CORE PROTOCOL V4.0
SIV VERSION 1.0
16TH APRIL 2026

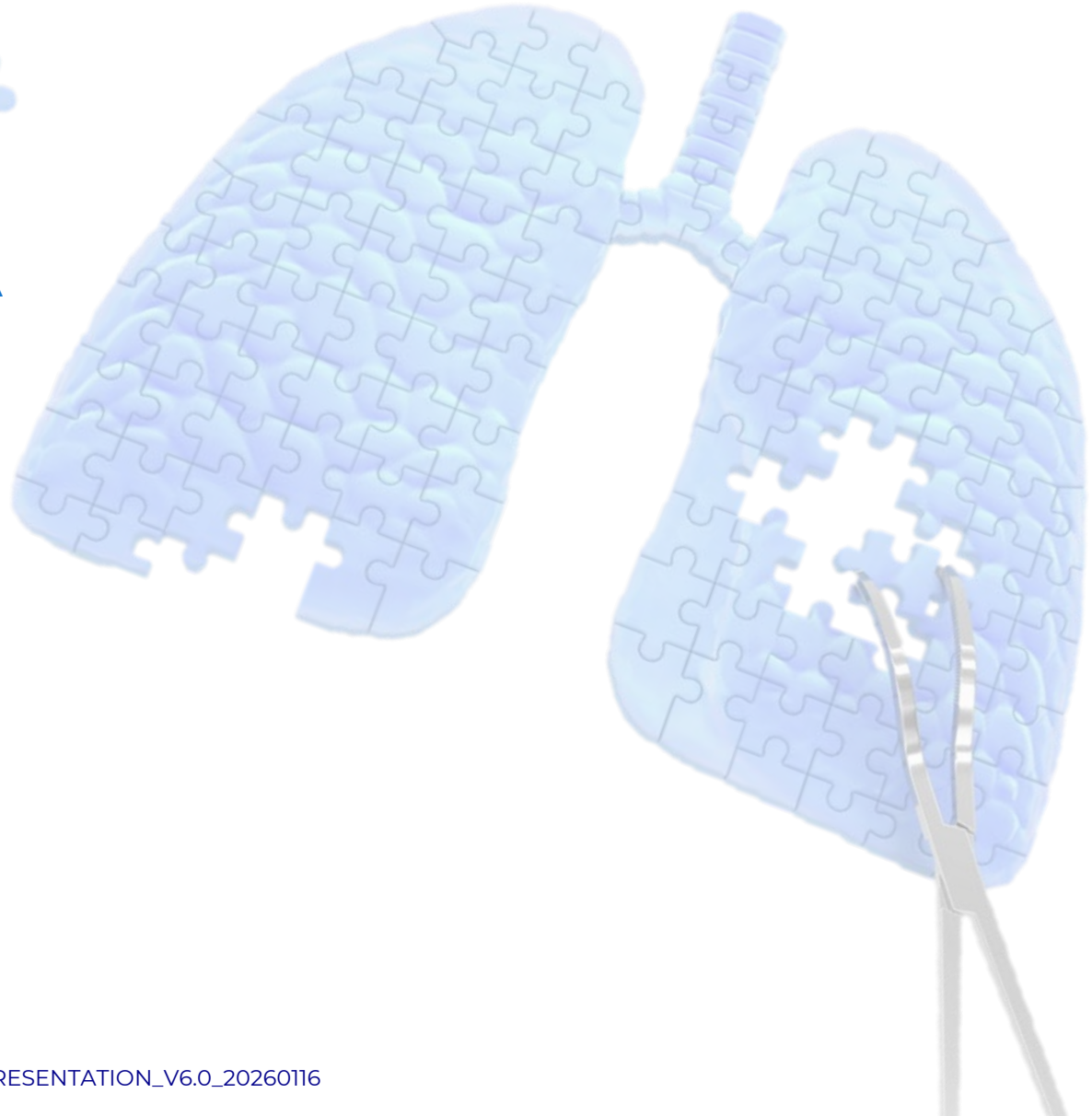
REMAP-CAP

SITE INITIATION VISIT – UK

ADULTS & PAEDIATRICS

AGENDA

- Meet the team
- Trial design
- Protocol - Core & PANDA
- Protocol - DSAs
- Safety
- Informed consent
- Study procedures
- ICH-GCP & GDPR
- Practical info



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MEET THE TEAM

MEET THE TEAM: SPONSORS AROUND THE GLOBE

PROJECT FUNDING

- REMAP-CAP is supported by the ECRAID-Base project which has received funding from the EU Horizon 2020 research and innovation program (grant number 965313).
- The UK Trial Management Team is funded by the NIHR.

MEET THE TEAM: SPONSOR

Sponsor: University Medical Center Utrecht, The Netherlands.

Ecraid: responsible for clinical trial operations

Sponsor

Lead Investigator European region: Lennie Derde

Sponsor Assessor(s): Lennie Derde, Marjolein Hensgens, Helen Leavis, Anthony Gordon

Ecraid:

Ecraid Clinical Trial Project Manager(s): Mina Jafarzadeh

Ecraid Country Clinical Trial Administrator(s): Sonal Patil

MEET THE TEAM: UK

Country Lead: Prof Anthony Gordon

UK Management: Imperial College London & ICNARC

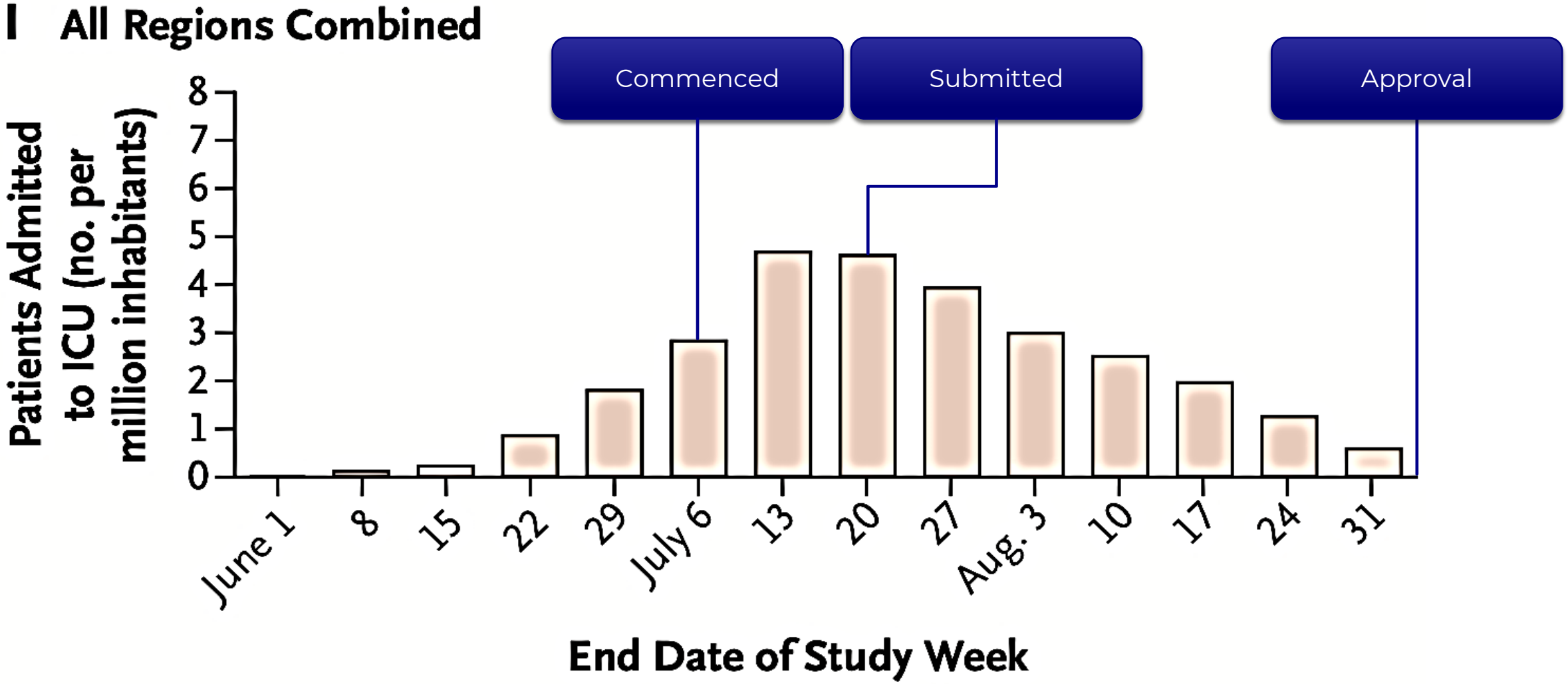
UK CTU: ICNARC

UK Management & Monitoring Team: Janis Best-Lane, Aisha Anjum, Lucy Stronach, Lindsay Jack, Tina Reetun, Ashley Alexander and Walton Charles

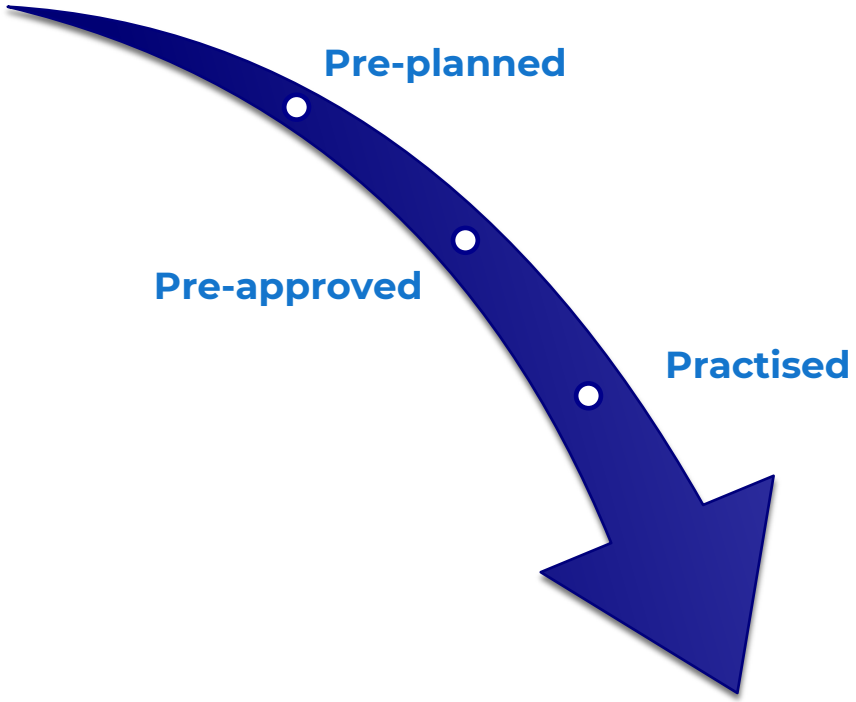
REMAP-CAP

TRIAL DESIGN

TRIAL DESIGN: TRADITIONAL



TRIAL DESIGN: HOW TO IMPROVE?



