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Region-Specific Appendix:

EUROPE

# Country Annex United Kingdom

# REMAP-CAP: Randomized, Embedded, Multifactorial Adaptive Platform trial for Community-Acquired Pneumonia

REMAP-CAP European Region-Specific Appendix - Country Annex UK Version 1.0 dated 07 August 2025

| Topic | Country specific details for topic |
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| National Coordinating Investigator | **Name**: Prof. Anthony Gordon<br>**Affiliation**: Chair in Anaesthesia and Critical Care, Department of Surgery & Cancer, Imperial College London<br>**Email**: anthony.gordon@imperial.ac.uk |
| Country Central Ethics Committee (CEC) | **Name**: London - Surrey Borders Research Ethics Committee<br>**Website**: London – Surrey Borders - Health Research Authority (hra.nhs.uk)<br>**Email**: surreyborders.rec@hra.nhs.uk |
| Country-Specific CEC Requirements | **Suspected Unexpected Serious Adverse Reaction (SUSARs):** Medicines & Healthcare products Regulatory Agency (MHRA) will liaise with CEC if required, no separate reporting needed.<br>**Urgent Safety Measures (USMs):** To be notified to CEC via email (above) within 3 days of measures being taken. Related substantial amendments to be submitted ASAP, if required.<br>**Annual Safety Report (ASR):** To be submitted to the CEC by email (surreyborders.rec@hra.nhs.uk).<br>**Serious Breach:** To report to CEC via 'notification of serious breaches of GCP or the trial protocol' form sent by email (surreyborders.rec@hra.nhs.uk ) within 7 days of becoming aware. Updates to initial (potential) serious breach reports are to be submitted without further delay. |
| Country Regulatory Authority (RA) | **Name**: MHRA<br>**Website**: Medicines and Healthcare products Regulatory Agency - GOV.UK (www.gov.uk)<br>**Email**: info@mhra.gov.uk / clintrialhelpline@mhra.gov.uk |

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| Country-Specific RA Requirements | **SUSARs**: To be reported to MHRA within 7 days of being aware if fatal/life threatening and additional info within 8 days of initial report. To be reported within 15 days if non-fatal/not life threatening via online MHRA submissions portal icsrsubmissions.mhra.gov.uk.<br><br>**USMs:** To be notified to MHRA via email at clintrialhelpline@mhra.gov.uk, within 3 days of measures being taken. Related substantial amendments to be submitted ASAP, if required.<br><br>**ASR:** To be submitted via the online MHRA submissions portal icsrsubmissions.mhra.gov.uk. Proof of payment is required for submission (refer to "Payment User reference guide – Paying online before submitting a Development Safety Update Report (DSUR)").<br><br>**Serious Breach:** To report to MHRA via email within 7 days of becoming aware using the MHRA Serious Breach Report template. Updates to initial (potential) serious breach reports are to be submitted without further delay. To report to MHRA via 'notification of serious breaches of GCP or the trial protocol' form sent by email to GCP.SeriousBreaches@mhra.gov.uk, within 7 days of becoming aware. |
| Country Data Protection Agency | **Name**: Information Commissioner's Office (ICO)<br>**Website**: https://ico.org.uk/<br>**Online contact form**: https://ico.org.uk/global/contact-us/contact-us-large-organisation/contact-us-organisation-advice/ |
| Country approved Informed Consent process | **UK Adults (aged ≥18 years):**<br>- Consent (general): Prospective written consent for capacitated, adult patients. |

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| | - Personal Legal Authorized Representative (PerLAR) consent: allowed for incapacitated patients.<br>- Professional LAR (ProLAR) consent (deferred consent): allowed for incapacitated patients.<br><br>**Deferred consent (ProLAR):**<br>- When patient does not have capacity and PerLAR is not available or not able to consent.<br><br>**Verbal/telephone consent (Patient or PerLAR):**<br>- When patient cannot physically write or be physically present (in case of retrospective consent).<br>- Requires impartial witness to sign.<br>- Obtain written consent ASAP.<br><br>**Delayed consent:**<br>- Allowed for incapacitated patients in emergency setting when prospective consent of any type is not possible.<br>- ProLAR or PerLAR consent to be obtained ASAP, preferably within 24 hours if possible.<br><br>**Retrospective written consent:**<br>- Obtained after already enrolled in trial, where deferred/delayed/verbal consent was obtained.<br>- Obtained if/when patient regains capacity, prior to hospital discharge or within D180 follow-up period.<br><br>**Information Sheet/Consent Forms (IS/CF) for adults:**<br>- Patient prospective/retrospective IS/CF<br>- PerLAR IS/CF<br>- PerLAR summary IS/CF<br>- ProLAR CF<br>- ProLAR summary IS/CF<br>- Telephone CF |

