_10-15_PIS_ICF v1.3 2023.08.02 (paed)	Changes to REMAP-CAP_Child_10-15_PIS_ICF
AM039	REC HRA MHRA	22.09.2023	21.11.2023	REMAP-CAP AM039 Amendment_Tool_v1_6_LOCKED Cysteamine_Nylexa IMPD_V5.1_27 Oct 2023_Final Cysteamine_Nylexa IMPD_V5.1_27 Oct 2023_track changed Cysteamine_Nylexa IMPD_Summary of changes_Oct 2023 REMAP-CAP_European RSA_Change History_20210910_eng_2 REMAP-CAP_Protocol_European RSA_V3.6_20201217_eng REMAP-CAP_Protocol_European RSA_V3.6_20201217_eng_TC	• IMPD update for cysteamine • European RSA V3.6 • Addition of abx and macrolides to COVID pts in PIS • Updated insurance certificate to Jun 2026 • DSMB letter

				Adults REMAP-CAP_PIS_ICF v1.15_19.09.2023 Clean REMAP-CAP_PIS_ICF v1.15_19.09.2023 TC REMAP-CAP_PerLIS_ICF v1.15_19.09.2023_Clean REMAP-CAP_PerLIS_ICF v1.15_19.09.2023_TC REMAP-CAP_PerLR Sum_ICF v1.3_19.09.2023_Clean REMAP-CAP_PerLR Sum_ICF v1.3_19.09.2023_TC REMAP-CAP_ProLR Sum_ICF v1.7_19.09.2023_Clean REMAP-CAP_ProLR Sum_ICF v1.7_19.09.2023_TC UK_REMAP-CAP_SubjectInsurance_Cert_20230110 DSMB_REMAP-CAP_20230808_ltr_No safety concerns	
NS07	REC HRA	19.10.2023	27.10.2023	Summary of changes to Corticosteroid Domain-Specific Appendix V5.0 - 16 October 2023 Summary of changes to Influenza Antiviral Domain-Specific Appendix V2.2 - 16 October 2023 REMAP-CAP Corticosteroid Domain-Specific Appendix V5.1_16 October 2023_CLEAN REMAP-CAP Corticosteroid Domain-Specific Appendix V5.1_16 October 2023_TC from V5 REMAP-CAP - Influenza Antiviral Domain-Specific Appendix - V2.2 - 16 October 2023_CLEAN REMAP-CAP - Influenza Antiviral Domain-Specific Appendix - V2.2 - 16 October 2023_TC from V2.1 DSMB_REMAP-CAP_20230922_ltr_pediatric incl and no safety concerns REMAP-CAP NSA07 Amendment Tool Locked	1. Update to the antiviral domain specific appendix - minor clarification to wording relating to paediatric participants 2. Update to the corticosteroid domain specific appendix - minor clarification to wording relating to paediatric participants
NSA08	HRA	23.11.2023	05.12.2023	Paed REMAP-CAP_YoungChild_PIS_ICF v1.2 2023.11.13_Clean REMAP-CAP_YoungChild_PIS_ICF v1.2 2023.11.13_tracked	The parent information / consent was mistakenly removed whilst under review for AM037 – this has been reinstated.