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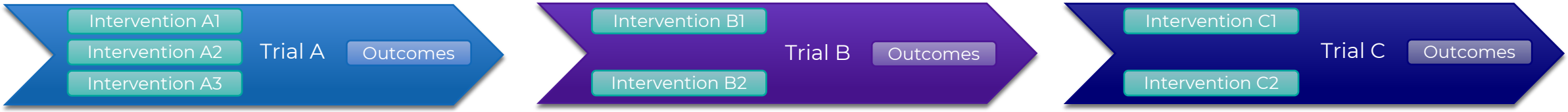
Randomised, Embedded, Multi-factorial, Adaptive, Platform

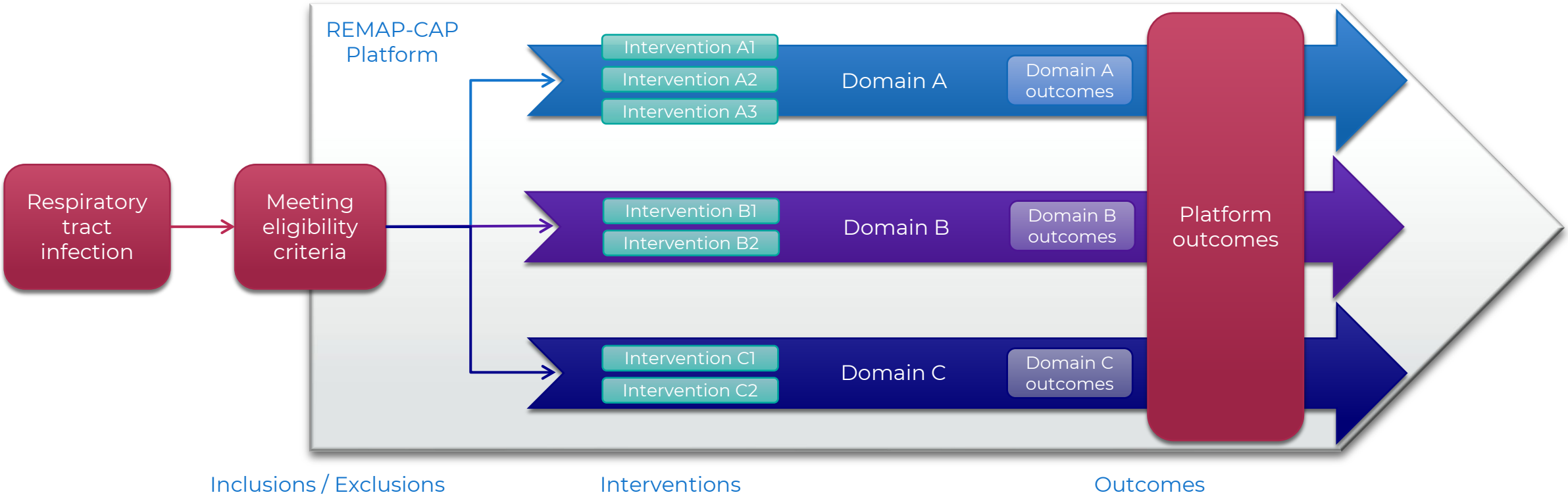
TRIAL DESIGN: TRADITIONAL RANDOMIZED CONTROLLED TRIAL

- **Serial testing** of single hypotheses
- Set randomization ratio



TRIAL DESIGN: ADAPTIVE PLATFORM TRIAL (APT)

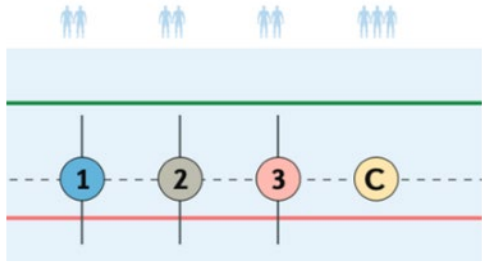
- **Parallel testing** of multiple hypotheses
- Response Adaptive Randomization (*RAR*)



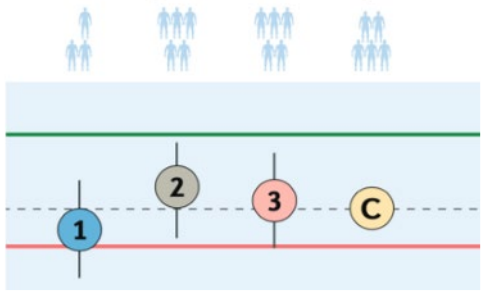
TRIAL DESIGN: RAR

Superiority

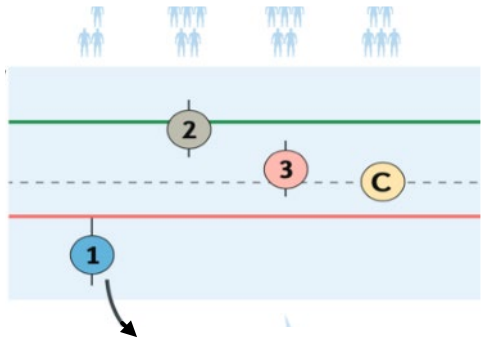
Inferiority



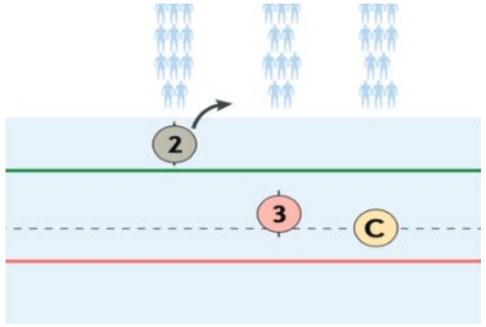
1. Study initiation



2. Following interim data update

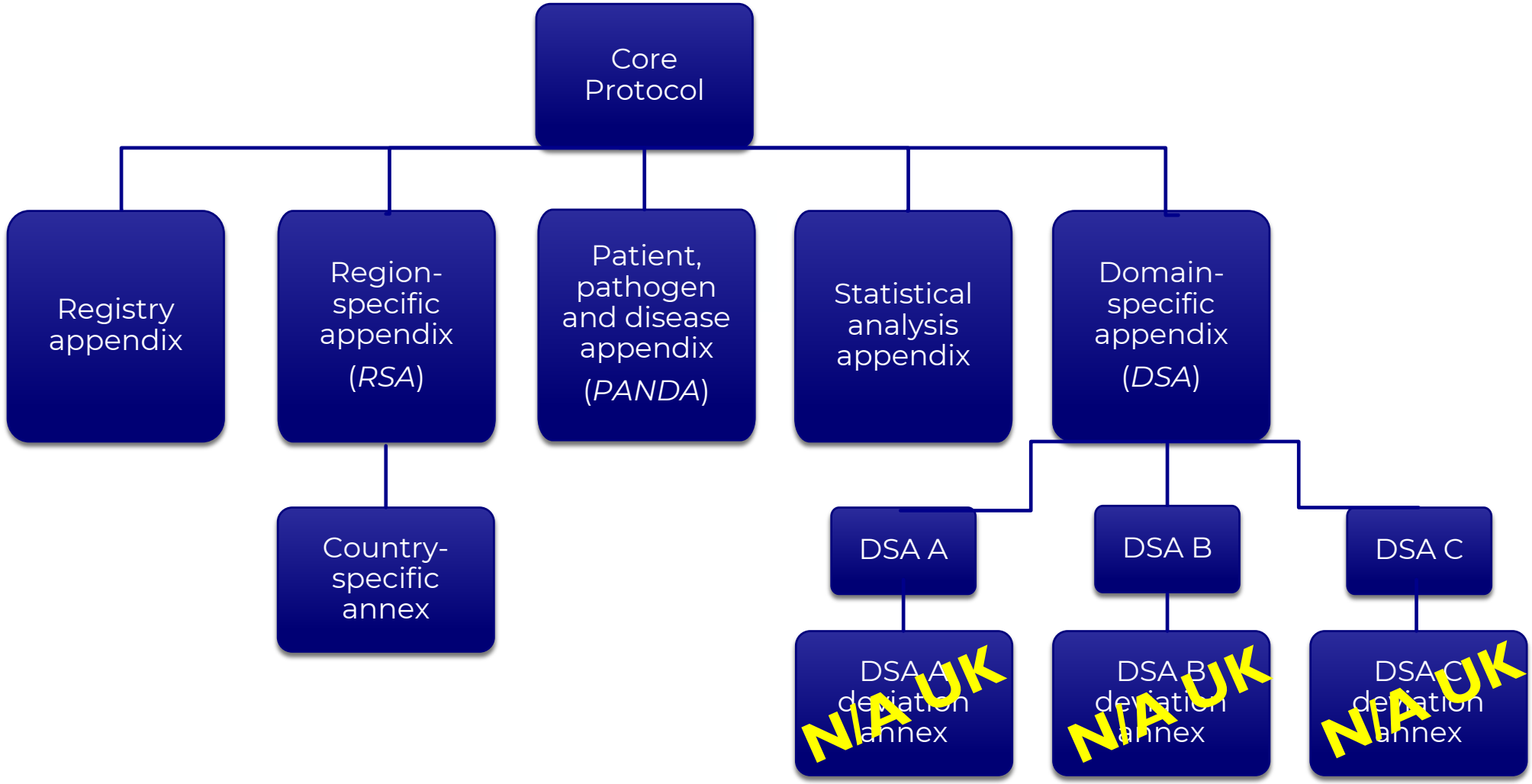


3. Discontinuation of inferior arm



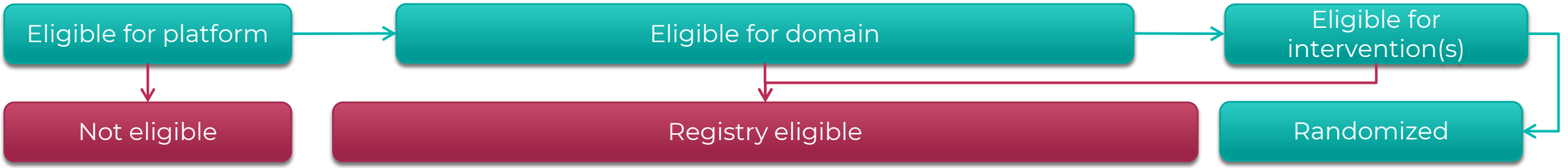
4. Arm graduation to the next phase

TRIAL DESIGN: MODULAR PROTOCOL STRUCTURE



TRIAL DESIGN: PARTICIPATION

Platform	Domain	*Example: Age Stratum*	*Example: Illness Severity State*	Intervention
Respiratory tract infection	Domain A	≥18 years old	Moderate	Intervention A1
				Intervention A2
			Severe	Intervention A1
				Intervention A2
	Domain B	≥18 years old	Moderate	Intervention B1
				Intervention B2
			Severe	Intervention B1
				Intervention B2
		<18 years old	Moderate	Intervention B1
				Intervention B2
			Severe	Intervention B1
				Intervention B2