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| | - Video CF<br><br>**<u>UK Paediatrics (aged <18 years):</u>**<br>- Consent (general): Prospective written consent for capacitated children or parent/guardian.<br>- ProLAR consent: Allowed for incapacitated child or parent/guardian. PerLAR not used.<br>- ProLAR consent (deferred consent): allowed when child/parent does not have capacity or is not available to consent.<br><br>**Deferred consent (ProLAR):**<br>- When child or parent/guardian does not have capacity or not able to consent.<br><br>**Verbal/telephone consent:**<br>- When child/parent cannot physically write or be physically present (in case of retrospective consent).<br>- Requires impartial witness to sign.<br>- Obtain written consent ASAP.<br><br>**Delayed consent:**<br>- Allowed for incapacitated child in emergency setting when prospective consent of any type is not possible.<br>- ProLAR or child/parent consent to be obtained asap, preferably within 24 hours if possible.<br><br>**Retrospective consent:**<br>- Obtained after already enrolled in trial, where deferred/delayed/verbal consent was obtained.<br>- Obtained if/when child/parent regains capacity, prior to hospital discharge or within D180 follow-up period.<br><br>**IS/CF for paediatrics:**<br>- Young Child and Guardian prospective/retrospective IS/CF. To be used where children are <10 yrs. |

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| | - Children and Guardian 10-15 prospective/retrospective IS/CF. For children 10-15 yrs.<br>- Child 16-17 prospective/retrospective IS/CF. For children between 16-17 yrs.<br>  - ProLAR CF<br>  - Telephone CF<br>  - Video CF<br><br>**<u>Withdrawal of consent</u>**:<br>Data use (subject withdrawn consent): The data/samples collected until the moment that trial consent is withdrawn will continue to be available to the Sponsor and will be utilized in trial analyses, unless patient/PerLAR specifies they wish for previously collected unused data/research samples, not to be used either.<br><br>Data use (subject deceased): The data collected during the trial may be used as long as ProLAR and/or PerLAR consent was collected, even if patient consent could not be collected prior to death.<br><br>Data use (subject decides to discontinue the treatment but no withdrawal of consent): Follow up and data use continues as normal. |
| Permitted LARs | **PerLAR:** Relative, carer, friend, court appointed representative.<br><br>**ProLAR:** Independent physician or matron (not part of the study). |
| IS/CF Requirements | **Language(s):**<br>1) English<br>2) Polish<br>3) Urdu<br>4) Arabic<br>5) Punjabi<br>6) Romanian<br>7) Bengali |

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| | 8) Portuguese<br>9) Gujarati<br>10) Spanish<br>11) Ukrainian<br>12) (Hindi)<br>13) (Mandarin)<br><br>Any IS/CF translation(s) will be submitted for ethics approval prior to implementation.<br><br>**UK template requirements:**<br><br><u>IS (HRA IS template V3.0, Jun-2024)</u><br><br>- Invitation / purpose of trial;<br>- Treatments being investigated;<br>- Who can participate and what it involves;<br>- Benefits / risks to taking part;<br>- Pregnancy risks / advice;<br>- Options to withdraw participation;<br>- Contact for trial questions or independent advice;<br>- Access to Privacy Notice (data protection, confidentiality);<br>- Access to results;<br>- Funding and Ethical review details.<br><br><u>CF (template V4.0)</u><br><br>- Participant trial ID/name, site name/number, PI name;<br>- Statements confirming information has been understood and consent is being given freely;<br>- Statements consenting to trial procedures, treatment options and contact for follow up;<br>- Statements giving permission for research staff, regulatory authorities and any third parties to access medical records for the research;<br>- Statement regarding use of results;<br>- Statement regarding transfer of any data outside of UK;<br>- Statement regarding patient consent superseding PerLAR/ProLAR consents; |