AM040	REC MHRA HRA	17.11.2023	29.01.2024	REMAP-CAP AM040 Amendment_Tool_v1_6_LOCKED REMAP-CAP AM040 cover letter 22.12.2023 AM040_MhraProductsForm_snapshot REMAP-CAP letter to sites - Anticoagulation and Antiplatelet Domain - 30 November 2023 REMAP-CAP letter to sites - Corticosteroid Domain_06 December 2023	• Submission of the Immune Modulation DSA • Updates to adult and children PIS documents (Telephone consent can now be used for legal

				Adults REMAP-CAP_Tel v2.0 2023.11.16_Clean REMAP-CAP_Tel v2.0 2023.11.16_Tracked REMAP-CAP_PerLR Sum_ICF v1.4_2023.11.16_Tracked REMAP-CAP_PerLR Sum_ICF v1.4_2023.11.16_Clean REMAP-CAP_PerLIS_ICF v1.16_2023.11.16_Tracked REMAP-CAP_PerLIS_ICF v1.16_2023.11.16_Clean REMAP-CAP_YoungChild_PIS_ICF v1.3 2023.12.13_Tracked REMAP-CAP_YoungChild_PIS_ICF v1.3 2023.12.13_Clean REMAP-CAP_ProLR Sum_ICF v1.8_2023.11.16_Tracked REMAP-CAP_ProLR Sum_ICF v1.8_2023.11.16_Clean REMAP-CAP_PIS_ICF v1.16_2023.11.16_Tracked REMAP-CAP_PIS_ICF v1.16_2023.11.16_Clean Paed REMAP-CAP_Child_16-17_PIS_ICF v1.2 2023.11.16_Tracked REMAP-CAP_Child_16-17_PIS_ICF v1.2 2023.11.16_Clean REMAP-CAP_Child_10-15_PIS_ICF v1.4 2023.11.16_tracked REMAP-CAP_Child_10-15_PIS_ICF v1.4 2023.11.16_Clean REMAP-CAP pharmacy guide - Version 4 - 26 October 2023 REMAP-CAP Immune Modulation Influenza DSA - V1.0 Adult + Paediatric patients - 29 September 2023 REMAP-CAP Immune Modulation Influenza DSA - V1.1 Adult patients only - 29 September 2023	representatives and patients) • Adding postal consent option. • Closure of fixed hydrocortisone intervention • Closure of the anticoagulation and antiplatelet domains • Submission of the pharmacy Manual v4.0
NSA09	HRA	16.04.2024	22.04.2024	UK_REMAP-CAP_mNCA_V2.4_20207XX_Template UK_REMAP-CAP_mNCA_V2.4_20207XX_Template_TC UK REMAP-CAP poster_Child_V2.0 2024.03.18- TC UK REMAP-CAP poster_Child_V2.0 2024.03.18- CLEAN UK REMAP-CAP poster V2.1_2024.03.18 - TC UK REMAP-CAP poster V2.1_2024.03.18 - CLEAN Adult REMAP-CAP-ProLR-Sum-ICF-v1.9-14.03.2024-CLEAN REMAP-CAP-ProLR-Sum-ICF-v1.9-14.03.2024-TC REMAP-CAP-PerLIS-ICF-v1.17-18.03.2024-CLEAN REMAP-CAP-PerLIS-ICF-v1.17-18.03.2024-TC REMAP-CAP-PerLR-Sum-ICF-v1.5-18.03.2024-TC	1. New Contract (mNCA) template 2. Updated adults and paediatric posters with QR code for new website. 3. PIS document updates - PerLR and ProLR add space to add name of patient and also remove Farah's number from all PIS documents 4. Acknowledgement of amendment still addressed

				REMAP-CAP-PerLR-Sum-ICF-v1.5-18.03.2024-CLEAN REMAP-CAP-PIS-ICF-v1.17-18.03.2024-TC REMAP-CAP-PIS-ICF-v1.17-18.03.2024-CLEAN Paed REMAP-CAP-Child-10-15-PIS-ICF-v1.5-19.03.2024-TC REMAP-CAP-Child-10-15-PIS-ICF-v1.5-19.03.2024-CLEAN REMAP-CAP-Child-16-17-PIS-ICF-v1.3-19.03.2024- TC REMAP-CAP-Child-16-17-PIS-ICF-v1.3-19.03.2024-CLEAN REMAP-CAP-Young-Child-PIS-ICF-v1.4-19.03.2024-TC REMAP-CAP-Young-Child-PIS-ICF-v1.4-19.03.2024-CLEAN	to Ms. W. van Bentum-Puijk. Change this in Ms. S. Peters 5. Clarification that consent forms can be sent by email or post