REMAP-CAP

PROTOCOL – CORE & PANDA

CORE PROTOCOL: PLATFORM ELIGIBILITY CRITERIA

Inclusion Criteria:

- ✓ Aged 28 days or older.
- ✓ Hospitalized patient;
- ✓ Acute respiratory tract infection*;

* This includes community + hospital acquired cases

Exclusion Criteria:

- × Death is deemed to be imminent and inevitable during the next 24 hours **AND** one or more of the patient, substitute decision maker or attending physician are not committed to full active treatment;
- × Patient is expected to be discharged from hospital within the next 24 hours;
- × Previous enrollment in this Platform within the last 90 days.

CORE PROTOCOL: ENDPOINTS & OUTCOMES

Description of endpoints and outcomes		
Primary Endpoint*	• Survival and Recovery Trajectory → a composite of 90-day all-cause mortality and, among survivors, a daily ordinal scale analyzed as a trajectory of illness and recovery to 28 days.	
Secondary Endpoint(s)*	• Hospital length-of-stay; • Mortality, censored at 90 days.	
Other Outcomes	• Domain-specific efficacy & safety outcomes, where applicable; • Hospital survival; • Survival, organ-support free days vasopressor-free days and ventilator-free days at day 28; • Progression to invasive mechanical ventilation/ extracorporeal life support / death;	• Survival at day 180; • Health-related quality of life at day 180 (using the EQ5D-5L, EQ-5D-Y or PedsQL-SF15 questionnaires); • Disability status at day 180 (using the WHODAS 2.0, 12-item instrument in participants aged 18 or older).

* Timely data entry of the endpoints is vital for RAR!

PANDA: FURTHER CATEGORIZATION OF POPULATION

Patient Characteristics

- Age
- Immune surpression
- Regional income level

Pathogens

- Influenza
- SARS-CoV-2
- MERS-CoV
- RSV
- Other recognized viral respiratory pathogens
- Other recognized bacterial respiratory pathogens
- Novel pandemic respiratory pathogens
- Co-infections

Diseases and Clinical Features

- Acquisition of infection
- Disease entity
- Illness severity
- Specific clinical features or syndromes

Domains may use these categories to constrain eligibility. This is specified in the eligibility section of the DSAs.

REMAP-CAP

DOMAIN PROTOCOLS - DSA

DSA: GENERAL INFORMATION

Refer to DSAs for:

- Domain-specific eligibility criteria;
- Domain rationale;
- Concomitant care;
- Potential domain-specific adverse events;
- Domain-specific endpoints;
- Domain-specific protocol deviations;
- Other domain-specific information.

DSA: AVAILABLE ILLNESS STATES PER DOMAIN

Domain	Moderate state?	Severe state?
Antibiotic Domain	✗	✓
Macrolide Duration Domain	✗	✓
Corticosteroid Domain	✓	✓
Influenza Antiviral Domain	✓	✓
Influenza Immune Modulation Domain	✗	✓
Immunoglobulin Domain PAUSED FOR NOW	✓	✓

DSA: AVAILABLE AGE STRATA PER DOMAIN

Domain	Paediatric (≥28 days)	Adolescent (≥12 years)	Adult (≥18 years)
Antibiotic Domain	✗	✗	✓
Macrolide Duration Domain	✗	✗	✓
Corticosteroid Domain	✓	✓	✓
Influenza Antiviral Domain	✓	✓	✓
Influenza Immune Modulation Domain	✓ (≥2 years)	✓	✓
Immunoglobulin Domain PAUSED FOR NOW	✗	✓ (≥16 years)	✓

DSA: ANTIBIOTICS DOMAIN (A) – ADULTS ONLY

Domain	Age Stratum	Illness Severity State	Intervention	Administration
Antibiotics (A)	≥18 years old	Severe	A1 - Ceftriaxone + Macrolide	IV, dose decided by treating clinician decision. Changes based on microbio results are permitted.
			A2 - Moxifloxacin or Levofloxacin	
			A3 - Piperacillin-Tazobactam + Macrolide	
			A5 - Amoxicillin-Clavulanate + Macrolide	

Domain objective

Determine the effectiveness of different antibiotic therapies for hospitalized patients with severe community-acquired pneumonia.

Hypothesis

The primary endpoint will differ based on domain intervention allocation.

ANTIBIOTICS DOMAIN ELIGIBILITY – ADULTS ONLY

Inclusion

- Severe illness state, admitted to ICU
- Patient has community-acquired respiratory tract infection
- Patient has pneumonia
- Empiric antibiotic therapy for bacterial pneumonia is considered appropriate

ANTIBIOTICS DOMAIN ELIGIBILITY – ADULTS ONLY

Exclusion

- Received more than 48 hours of intravenous antibiotic treatment for this index illness
- More than 24 hours has elapsed since commencement of sustained organ failure support
- A specific antibiotic choice is indicated, for example:
    - Suspected or proven **concomitant infection** such as meningitis
    - Suspected or proven **infection with resistant bacteria** where agents being trialled would not be expected to be active. This includes cystic fibrosis, bronchiectasis or other chronic suppurative lung disease where infection with Pseudomonas may be suspected but **does not include** patients with suspected methicillin-resistant staphylococcus aureus (MRSA) infection.
    - **Febrile neutropenia or significant immunosuppression** (including organ or bone marrow transplantation, human immunodeficiency virus (HIV) Infection with CD4 cell count <200 cells/μL, systemic immunosuppressive, systemic corticosteroids comprising prednisolone, or equivalent, ≥20mg/day for > 4 preceding weeks).
    - Suspected melioidosis
    - Specific microbiological information available to guide specific antibacterial therapy
- The treating clinician believes that participation in the domain would not be in the best interests of the patient.

ANTIBIOTICS DOMAIN ELIGIBILITY – ADULTS ONLY

Intervention Specific Exclusions

- Known non-serious hypersensitivity to penicillins will result in exclusion from receiving interventions that include piperacillin and amoxicillin
- Known non-serious hypersensitivity to cephalosporins will result in exclusion from receiving interventions that include ceftriaxone
- Known serious hypersensitivity to beta-lactams, including penicillins or cephalosporins, will result in exclusion from interventions that include piperacillin, amoxicillin, and ceftriaxone
- Known hypersensitivity to moxifloxacin or levofloxacin will result in exclusion from moxifloxacin or levofloxacin intervention.
- Known serious hypersensitivity to the macrolide will result in exclusion from interventions that include piperacillin, amoxicillin and ceftriaxone
- Known or suspected **pregnancy** will result in exclusion from **moxifloxacin or levofloxacin**-interventions. It is normal clinical practice that women admitted who are in an age group in which pregnancy is possible will have a pregnancy test conducted. The results of such tests will be used to determine interpretation of this exclusion criteria.

DSA: MACROLIDE DURATION DOMAIN (M) – ADULTS ONLY

Domain	Age Stratum	Illness Severity State	Intervention	Administration
Macrolide (M)	≥18 years old	Severe	M1 – Standard course macrolide	Between D3 & D5 / discharge
			M2 – Extended course macrolide	For 14 days / discharge

Macrolide Options
Azithromycin 500mg daily
Clarithromycin 500mg daily
Roxithromycin 150mg q12hr
Can switch from IV to enteral

Domain objective

Determine the effectiveness of standard course versus extended course macrolide treatment for hospitalized patients with severe community-acquired pneumonia, who have received an allocation to a macrolide-containing intervention in an Antibiotic Domain of this Platform.

Hypothesis

Primary endpoint specified in relevant Core Protocol documents will differ based on the duration of administration of a macrolide.

MACROLIDE DOMAIN ELIGIBILITY – ADULTS ONLY

Inclusion

- Severe illness state, admitted to ICU
- Patient has been allocated a macrolide intervention within the antibiotic domain

Exclusion

- There is microbiological confirmation or the clinician strongly suspects Legionella or any other form of **atypical pneumonia**.
- Macrolide antibiotics have already been discontinued for more than 36 hours.
- The treating clinician believes that participation in the domain would not be in the best interests of the patient.

DSA: CORTICOSTEROID DOMAIN (C) – ADULTS & PAEDS

Domain	Age Stratum	Illness Severity State	Intervention	Administration
Corticosteroid (C)	≥18 years old / <18 years old	Moderate	C1 - No corticosteroid	Steroids can be given if new condition develops, not flu.
			C4 - Fixed-course dexamethasone	For 10 days, **Adults:** 6mg daily **Paeds:** 0.15 mg/kg (max 6mg/day). IV or enteral
		Severe	C1 - No corticosteroid	As above
			C3 - Shock-dependent hydrocortisone **Adults only**	During septic shock 50 mg every 6 hours IV
			C4 - Fixed-course dexamethasone	For 10 days Dosing as above, IV or enteral

Domain objective

Determine the effectiveness of different strategies of corticosteroid utilization for hospitalized patients with severe lower-respiratory tract infection.