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| | - Statement relating to blood samples or data being stored/used for future research, if applicable. |
| Country Safety Reporting Requirements (beyond Core Protocol/EU RSA/ICH GCP) | As per Country-Specific CEC requirements and Country-Specific RA requirements sections above.<br><br>For the Immunoglobulin domain, all transfusion related Serious Adverse Events/Reactions and/or errors, are to be reported to SHOT/MHRA via the SABRE portal within 48 hours of being known by transfusion teams. |
| Country Investigational Medicinal Product (IMP) Requirements | Clinical trial labelling must be compliant with EU GMP Annex 13.<br><br>**Unmarketed IMP**:<br><br>- Requires full clinical trial labelling;<br>- Trial-specific storage/temperature monitoring required;<br>- Trial-specific accountability and authorisation for destruction required.<br><br>**Marketed IMP** used outside the Marketing Authorization (MA):<br><br>- Can include a reduced label (name of investigator, trial code/name, patient ID);<br>- Trial-specific storage/temperature monitoring required;<br>- Trial-specific accountability and authorisation for destruction required.<br><br>**Marketed IMP** used within the MA, via routine hospital supply:<br><br>- No clinical trial labelling or simplified labelling required;<br>- Trial-specific storage/temperature monitoring not required;<br>- No trial-specific accountability or authorization for destruction required – routine hospital procedures apply. |

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| | **Marketed IMP** used within MA, but via external supply:<br>- Trial-specific storage/temperature monitoring not required;<br>- Trial-specific accountability required at pharmacy level only, authorization for destruction also required;<br>- If clinical trial labelling present, full study specific accountability and temperature monitoring may be required. |
| Country Insurance Requirements | Subject liability and indemnification insurance (combined). |
| Country-Level Domain-Specific Requirements and Exceptions | - For the Tocilizumab intervention, pregnancy outcome data will be collected as per the EU RSA.<br>- Pregnancy outcome data will be monitored as per the Monitoring Plan.<br>- Patients will be informed of the potential for neonatal/infant immunosuppression and that they may be advised to avoid use of live vaccines until the infant is 6 months old, in the IS/CF, as per request of the MHRA. |
| Health Related Quality of Life (HRQoL) at 6 months after enrolment using the EQ5D-5L approval status | Applicable.<br>**EQ-5D-5L (adults) approved for use:**<br>- Paper Proxy 1 administration (English) v1.4<br>- Paper Proxy 2 administration (English) v1.5<br>- Paper Interviewer Administration (English) v1.4<br>- Paper Telephone (English) v1.3<br>- Paper Self-complete (English) v1.2<br>**EQ-5D-Y (paediatrics) approved for use:**<br>- Paper Proxy 1 Interviewer administration (English) v1.3<br>- Paper Proxy 2 Interviewer administration (English) v1.2 |

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| | - Paper Interviewer Administration (English) v1.3<br>- Paper Proxy 1 (English) v2.1<br>- Paper Proxy 2 (English) v2.1<br>- Paper Self-complete (English) v2.3<br><br>**PedsQL-SF15 (paediatrics) to be approved for use:**<br><br>• Adolescent Self and Parent<br>• Child Self and Parent<br>• Young Child Self and Parent<br>• Toddler Parent |
| Disability status measured at 6 months after enrolment using the WHODAS 2.0, 12-item instrument approval status | Applicable.<br><br>**WHODAS v2.0 (adults) approved for use:**<br><br>- 12-item Self, Proxy and Interviewer administered<br>- 12+24-item Interviewer administered<br>- 36-item Self, Proxy and Interviewer administered |
| Other Relevant Country-Specific Requirements/Regulations | **ClinialTrials.gov Identifier:** NCT02735707<br><br>**ISRCTN Registry Number:** ISRCTN67000769<br><br>**NIHR RDN site accruals:** Sent monthly via email at rdncc.portfolioa@nihr.ac.uk who upload onto Open Data Platform (ODP).<br><br>**NIHR Funder:** Recruitment numbers per domain uploaded monthly on REALMS platform, as well as annual progress reports. |

**Version History**

| Version | Summary of Changes |
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| Version 1.0 | N/A |