AM41	REC HRA MHRA	20.05.2024	27.06.2024	REMAP-CAP AM041 Amendment_Tool_v1_6_LOCKED REMAP-CAP letter to sites - Antibiotic and Macrolide Domains REMAP-CAP letter to sites - Cysteamine Domain Roche_REMAP-CAP_MA compliance Baloxavir UK_REMAP-CAP_SubjectInsurance_Cert_20240205 UK_REMAP-CAP_SubjectInsurance_Endorsement 4_20240205 Effective_UK (English) EQ-5D-Y Paper Interviewer Administration v1.3 Effective_UK (English) EQ-5D-Y Paper Proxy2 Interviewer Administration v1.2 Adult REMAP-CAP-PerLIS-ICF-v1.18-07.05.2024 Clean REMAP-CAP-PerLIS-ICF-v1.18-07.05.2024-TC REMAP-CAP-PerLR-Sum-ICF-v1.6-07.05.2024- Clean REMAP-CAP-PerLR-Sum-ICF-v1.6-07.05.2024- TC REMAP-CAP-PIS-ICF-v1.18 07.05.2024 Clean REMAP-CAP-PIS-ICF-v1.18 07.05.2024 TC REMAP-CAP-ProLR-Sum-ICF-v1.10 07.05.2024 Clean REMAP-CAP-ProLR-Sum-ICF-v1.10 07.05.2024 TC GxP-0556690_MV43976_BALO_2FC_20MG_BL_39029775 Primary Packaging GxP-0556691_MV43976_BALO_2FC_20MG_BL_39029775_BFP Booklet front page for primary packaging GxP-0556692_MV43976_BALO_2FC_20MG_BX_39029774 Secondary Packaging GxP-0556693_MV43976_BALO_2FC_20MG_BX_39029774_BFP Booklet frontpage for secondary packaging	• Change of baloxavir supply from Roche UK to Roche global • Addition of releasing site information to section D9 of the MHRA CTA for licensed Baloxavir • Submission of clinical trial labelling for baloxavir • Closure of the cysteamine domain • Closure of the antibiotics and macrolide domains for COVID patients. • Submission of the updated Insurance certificate • Matrons can act as ProLRs • Clarification that appropriately trained individuals can obtain consent • Submission of the EQ-5D-Y Questionnaire

NSA10	HRA	31.10.2024	31.10.2024	237150_NSA10_locked_PDF Grant agreement letter until Nov24	Correction of study end date to 30 th Nov 2024
NSA11	HRA	27.11.2024	27.11.2024	237150_NSA11_locked Grant agreement letter until Nov25	Study end date extended until 30 th Nov 2025
AM42	REC HRA MHRA	13.12.2024	01.04.2025	Paed REMAP-CAP-Child 16-17-Video-CF-v1.0-20.11.2024 REMAP-CAP-Child 0-15-Video-CF-v1.0-20.11.2024 REMAP-CAP-Child 0-17 Tel-CF-v1.0-20.11.2024 REMAP-CAP-Child 0-17-ProLR-Sum-ICF-v1.0-13.11.2024 REMAP-CAP-Child 0-9-PIS-ICF-v1.5-13.11.2024 clean (not active) REMAP-CAP-Child 0-9-PIS-ICF-v1.5-13.11.2024 TC REMAP-CAP-Child 10-15-PIS-ICF-v1.6-13.11.2024 clean (not active) REMAP-CAP-Child 10-15-PIS-ICF-v1.6-13.11.2024 TC REMAP-CAP-Child 16-17-PIS-ICF-v1.4-13.11.2024 clean (not active) REMAP-CAP-Child 16-17-PIS-ICF-v1.4-13.11.2024 TC Adult REMAP-CAP-Patient-Video-CF-v1.2-13.11.2024 clean REMAP-CAP-Patient-Video-CF-v1.2-13.11.2024 TC REMAP-CAP-PerLR-Video-CF-v1.2-13.11.2024 clean REMAP-CAP-PerLR-Video-CF-v1.2-13.11.2024 TC REMAP-CAP-Tel-CF-v2.1-13.11.2024 clean REMAP-CAP-Tel-CF-v2.1-13.11.2024 TC