Hypothesis

Probability of the occurrence of the primary endpoint specified in the Core Protocol documents will differ based on the allocated corticosteroid strategy

CORTICOSTEROID DOMAIN ELIGIBILITY – ADULTS & PAEDS

Inclusion

- Aged ≥ 28 days old (corrected gestational age)

If in moderate state

- Patient is receiving some form of supplemental oxygen (simple facemask, low or high flow nasal oxygen, or non-invasive ventilation)

If in severe state

- Patient has pneumonia

CORTICOSTEROID DOMAIN ELIGIBILITY – ADULTS & PAEDS

Exclusion

- Confirmed SARS-CoV-2 infection
- Hospital-acquired respiratory tract infection, except where the patient has confirmed influenza infection
- Known hypersensitivity to any corticosteroid
- Indication to prescribe **systemic corticosteroids** for a reason that is **unrelated to the respiratory tract infection**, such as chronic corticosteroid use before admission, acute severe asthma, or suspected or proven Pneumocystis jirovecii or COVID-19 pneumonia
- The treating clinician believes that participation in the domain would not be in the best interests of the patient

If in Severe state

- More than 24 hours have elapsed since commencement of sustained organ failure support in an ICU.

DSA: INFLUENZA ANTIVIRAL DOMAIN (I) – ADULTS

Domain	Age Stratum	Illness Severity State	Intervention	Administration
Antiviral (I)	**≥18 years old (adults)**	Moderate / Severe	I1 - No antiviral for influenza	No flu antivirals for 28 days /discharge
			I2 – Oseltamivir **CLOSED IN SEVERE ADULTS**	For 5 days / discharge 10 doses, BD. Dosing by clinician. Enteral
			I3 - Oseltamivir **CLOSED IN SEVERE ADULTS** **PAUSED IN MODERATE ADULTS**	For 10 days / discharge 10 doses, BD. Dosing by clinician. Enteral
			I4 - Baloxavir	On D1 & D4 / discharge Dosing based on weight. Enteral
			I5 - Oseltamivir + Baloxavir	Respectively for 5 days AND on D1 & D4 / discharge. Dosing as above
			I6 - Oseltamivir + Baloxavir	Respectively for 10 days AND on D1 & D4 / discharge. Dosing as above

Domain objective	Determine the effectiveness of different antiviral strategies for hospitalized patients with microbiological testing-confirmed influenza virus infection.
Hypothesis	Probability of improvement in the primary outcome after enrollment will differ based on domain intervention allocation.

DSA: INFLUENZA ANTIVIRAL DOMAIN (I) – PAEDS

Domain	Age Stratum	Illness Severity State	Intervention	Administration
Antiviral (I)	**<18 years old (children)**	Moderate / Severe	I1 - No antiviral for influenza	No flu antivirals for 28 days /discharge
			I2 – Oseltamivir	For 5 days / discharge 10 doses, BD. Dosing by clinician. Enteral
			I3 - Oseltamivir **PAUSED IN MODERATE CHILDREN**	For 10 days / discharge 20 doses, BD. Dosing by clinician. Enteral
			I4 - Baloxavir	On D1 & D4 / discharge Dosing based on weight. Enteral
			I5 - Oseltamivir + Baloxavir	Respectively for 5 days AND on D1 & D4 / discharge. Dosing as above
			I6 - Oseltamivir + Baloxavir	Respectively for 10 days AND on D1 & D4 / discharge. Dosing as above

Domain objective	Determine the effectiveness of different antiviral strategies for hospitalized patients with microbiological testing-confirmed influenza virus infection.
Hypothesis	Probability of improvement in the primary outcome after enrollment will differ based on domain intervention allocation.

ANTIVIRAL DOMAIN ELIGIBILITY – ADULT & PAEDS

Inclusion

- Aged ≥ 28 days old (corrected gestational age)
- Influenza infection has been confirmed by microbiological testing.

Exclusion

- Patient has already received **two or more doses of oseltamivir or other neuraminidase inhibitors**
- Patient has already received **one or more doses of baloxavir**
- Patient is already receiving, or a clinical decision has been made to commence, an antiviral active against influenza other than oseltamivir or baloxavir, or both.
- The treating clinician believes that participation in the domain would not be in the best interests of the patient

ANTIVIRAL DOMAIN ELIGIBILITY – ADULTS & PAEDS

Exclusions if in Moderate State

- More than 96 hours has elapsed since hospital admission

Exclusions if in Severe state

- More than 48 hours has elapsed since commencement of sustained organ failure support in an ICU

Intervention Specific Exclusions

- Known hypersensitivity to oseltamivir or baloxavir
- Known or suspected **pregnancy** will result in exclusion from interventions that include **baloxavir**

DSA: INFLUENZA IMMUNE MOD DOMAIN (N) – ADULTS & PAEDS

Domain	Age Stratum	Illness Severity State	Intervention	Administration
Immune Modulation (N)	≥18 years old / ≥2 years and <18 years old	Severe	N1 - No immune modulation	No immune mods for 28 days/discharge. Steroids can be given clinically or via study steroid domain.
			N2 – Tocilizumab	**Adults:** 8mg/kg up to 800mg, single dose over 1 hour - IV **Paeds:** If ≥30kg, adult dosing - IV If < 30 k, single dose 12mg/kg - IV
			N3 – Baricitinib	For 10 days / discharge Based on age and eGFR. Enteral

Domain objective

Determine the effectiveness of immune modulation interventions for severely ill hospitalized patients with microbiological testing confirmed influenza virus infection.

Hypothesis

Probability of the occurrence of the primary endpoint specified in the relevant Core Protocol documents will differ based on allocation to influenza immune modulation therapy.

IMMUNE MODULATION DOMAIN ELIGIBILITY – ADULTS & PAEDS

Inclusion

- Aged ≥2 years old
- Influenza infection has been confirmed by microbiological testing
- In the opinion of the treating clinician, the primary contributor to the patient's Severe Illness State is a respiratory tract infection
- Patient has community-acquired respiratory tract infection
- Patient has pneumonia

IMMUNE MODULATION DOMAIN ELIGIBILITY – ADULTS & PAEDS

Exclusion:

- SARS-CoV-2 infection has been confirmed by microbiological testing
- More than 48 hours has elapsed since commencement of sustained organ failure support
- Known condition or treatment resulting in ongoing **immune suppression** including neutropenia prior to this hospitalization
- A neutrophil count <1.0 x 10^9 / L
- Confirmed or strongly-suspected active mycobacterial infection or invasive fungal infection
- Patient has already received **any dose of one or more of tocilizumab (or another IL-6 receptor antagonist) or baricitinib (or another JAK inhibitor)** during this hospitalization or is on long-term therapy with any of these agents prior to this hospital admission.
- The treating clinician believes that participation in the domain would not be in the best interests of the patient

IMMUNE MODULATION DOMAIN ELIGIBILITY – ADULTS & PAEDS

Intervention-level exclusion criteria:

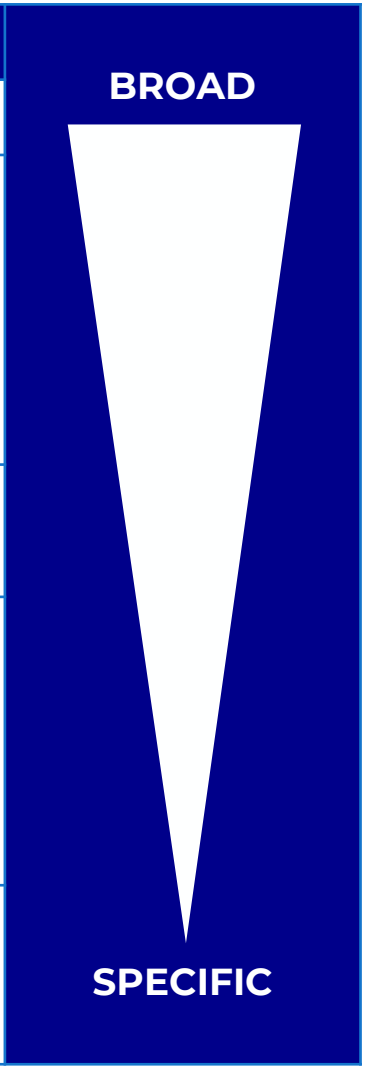
- Known hypersensitivity to an agent specified as an intervention in this domain will exclude a patient from receiving that agent
- Known or suspected **pregnancy** will result in exclusion from **baricitinib (and tocilizumab for now)**
- An alanine aminotransferase or an aspartate aminotransferase that is more than five times the upper limit of normal will result in exclusion from receiving **tocilizumab**
- A platelet count < 50 x 10^9 / L will result in exclusion from receiving **tocilizumab**
- Renal impairment at baseline will result in exclusion from the **baricitinib** intervention:
  - For adults and children ≥ 9 years of age, eGFR <15 mL/min/1.73m^2 and/or receipt of RRT (including long-term)
  - For children ≥2 years and <9 years of age, eGFR <30 mL/min/1.73m^2 and/or receipt of RRT (including long-term)

REMAP-CAP

SAFETY

SAFETY: DEFINITIONS

Event	Definition
Adverse Event (AE)	Any untoward medical occurrence.
Serious Adverse Event (SAE)	Any untoward medical occurrence that is fatal, life-threatening or results in persistent or significant disability / inpatient hospitalization or prolongation of existing hospitalization / a congenital anomaly or birth defect.
Serious Adverse Drug Reaction (SADR/SAR)	A SAE that is **possibly, probably or definitely related** to drug administration.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A SAE that is **unexpected** (not previously described in Summary of Product Characteristics / Investigator Brochure) and **possibly, probably or definitely related** to study treatment/participation.
Domain-specific SAE	Safety events defined in the DSAs, that should **always** be reported, regardless of relatedness.



SAFETY: REPORTING REQUIREMENTS

There are two categories of SAEs for REMAP-CAP:

- DSAs may pre-specify SAEs that must be reported for all participants enrolled in that domain, regardless of relatedness or suspected relationship to participation in the domain.
- Other SAEs (not specified in DSAs) should be reported only where they are deemed to be possibly, probably or definitely related to study treatment / participation.

Event type	Reporting required?*
SAEs related to a study intervention or study participation (including SUSARs)	YES
SAEs **not** related to study intervention or study participation	NO
AEs	NO
Domain-specific SAEs	YES
Domain-specific secondary endpoints related to study intervention or study participation	YES
Domain-specific secondary endpoints **not** related to study intervention or study participation	NO

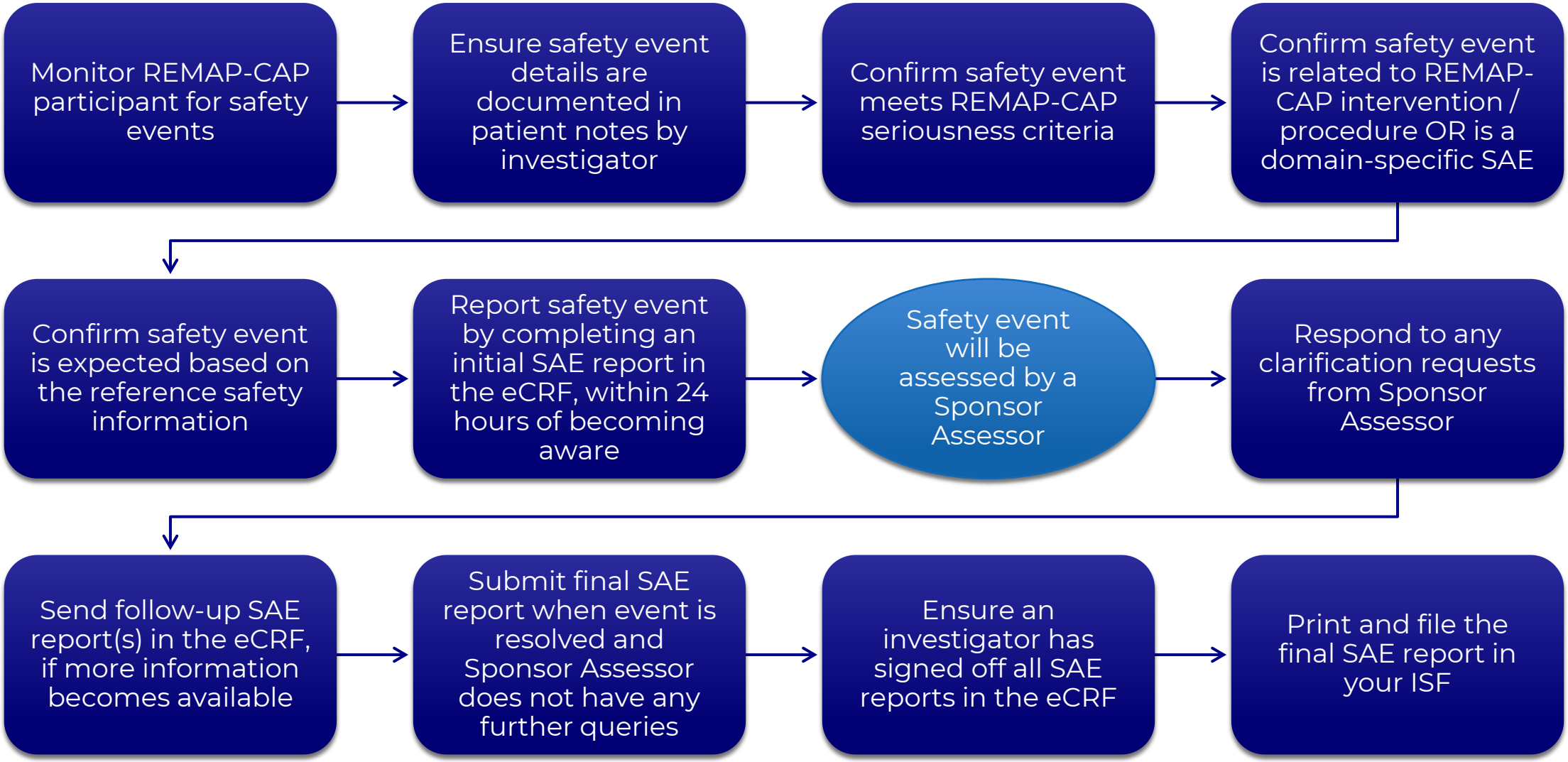
* Reporting is only required for events that occur between randomization and hospital discharge!

SAFETY: REPORTING EXPECTATIONS

- Report safety event **within 24 hours of becoming aware**.
- Complete the SAE form in the electronic case report form (*eCRF*). Different SAE report types can be entered in the eCRF:
  - Initial SAE report;*
  - Follow-up SAE report;*
  - Final SAE report.
- Only in case the eCRF is **not** working:
  - Use back-up SAE form available in investigator site file (*ISF*).
  - E-mail a copy to eu.remapcap@umcutrecht.nl and monitor or project manager.
- Document relevant information and SAE assessment in the patient files.
- Follow-up with patient until SAE is resolved.

* Send a follow-up report when more info is available, instead of editing initial report.

SAFETY: REPORTING FLOWCHART



DOMAIN SPECIFIC SAES

The following should be screened for and reported as SAEs for all patients, irrespective of intervention allocation:

- **MACROLIDE:**
  - Cardiac arrhythmia (particularly torsades de pointes)
  - Gastrointestinal intolerance
  - Hypersensitivity
  - Abnormal liver function

- **IMMUNE MODULATION**: The following should be screened for and reported as SAEs for all patients in this domain, irrespective of intervention allocation:
  - Severe thrombocytopenia, out of keeping with clinical disease
  - Severe neutropenia, out of keeping with clinical disease
  - Increase in LFTs to 5x upper limit of normal
  - Gastrointestinal perforation

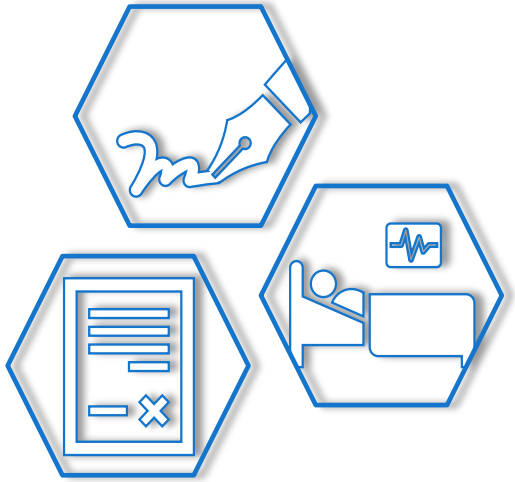
- **ANTIBIOTICS, ANTIVIRAL, CORTICOSTEROID DOMAINS:** None

REMAP-CAP

INFORMED CONSENT

INFORMED CONSENT: DEFINITION

*'A process by which a participant or their legally accepted representative **voluntarily confirms their willingness** to participate in a trial after having been informed and been provided with the opportunity to discuss all aspects of the trial that are relevant to the participant's decision to participate. (...) Informed consent is documented by means of a written or electronic, signed and dated informed consent form. (...)' International Council for Harmonisation – Good Clinical Practice (ICH-GCP)*



INFORMED CONSENT: WHO?

Type of consent?	Who is involved?	Situation
Participant or Parent/guardian	A patient/participant or A parent/guardian (for children)	When patient has capacity. **Default consent type.** or When parent/guardian is available, if child is too young or incapable of providing consent.
Personal Legal Representative (PerLR)* *PerLR does not apply to children	A personal relationship with the patient who does not have a conflict of interest i.e. friend/relative/legal guardian	When patient doesn't have capacity and PerLR* is available in person or remotely. *This scenario does not apply for children, only a parent/guardian would be approached.
Professional Legal Representative (ProLR)	Independent physician or matron who is not involved in the trial nor listed on the delegation log.	When patient does not have capacity and PerLR (or parent/guardian, for children) is not available, but ProLR is available.
Witnessed consent	A person independent of the trial, who is not unfairly influenced by people involved in the trial i.e. Independent nurse or admin	Required when a patient (or parent/guardian, for children) or PerLR cannot read/write and **verbal consent** is taken instead of written consent or When **remote consent** is obtained (via telephone)

INFORMED CONSENT: WHEN?

Timing of consent	Description	Situation
Prospective consent	Consent obtained from patient or parent/guardian, prior to start of screening activities.	When patient has capacity. **Default consent type.** When parent/guardian is available, if child is too young or incapable of providing consent.
Deferred consent	Consent obtained from PerLR* or ProLR prior to start of screening activities.	When patient doesn't have capacity and PerLR or ProLR is available in person or remotely.
Delayed consent	Consent obtained on behalf of the patient by a PerLR*/ProLR after screening or randomisation *PerLR consent is not applicable for children, only a ProLR would be approached	○ Emergency situation i.e. timeframe is short, PerLR (or parent/guardian) and ProLR are BOTH not immediately available . ○ Patient is enrolled with NO consent in place. ○ Consent must be obtained from PerLR (or parent/guardian), or ProLR as soon as possible preferably within 24 hours. ○ Once the patient regains capacity, the patient should sign the CF retrospectively.
Retrospective patient consent (or parent/guardian)	Consent obtained after patient is enrolled in study, if/when patient has regained capacity or parent/guardian is available (for children)	Obtained if patient (or parent/guardian) did not provide prospective consent, where deferred/delayed consent was obtained.

INFORMED CONSENT: HOW?

How?	Description?	Situation
Written consent	Fully completed paper consent form either using the full or the summary information sheet.	Patient or parent/guardian or PerL/ProLR can read and write and are physically able to complete the CF..
Verbal consent	Each consent statement is agreed to verbally by the patient (or parent/guardian, for children) or PerLR, in the presence of an impartial witness who signs the CF.	Patient (or parent/guardian) or PerLR are present in person but cannot read/write, or are not physically able to do so.
Remote verbal consent (telephone)	Consent is obtained via telephone call to the patient (or parent/guardian) or PerLR, in the presence of an impartial witness who also signs the telephone CF. Must be followed up with written consent where/when possible.	Patient is unable to consent. Parent/ guardian or PerLR are not immediately available in person. or When patient is d/c from hospital promptly and retrospective consent is pending.
Video animation consent	Patient (or parent/guardian) or PerLR is shown the study animation video in English and signs the Video CF. They are also given a copy of the full written information sheet.	Patient (or parent/guardian) or PerLR requests a format other than the written PIS to view information.