REMAP-CAP-ProLR-Sum-ICF-v1.11-13.11.2024 clean REMAP-CAP-ProLR-Sum-ICF-v1.11-13.11.2024 TC REMAP-CAP-PerLR-Sum-ICF-v1.7-13.11.2024 clean REMAP-CAP-PerLR-Sum-ICF-v1.7-13.11.2024 TC REMAP-CAP-PerLRIS-ICF-v1.19-13.11.2024 clean (not active) REMAP-CAP-PerLRIS-ICF-v1.19-13.11.2024 TC REMAP-CAP-PIS-ICF-UK-v1.19-13.11.2024 clean (not active) REMAP-CAP-PIS-ICF-UK-v1.19-13.11.2024 TC REMAP-CAP-PIS-Sum-ICF-v1.0-20.11.2024 REMAP-CAP-Privacy-Notice-v1.2-25.11.2024 Changes requested from ethics, final versions of PIS/CFs along with the above: Adults REMAP-CAP-PerLRIS-ICF-v1.20-17.01.2025 REMAP-CAP-PIS-ICF-UK-v1.20-17.01.2025	• Changes to the Summary of Product Characteristics (SmPC) for REMAP-CAP Investigational Medicinal Products (IMPs) • Submission of Tocilizumab labels • Submission of SOECAT V1.0 & V2.0 • Submission of the RCC and QP declaration for Baloxavir paediatric formulation and labels • Updates to all PIS-CF versions and the privacy notice • Retrospective consent can now be obtained for paediatric patients • Telephone and video consent forms for paediatrics • Professional legal representative consent form for paediatrics • PIS summary sheet and consent form • DMSB Letter

				Paed REMAP-CAP-Child 0-9-PIS-ICF-v1.6- 17.01.2025 REMAP-CAP-Child 10-15-PIS-ICF-v1.7-17.01.2025 REMAP-CAP-Child 16-17-PIS-ICF-v1.5-17.01.2025 REMAP-CAP_SmPC_Levofloxacin_20230923 REMAP-CAP_SmPC_Piperacillin-Tazobactam_20230103 REMAP-CAP_SmPC_Ceftriaxone_20230221 REMAP-CAP_SmPC_Azithromycin powder_20220622 REMAP-CAP_SmPC_Azithromycin tablet_20220519 REMAP-CAP_SmPC_Clarithromycin powder_20230127 REMAP-CAP_SmPC_Clarithromycin tablet_20230715 REMAP-CAP_SmPC_Erythromycin powder_20220622 REMAP-CAP_SmPC_Erythromycin tablet_20230602 REMAP-CAP_SmPC_Baricitinib (Olumiant)_20240730 REMAP-CAP_SmPC_Tocilizumab_20241031 REMAP-CAP_SmPC_Hydrocortisone_20230607 REMAP-CAP_SmPC_Dexamethasone_20240910 REMAP-CAP_SmPC_Baloxavir_20230615 xofluza-epar-product-information_en_incl paediatric formulation FM-0061 Regulatory Compliance Confirmation Letter CTR switch MV43976_Baloxavir GxP-0566740_MV43976_QP_Baloxavir_2MG_719-1686/F08-01 Secondary packaging MV43976_BALO_2G_40MG_20ML_BX_39030769 MV43976_BALO_2G_40MG_20ML_BX_39030769_BFP MV43976_BALO_2G_40MG_20ML_VL_39030770 MV43976_BALO_2G_40MG_20ML_VL_39030770_BFP GxP-0556697_MV43976_TOCI_200MG_10ML_BX_39029772 GxP-0556698_MV43976_TOCI_200MG_10ML_BX_39029772_BFP GxP-0556699_MV43976_TOCI_200MG_10ML_VL_39029773 GxP-0556700_MV43976_TOCI_200MG_10ML_VL_39029773_BFP REMAP-CAP_DSMB Letter_20241107 REMAP-CAP SoECAT v1.0 REMAP-CAP SoECAT v2.0	
NSA12	HRA	07.05.2025	07.05.2025	Adult REMAP-CAP-Patient-Video-CF-v2.0- 07.05.2025 CLEAN REMAP-CAP-Patient-Video-CF-v2.0- 07.05.2025 TC REMAP-CAP-PerLRIS-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-PerLRIS-ICF-v2.0-07.05.2025 TC	Administrative/formatting changes to PIS/CFs previously submitted and approved in SA042.