Please note: All references to 'PerLR' are not applicable to children

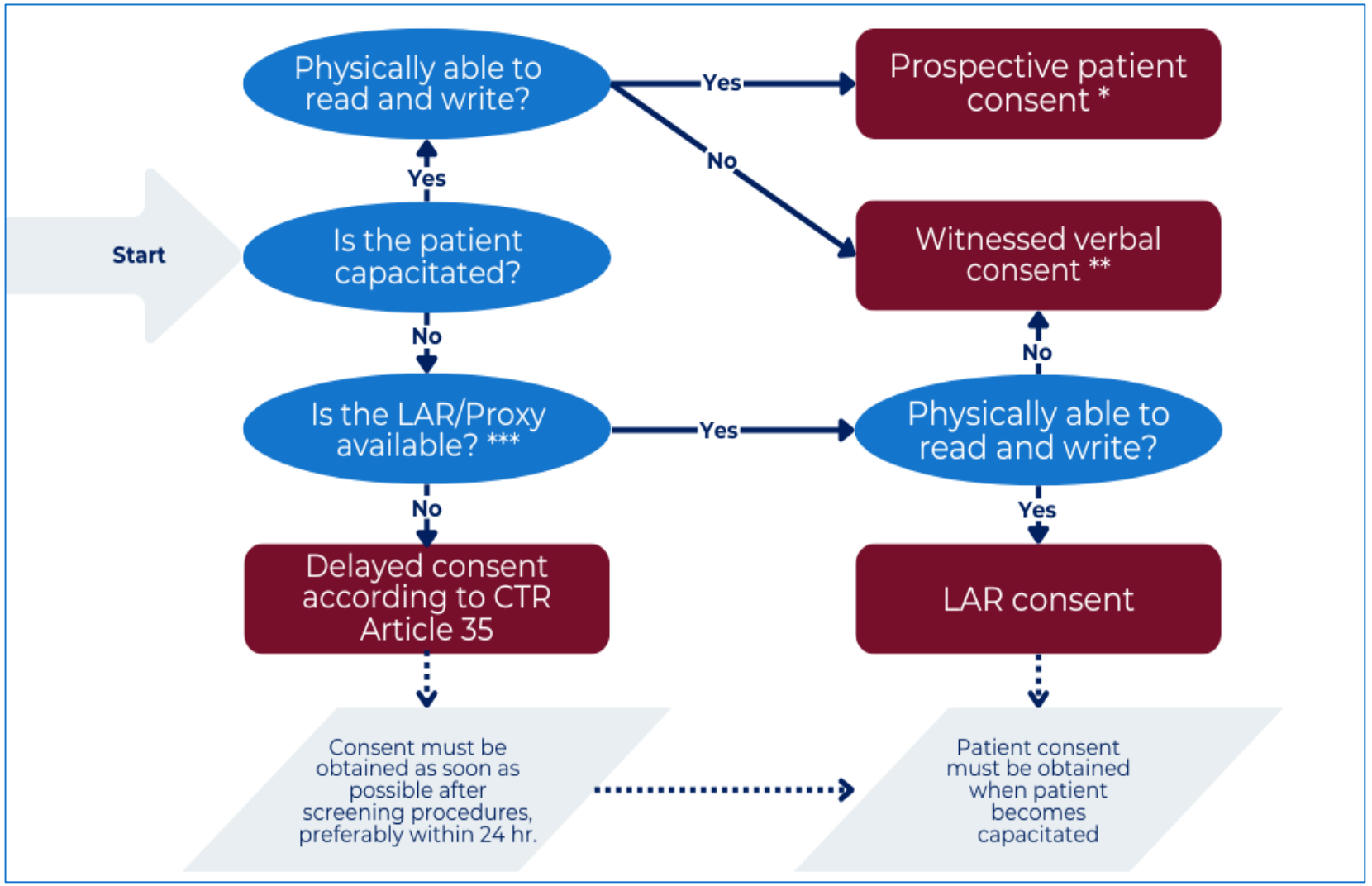
INFORMED CONSENT: RETROSPECTIVE

If ProLR consent has been taken:

- Attempts MUST be made to obtain consent from the Patient (or parent/guardian, for children) or PerLR as soon as available, ideally before hospital discharge
- If not, attempts MUST be made to obtain consent after discharge:
  - In person if they have a follow up appointment
  - Via telephone, followed by written consent by post/email

Please try to obtain telephone (remote) consent prior to postal written consent in case this is not returned or received (even if they have agreed they will send it back)

INFORMED CONSENT: FLOWCHART



LAR: Legally Authorised Representative

For adults this can be a PerLR (any relative or friend etc) or ProLR.

For children this can only be a parent/guardian or ProLR.

INFORMED CONSENT: SITE PROCESS

- Procedures for obtaining informed consent in an emergency setting
- Procedures for documentation of method /type of consent i.e. completion of consent statement
- Procedures for checking validity of PerLR/ProLR signing CFs on behalf of patients
- Procedures for where CFs are collected/placed out of hours when research nurses or access to study files are not available, to avoid loss of forms

INFORMED CONSENT: DOCUMENTATION

Documentation must include information on:*

- **Who informed the participant/PerLR or ProLR** about the trial **and when/how** was this done
- **Method for obtaining informed consent** (including alternative methods).
- Confirmation of **patient/PerLR capacity**, to what degree and why
- For ProLR consent: Verification that they are **not listed on delegation log** and are **independent of study**

Additional preferred items:

- Participant/PerLR was **able to ask questions** to a study investigator
- Participant/PerLR was **given enough time** to consider study participation
- **Which version** of the PIS/CF was signed
- Participant/PerLR were **given a copy** of the completed PIS/CF

* It should be clear from the source documentation that the site adhered to site- and REMAP-CAP approved procedures for obtaining Informed Consent.

CONSENT STATEMENT TEMPLATE

Optional - sites may use their own paper/digital template or write directly in medical notes.

Site Name	
Patient Trial ID	

REMAP-CAP Consent Statement

One statement to be completed per consent.

To be filed in patient medical records alongside copy of signed consent form and patient information sheet used. The purpose of this statement is to ensure the consent process is followed and documented in a GCP compliant manner.

Study Title:	**Randomised, Embedded, Multifactorial Platform Trial for Community Acquired Pneumonia (REMAP-CAP)**		
IRAS Number:	**237150**	**Protocol Version and Date:**	

Before written and informed consent to participate is obtained from the patient or PerLR/ProLR, the study is introduced by a delegated member of the study team using an approved version of the information sheet.

INFORMED CONSENT: WITHDRAWING PARTICIPATION

What if patient or personal LR does not wish for the patient to continue trial participation?

The patient will have trial treatment discontinued, unless this may cause harm to the patient (to be determined by treating clinician).

The patient or personal LR can indicate if they also want to withdraw consent for:

- further data collection / use of the patient's data, and
- the patient to be contacted for follow-up checks on quality of life.

Site staff should ensure that:

- a new consent event is created in the eCRF, to indicate that consent was revoked*
- withdrawal of consent (and reason if provided) is clearly documented in the source documentation.

* The system will lock the patient's eCRF, if they also revoked consent for further data collection.

INFORMED CONSENT: MISTAKES

- Incorrect or missing study details (site name/number, investigator name, pt ID)
- Boxes ticked rather than initialled or blank boxes
- Missing signatures or dates/times, incorrect dates
- Incomplete names i.e. 'J. Kim' or nicknames
- Wrong version of the PIS/CF used
- Original Consent Forms not filed in the ISF
- Consent process not documented in medical records
- Retrospective consent not attempted
- Lost PIS/CFs

INFORMED CONSENT: MISTAKES

Imperial College London

[Insert hospital/ trust logo here]

PROTECT HF

Full Title of Project: Physiological versus Right ventricular pacing Outcome Trial Evaluated for bradycardia Treatment (PROTECT-HF)

Chief Investigator: Dr Daniel Keene
Study Protocol Number: 22HH7931
IRAS ID: 312355

Participant Study ID Number:	
Site Number/Name:	001 - HAMMERSMITH HOSP
Name of Principle Investigator:	Dr J Smith

Participant Consent Form

Please initial each box if you agree with the following:

1. I confirm that I have read and understand the participant information sheet version 3.0 dated 29/02/2024 for (Physiological versus Right ventricular pacing Outcome Trial Evaluated for bradycardia Treatment (PROTECT-HF)) and have had the opportunity to ask questions which have been answered fully.	SS
2. I understand that my participation is voluntary, and I am free to withdraw at any time, without giving any reason and without my legal rights nor treatment / healthcare being affected. If I withdraw, I understand that the data collected whilst I was on the study will be retained and used by the research team who are obliged to keep my identity confidential.	SS
3. I understand that sections of any of my medical notes may be looked at by responsible individuals from Imperial College London, from NHS Trust or from regulatory authorities where it is relevant to my taking part in this research. I understand that if I have Medtronic CareLink, the coordinating study team will access my Cardiac Compass data (CCD) to obtain my remote pacemaker follow-up data (I understand that my personally identifiable data will not be shared with Medtronic).	SS

Version 3.0, 29 February 2024	Page 1 of 3
Participant Consent Form England	PROTECT-HF Study

1 copy for participant; 1 copy for Investigator Site File; 1 copy for participant notes
To ensure confidence in the process and minimise risk of loss, all consent forms must be printed, presented and stored in double sided format

4. I agree to my data (which includes my identifiable data [name, email address and contact telephone numbers]), and that of my nominated other if applicable, being entered onto a secure database, held at Imperial College London, in accordance with the Data Protection Act 2018.	SS
5. I understand that if I am eligible for the study, a member of the coordinating research team from Imperial College London will have access to my identifiable data (and my nominated other if applicable) to allow contact (via telephone and email) for follow up purposes as specified in the Participant Information Sheet.	SS
6. I agree to my GP being informed about my participation in this research study and any incidental findings to be conveyed to them.	SS
7. I understand that data collected from me is a gift donated to Imperial College and that I will not personally benefit financially if this research leads to an invention and/or the successful development of a new test, medication treatment, product or service.	SS
8. I give consent for identifiable data to be stored and shared securely with NHS Digital. This data will include my NHS number, date of birth, postcode and gender. This secure sharing of data with NHS Digital will be used to link information regarding hospital admissions, emergency care and civil registration.	SS
9. I give consent for information collected about me to be used to support other research or in the development of a new test, medication, medical device or treatment by an academic institution or commercial company in the future, including those outside of the United Kingdom (which Imperial has ensured will keep this information secure).	SS
10. I agree to the central study team to contact me via email/phone for follow up purposes as specified in the Patient Information Sheet.	SS
11. Should I lose capacity during the study, and only if this occurs after my pacemaker implantation, I understand that my health status related data will still be collected by the coordinating research team at Imperial College London from my medical notes by contacting my local clinical and research teams and from NHS Digital. This will include data from my pacemaker device checks and any hospital visits or admissions. Attempts would not be made to contact me or my nominated other directly after this time. I will no longer be asked to complete study related questionnaires. If I lose capacity prior to my pacemaker device implant, I will be withdrawn from the study and receive the standard of care treatment.	SS
12. I consent to take part in the PROTECT-HF study.	

Version 3.0, 29 February 2024	Page 2 of 3
Participant Consent Form England	PROTECT-HF Study

1 copy for participant; 1 copy for Investigator Site File; 1 copy for participant notes
To ensure confidence in the process and minimise risk of loss, all consent forms must be printed, presented and stored in double sided format

The following is an optional aspect of the trial, please initial the appropriate box:

	Yes	No
1. I give consent to being contacted about the possibility to take part in other research studies.	✓	
2. I agree for study related questionnaires to be sent to me via electronic means.		✓

SANDRA SMITH — Name of participant — Signature — 01 SEP 2024 — Date & Time

J. Kim — Name of person taking consent — Signature — 01 OCT 2024 11:30 — Date & Time

INFORMED CONSENT: MISTAKES

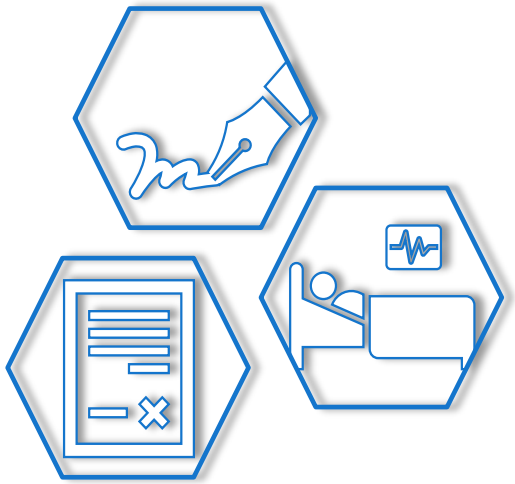
- Incorrect or missing study details (site name/number, investigator name, pt ID) - correction initialled/dated
- Boxes ticked rather than initialled or blank boxes - NTF
- Missing signatures or dates/times, incorrect dates - Re-consent/PD
- Incomplete names i.e. 'J. Kim' or nicknames - correction initialled/dated
- Wrong version of the PIS/CF used - PD
- Original Consent Forms not filed in the ISF - NTF + locate/swap
- Consent process not documented in medical records - PD + retrospective entry if possible
- Retrospective consent not attempted – PD
- Lost PIS/CFs - PD + potential data breach

WI APPENDIX III (2 PAGES)

Study	Category	Finding summary	Finding detail	Site Action	PD / NO PD
REMAP-CAP	Process	No consent obtained	No informed consent obtained to confirm subject/LAR has agreed to study participation. - subject alive	Obtain subject/LAR consent as soon as possible. After D180: Add no patient consent expected to eCRF	PD
REMAP-CAP	Process	No consent obtained	No informed consent obtained to confirm subject/LAR has agreed to study participation. - subject deceased	In countries with no approved delayed consent process: Obtain personal LAR consent to use subject data as soon as possible. In countries with approved delayed consent process: if required by local law in country, obtain personal LAR consent to use subject data as soon as possible Add no patient consent expected to eCRF	PD
REMAP-CAP	Process	No patient consent obtained	No patient consent after LAR consent even though subject has the capacity/became capacitated to provide consent – during hospitalisation	Obtain patient consent.	PD
REMAP-CAP	Process	No patient consent obtained	No patient consent after LAR consent even though subject has the capacity/became capacitated to provide consent – after hospital discharge prior day 180	Obtain patient consent (remotely). For subjects that remain incapacitated at hospital discharge sites are expected to check at least at day 90 and day 180 if the subject has regained capacity to provide consent, if still alive. Document the reason why no consent was	Possibly

INFORMED CONSENT: TAKEAWAYS

- Check the **EU RSA: UK Country Annex** for approved consent types and procedures
- Use the most recent approved site-specific PIS/CF.
    - The treatment-related parts of the PIS will cover all treatments across the study and will NOT need amending per site. Relevant domains may be circled on the CF but nothing can be deleted.
    - Sites will be asked to add in Trust header, local contact/PALS details and site/PI details.
- Collect prospective patient consent unless (temporarily) not possible
- Document the consent **process** in the source documentation
- Enter **each** consent event in the eCRF.
- Use the REMAP-CAP work instruction on Informed Consent (in your ISF) as a reference document.



REMAP-CAP

SCREENING, RAND & DATA ENTRY

SCREENING

Screening method	Screening tool	Screening documentation	Screening outcome
Screening in the eCRF*	Digital eligibility assessment is an automated process in eCRF	Patient is added to the master screening and enrolment log in eCRF	Participant will be randomized / a screen failure in eCRF
Screening on paper	Site-specific eligibility checklist (can be printed / downloaded from eCRF)	Complete the paper screening and enrolment log	Patient is deemed eligible or not, in line with eligibility checklist

Continue with screening in eCRF & ensure the **eligibility assessment is documented in source** by the investigator.

* In most countries informed consent is needed before entering participant data in the eCRF.

PARTICIPANT RECRUITMENT

It is important to have a clear recruitment strategy:

- **Who is involved** in participant recruitment?
- **Who is responsible** for participant recruitment?
- What is your **target recruitment frequency**?
- Any expected **challenges**?
- How is information on REMAP-CAP **shared with non-study staff**?
- Can the sponsor team provide **support**?

ELIGIBILITY CHECKLIST & STATEMENT TEMPLATE

Optional - sites may use their own template or write directly in medical notes

Site Name	
Patient Trial ID	

REMAP-CAP Eligibility Checklist and Statement

Please complete this form as part of the screening process for the REMAP-CAP trial, Core Protocol v3.1 dated 9th Nov 2022.

To be signed by a **clinician or doctor** who has undergone the **REMAP-CAP eligibility assessor training** and is listed on the **delegation log** (but does not necessarily require GCP training).

Here, clinician is defined as any role who has **prescribing rights** i.e. nurses, practitioners.

Once completed/signed, this form should be filed in the patient's medical records.

Platform Inclusion:

Inclusion Criteria	Please circle which apply	
Adult or paediatric patient (28 days or older) hospitalized with an acute illness due to a lower respiratory tract infection	Yes	No

Exclusion Criteria	Please circle which apply	
More than 14 days has elapsed since admission to hospital	Yes	No
If receiving organ failure support in an ICU, more than 48 hours has elapsed since admission to ICU	Yes	No

RANDOMISATION & DATA ENTRY

- Treat patients according to protocol and randomisation result.
- Study participation and randomisation results must be documented in (electronic) patient notes.
- Timely data entry is important:
  - Ensure timely completion of eCRF pages (e.g. enter data weekly).
  - Ensure timely entry of safety events and protocol deviations (*PDs*).
  - Ensure timely entry of primary endpoint data (notifications sent as reminder).
  - Ensure timely resolution of monitoring queries and automated system alerts.
  - Ensure timely sign-off and locking of participant eCRFs by Principal Investigator. Minimum requirement for sign-off:
    - After data completion of day 90 / day 180
    - After closure of a domain / platform conclusion has been made

DATABASE ACCESS

User Role	Functions	eCRF training required
Rand user	Screening & randomisation only	eCRF training slides Dummy randomisation
Research coordinator	All functions except SAE / eCRF sign offs	eCRF training slides Dummy randomisation
Investigator	All functions including SAE / eCRF sign offs	eCRF training slides Dummy randomisation
Data collector	Data entry only	eCRF training slides

For guidance:

- eCRF Data Completion Guidelines
- eCRF Spiral Database User Guide
- 2FA Quick Guide

REMAP-CAP

NASAL SWABS

SWAB COLLECTION

- After site activation nasal swab kits/safe boxes will be provided to site.
- Please collect nasal swabs from ALL positive influenza patients on the following days:-
  - Day 1 (soon after randomisation)
  - Day 3 (+/- 24 hrs or asap if D3 not possible)
  - Day 7 (+/- 24 hrs or asap if D7 not possible)

- Please post patients' Day 1 and Day 3 samples together in one safe box. Do not wait for Day 7 sample to be taken as samples are not viable after 5 days. Day 7 sample to be sent separately.
- Please enter sample collections on the eCRF

Notes:

- Subsequent sample(s) should be taken even if a sample is missed.

- Please do not use hospital swabs as these are not the correct type that we require for the study

- Sites may use the study specific sample tracker if they wish

Xmas/Easter

Do not send swab samples as central labs are closed – keep refrigerated until labs are open.

If you have no refrigeration space, miss the samples, it will not be classed as a Protocol Deviation

REMAP-CAP

PROTOCOL DEVIATIONS

PROTOCOL DEVIATIONS

- **Protocol Deviations** (*PDs*) are defined as any change, divergence, or departure from laws, regulations, local requirements as well as the Trial Protocol and trial-specific documents.
- All PDs must be:
  - Reported to the trial management team;
  - Entered in the eCRF (per eCRF completion guideline);
  - Signed off by the Principal Investigator.

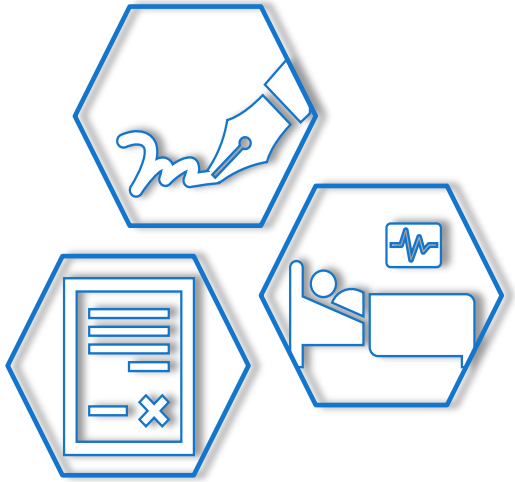
- PD entry in the eCRF is only possible at **patient-level**.
  - categorised e.g. platform or domain-specific deviation, trial procedure deviation, etc.
  - If in doubt of category, use the 'OTHER' subcategory as part of the 'Platform eligibility deviation' option.