				REMAP-CAP-PerLR-Sum-ICF-v2.0 07.05.2025 CLEAN REMAP-CAP-PerLR-Sum-ICF-v2.0 07.05.2025 TC REMAP-CAP-PerLR-Video-CF-v3.0-07.05.2025 CLEAN REMAP-CAP-PerLR-Video-CF-v3.0-07.05.2025 TC REMAP-CAP-PIS-ICF-UK-v2.0 07.05.2025 CLEAN REMAP-CAP-PIS-ICF-UK-v2.0 07.05.2025 TC REMAP-CAP-PIS-Sum-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-PIS-Sum-ICF-v2.0-07.05.2025 TC REMAP-CAP-ProLR-Sum-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-ProLR-Sum-ICF-v2.0-07.05.2025 TC REMAP-CAP-Tel-CF-v3.0-07.05.2025 CLEAN REMAP-CAP-Tel-CF-v3.0-07.05.2025 TC Paed REMAP-CAP-Child 0-15-Video-CF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 0-15-Video-CF-v2.0-07.05.2025 TC REMAP-CAP-Child 0-17 Tel-CF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 0-17 Tel-CF-v2.0-07.05.2025 TC REMAP-CAP-Child 0-17-ProLR-Sum-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 0-17-ProLR-Sum-ICF-v2.0-07.05.2025 TC REMAP-CAP-Child 0-9-PIS-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 0-9-PIS-ICF-v2.0-07.05.2025 TC REMAP-CAP-Child 10-15-PIS-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 10-15-PIS-ICF-v2.0-07.05.2025 TC REMAP-CAP-Child 16-17-PIS-ICF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 16-17-PIS-ICF-v2.0-07.05.2025 TC REMAP-CAP-Child 16-17-Video-CF-v2.0-07.05.2025 CLEAN REMAP-CAP-Child 16-17-Video-CF-v2.0-07.05.2025 TC	
AM43	REC HRA MHRA	23.09.2025	10.11.2025	237150_AM043 REMAP-CAP AM043 cover letter Adult REMAP-CAP-Patient-Video-CF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-PerLRIS-ICF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-PerLR-Sum-ICF-v3.0 01.07.2025_CLEAN/TC REMAP-CAP-PerLR-Video-CF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-PIS-ICF-UK-v3.0 01.07.2025 CLEAN/TC REMAP-CAP-PIS-Sum-ICF-v3.0- 01.07.2025 CLEAN/TC REMAP-CAP-ProLR-Sum-ICF-v3.0- 01.07.2025 CLEAN/TC REMAP-CAP-Tel-CF-v4.0-01.07.2025 CLEAN/TC Paed REMAP-CAP-Child 0-9-PIS-ICF-v3.0- 01.07.2025_CLEAN/TC	• Protocol v4.0 and updates to DSAs • EU RSA + UK appendix updates • Immune modulation DSA V2.1 • PedsQL • PANDA • UMC Utrecht CT - Endorsement Doc • Updates to Adult and Paeds PIS-CF to include pregnancy

				REMAP-CAP-Child 0-15-Video-CF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-Child 0-17 Tel-CF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-Child 0-17-ProLR-Sum-ICF-v3.0-01.07.2025_CLEAN/TC REMAP-CAP-Child 10-15-PIS-ICF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-Child 16-17-PIS-ICF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-Child 16-17-Video-CF-v3.0- 01.07.2025_CLEAN/TC REMAP-CAP-Privacy-Notice-v2.0-27Aug25_CLEAN/TC UMC Utrecht CT - Endorsement Doc REMAP-CAP Core Protocol V4 - 05 November 2024_CLEAN/TC REMAP-CAP Core Protocol V4 SoC - 05 November 2024 REMAP-CAP_Protocol_European RSA_V4.0_20241106_eng/TC UK_REMAP-CAP_EU RSA Country Annex_V1.0_20250807 REMAP-CAP_Protocol_Stat.Anal.App._V4.0_20241105/TC REMAP-CAP_Protocol_Stat.Anal.App._V4.0_20241105_SoC REMAP-CAP_Protocol PANDA_V1.0_20241105 [UK_REMAP-CAP_Protocol Registry Appendix_V2.0_20241105 REMAP-CAP_Protocol_DSA A_V4.0_20241105 / TC REMAP-CAP_Protocol_DSA A_V4.0_20241105_SoC REMAP-CAP_Protocol_DSA C_V6.0_20241105 /TC REMAP-CAP_Protocol_DSA C_V6.0_20241105_SoC REMAP-CAP_Protocol_DSA I_V3.0_20241105 /TC REMAP-CAP_Protocol_DSA I_V3.0_20241105_SoC REMAP-CAP_Protocol_DSA M_V4.0_2241105 /TC REMAP-CAP_Protocol_DSA M_V4.0_2241105_SoC REMAP-CAP_Protocol_DSA_N_V2.1_20250509 / TC REMAP-CAP_Protocol_DSA P_V4.0_20241105 /TC REMAP-CAP_Protocol_DSA P_V4.0_20241105_SoC PedsQL-4.0-SF-15-Core-A_AU4.0_eng-GB 13-18yrs PedsQL-4.0-SF-15-Core-C_AU4.0_eng-GB 8-12yrs PedsQL-4.0-SF-15-Core-PA_AU4.0_eng-GB 13-18yrs parent PedsQL-4.0-SF-15-Core-PC_AU4.0_eng-GB 8-12yrs parent PedsQL-4.0-SF-15-Core-PT_AU4.0_eng-GB 2-4 yrs parent PedsQL-4.0-SF-15-Core-PYC_AU4.0_eng-GB 5-7yrs parent PedsQL-4.0-SF-15-Core-YC_AU4.0_eng-GB 5-7 yrs	updates and administrative changes.
NSA13	HRA	27.10.2025	04.11.2025	N/a	Update to sponsor contact details.
NSA14	HRA	05.01.2026	05.01.2026	FW_HTA Project_NIHR155209 – Contract Variation Request Outcome MV43976_BALOX_paed granule labels_Approval_signed REMAP-CAP_Protocol_DSA I_V3.0_20241105_TC V2.2	Submission of 8-month (no cost) contract variation approval.

				REMAP-CAP_Protocol_DSA_N_V2.0_20241105 REMAP-CAP_Protocol_DSA_N_V2.0_20241105_TC V1.1 REMAP-CAP_UK_leaflet_V3.0_2025.12.19 MV43976_RCC Xofluza GfOS 2mg_mL_UMCU_highlighted 237150_NSA14_locked 31Dec25 IRAS 237150. Amendment	• Submission of amended patient leaflet. • Submission of updated Regulatory Compliance Confirmation for Baloxavir granules • Submission of some previously missed tracked changes for study documents submitted in AM43 • Updated IMP labels for Baloxavir granules
AM44	Ethics MHRA HRA	01.04.2026 Issue with MHRA submission missed – submitted separately on 23 rd June using new mod form	12.08.2026	Completed Amendment Tool [237150_SA044] 1.8 31 March 2026 REMAP-CAP AM044 cover letter signed 01 April 2026 REMAP-CAP letter to sites - Pause of Influenza Antiviral Domain - 14 MAR 2026 Adults REMAP-CAP-PIS-ICF-UK-v4.1 22.04.2026_TC REMAP-CAP-PIS-ICF-UK-v4.1 22.04.2026_clean REMAP-CAP-PerLRIS-ICF-v4.1-22.04.2026_TC REMAP-CAP-PerLRIS-ICF-v4.1-22.04.2026_clean REMAP-CAP-PerLR-Sum-ICF-v4.0 25.03.2026_clean REMAP-CAP-PerLR-Sum-ICF-v4.0 25.03.2026_TC REMAP-CAP-PerLR-Video-CF-v4.0-25.03.2026_clean REMAP-CAP-PerLR-Video-CF-v4.0-25.03.2026_TC REMAP-CAP-PIS-Sum-ICF-v4.0-25.03.2026_clean REMAP-CAP-ProLR-Sum-ICF-v4.0-25.03.2026_clean REMAP-CAP-PIS-Sum-ICF-v4.0-25.03.2026_TC REMAP-CAP-ProLR-Sum-ICF-v4.0-25.03.2026_TC REMAP-CAP-Tel-CF-v5.0-25.03.2026_clean REMAP-CAP-Tel-CF-v5.0-25.03.2026_TC REMAP-CAP-Patient-Video-CF-v4.0-25.03.2026_clean REMAP-CAP-Patient-Video-CF-v4.0-25.03.2026_TC Paeds REMAP-CAP-ChildrenYoungPpl 0-17 Tel-CF-v4.0-25.03.2026_clean REMAP-CAP-ChildrenYoungPpl 0-17 Tel-CF-v4.0-25.03.2026_TC	Information added to adult and paediatric PIS re Oseltamivir findings (stats trigger for inferiority) in severely ill ICU patients.

				REMAP-CAP-ChildrenYoungPpl 0-17-PIS-ICF-v4.0-25.03.2026_TC REMAP-CAP-ChildrenYoungPpl 0-17-ProLR-Sum-ICF-v4.0-25.03.2026_clean REMAP-CAP-ChildrenYoungPpl 0-17-ProLR-Sum-ICF-v4.0-25.03.2026_TC REMAP-CAP-ChildrenYoungPpl 0-17-Video-CF-v4.0-25.03.2026_clean REMAP-CAP-ChildrenYoungPpl 0-17-Video-CF-v4.0-25.03.2026_TC REMAP-CAP-ChildrenYoungPpl 0-17-PIS-ICF-v4.1-22.04.2026_TC REMAP-CAP-ChildrenYoungPpl 0-17-PIS-ICF-v4.1-22.04.2026_clean	

FYI, during the approval process for the 1st three substantial amendments, the HRA's incorrectly labelled every amendment as Amendment 01 on the approval letter. They were made aware of this, but as all the other pertinent information on the document was correct, they did not feel the need to re-issue the approval letters.