IMPORTANT PROTOCOL DEVIATIONS

- **Important PDs** are a subset of PDs that may significantly **impact the completeness, accuracy, and/or reliability of the trial data** or that may **significantly affect a participant's rights, safety, or well-being**. An important PD may also be a Serious Breach and/or a Personal Data Breach.
- Assess for all PDs whether the deviation may qualify as an important PD. Important PDs should be reported to the TM team no later than 2 business days after discovery.
- **In case of an important PD**:
  - Take immediate action to prevent (further) negative impact on the participant's rights, safety or well-being and data integrity.
  - An Important Protocol Deviation Form will be sent to the site and should be completed by the investigator.
  - A Corrective and Preventive Action (*CAPA*) plan would be required

SERIOUS BREACH DEFINITION

‘ (…) means a breach from approved protocol, ICH-GCP and/or relevant legislation ***likely to affect to a significant degree the safety and rights of a participant or the reliability and robustness of the data generated*** *in the clinical trial (…)’ article 52.2 of the Clinical Trial Regulation (EU) No 536/2014*



SERIOUS BREACH

- Sponsor / Ecraid will assess whether an Important PD qualifies as a Serious Breach (*SB*) and will ensure proper reporting to relevant parties / authorities. In the EU and UK, a Serious Breach needs to be reported to the regulatory authorities **within 7 calendar days from awareness.**

Examples of PDs

- Failure to collect a patient questionnaire;
- Missed administration of one dose of IMP.

Examples of important PDs (and potential SBs)

- Failure to relay updated patient information leaflet / ICF to participants 2-3 months after approval;
- Non-compliance to in/exclusion criteria;
- Late reporting of / unreported SAEs.

REMAP-CAP

PHARMACY & IMP

IMP ORDERING & SHIPMENT

IMP from local hospital pharmacy stock

- Follow regular local procedures to order all IMP (except Baloxavir and Tocilizumab).

IMP from external supplier (Roche)

- Use the study specific **order form** for Baloxavir/Tocilizumab.
- Delivery timeline: Max. 7 days (turnaround time is usually 1-2 days).
- See ***'Roche Manual Extract for Sites'*** for info on the temp logger.
- Complete and return the ***'IMP Acknowledgement of Receipt'***.

IMP STORAGE CONDITIONS & QUALITY

IMP from local hospital pharmacy stock

- Store IMP in line with **SmPCs** and the REMAP-CAP **pharmacy guide**.
- Temperature monitoring log(s) to be made available to Sponsor upon request.
- Report storage temperature deviations of concern to Sponsor.
- Monitor expiration dates of IMP throughout the study.

IMP from external supplier (Roche)

- Store IMP in line with **SmPCs** and the REMAP-CAP **pharmacy guide**.
- Use the REMAP-CAP ***'IMP Temperature Monitoring Log'*** if manually monitoring.
- Use the REMAP-CAP ***'IMP Temperature Deviation Form'*** if necessary.
- Monitor expiration dates of IMP throughout the study.
- **Quarantine** IMP in cases of temperature deviations or quality issues, until Sponsor shares the **"Use/Do not use-decision".**

IMP PREPARATION & ADMINISTRATION

IMP from local hospital pharmacy stock

- Prepare and administer the IMP in line with the REMAP-CAP DSAs, administration guide and pharmacy guide (if applicable).
- Additional study labelling is not required.

IMP from external supplier (Roche)

- Ensure stock provided by external supplier is separated from local stock and used for trial purposes only.
- External supplier will ensure IMP study labelling prior to shipment.
- Prepare and administer the IMP in line with the REMAP-CAP DSAs, pharmacy guide and administration guide.

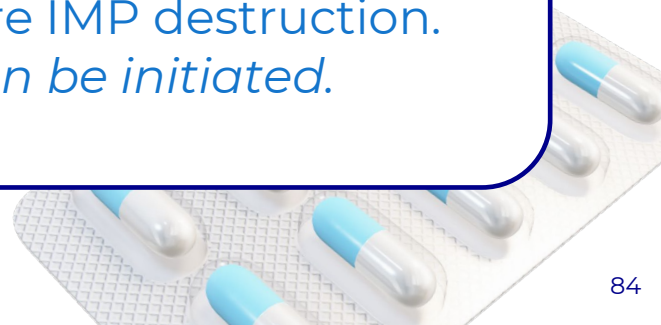
IMP ACCOUNTABILITY & DESTRUCTION

IMP from local hospital pharmacy stock

- Follow regular local procedures to account for IMP.
- Ensure drug accountability / inventory log(s) can be made available to Sponsor upon request.
- Follow regular local procedures to destroy IMP.

IMP from external supplier (Roche)

- Use the REMAP-CAP ***'IMP Inventory Log'*** to capture IMP accountability. Individual patient level accountability not required.
- Use the REMAP-CAP ***'IMP Destruction Log'*** to capture IMP destruction. *Note that only after our review should IMP destruction be initiated.*



REMAP-CAP

D90 + D180 FOLLOW UP

DAY 90 + DAY 180 FOLLOW UP

Day 90:

Completed by sites for flu and CAP patients:

Survival status to be entered on eCRF, from medical records

No patient contact

Day 180:

Completed by sites for flu patients, completed by ICNARC for CAP patients

Survival status to be entered on eCRF

Adults: EQ-5D-5L and WHODAS questionnaires by telephone

Paeds: EQ-5D-5Y / PedsQL by telephone

3 attempts to patient/proxy - 2 week window to complete f-up

Day 180: Questionnaires and training not available on study website, please request from study team at ukremap-cap@icnarc.org

The study team will send through to you:

- Telephone scripts + telephone contact log
- EQ-5D-5L and WHODAS questionnaires for adults
- EQ-5D-5Y / PedsQL for paediatrics
- D180 follow up instructions/training slides + training log

REMAP-CAP

INVESTIGATOR SITE FILE

INVESTIGATOR SITE FILE

- An ISF is provided to your site.
- It is the site's responsibility to keep the ISF up-to-date.
- ISF tasks include:
  - File received ISF document updates and important correspondence regarding the study;
  - Add sign/dated CVs of team members;
  - Add updates of GCP certificates and training;
  - Keep study logs up-to-date;
  - Use document referral notes to document where to find specific documents (if not filed in the ISF);
  - File printed SAEs & PD forms from eCRF;
- Consult ISF Index for other essential records that should be retained in the ISF.

ISF INDEX

1. Contact Information Study
2. Regulatory and Ethical documents
3. Financial Contracts / Signed Agreements
4. Study Protocols
5. Research Participant Information
6. Participant Insurance
7. Site Personnel
8. Monitoring / Audit / Inspection
9. Working Procedures
10. Product Information / Pharmacy
11. Laboratory
12. Safety (including SAE forms)
13. Database / Case Report Forms
14. Protocol Deviations / File Notes
15. Attended meetings
16. Correspondence
17. Other

E-ISF

- Using Trust eISF is permitted – must be a GCP compliant, validated system e.g. Florence
- A shared drive is NOT an eISF!

SITE WORKING FILE

- Teams working across multiple sites or departments within the same Trust may have ONE main ISF at a site, and then 'working files' at other sites.
- Reduced index only requiring localised documents and local logs etc.

REMAP-CAP

ICH-GCP & GDPR

ICH-GCP: BASICS

- GCP is:
  - an international,
  - ethical,
  - scientific and
  - quality standard
  - for the conduct of trials that involve human participants.

- These guidelines help to assure that the rights, safety and well-being of trial participants are protected.

- Latest iteration is **ICH-GCP E6(R3);** effective as of 23rd July 2025; mandated in the UK as of **28th April 2026**.

- A free course can be done via: https://globalhealthtrainingcentre.tghn.org/ich-gcp-r3/

ICH-GCP: INVESTIGATOR RESPONSIBILITIES

- The Local PI should supervise and delegate their site as appropriate
- The Local PI remains ultimately responsible for their site and should maintain appropriate oversight.

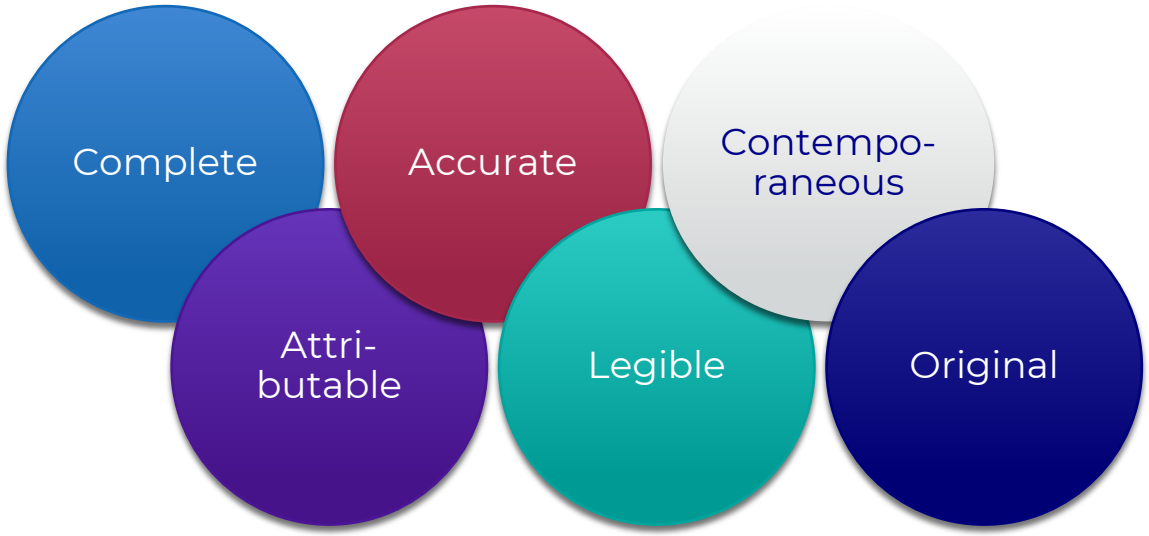
The investigator is **responsible for supervising** any qualified individual or party to whom the investigator delegates **trial-related duties and functions** conducted at the trial site.

The investigator should protect the **rights, safety and well-being of trial participants**, and ensure **integrity of trial data**, and accurate & complete source records

The investigator must ensure the trial is conducted in accordance with the **Protocol and applicable regulations (**GCP, CTR, GDPR, local)**.**

ICH-GCP: SOURCE DATA

- The investigator should maintain **adequate source documents** and **trial records**.
- **Changes** to source data should be:
  - **traceable** (with date and signed initials),
  - **not obscure** the original entry,
  - and be **explained if necessary**.
- **Direct entry of data** is permissible for some data.
- The source documents must be clear from the **source document location log**.



GDPR: BASICS

General Data Protection Regulation (*GDPR*)			
Applicable in the **European Union**	Requirements for processing (collecting, using and retaining) **personal data and the rights of data participants**	Participants give explicit **permission** to use their data for the study on the **ICF**	**Refer to https://gdpr-info.eu/ for more information**

Reminders for site:

- Ensure personal documents and data of participants are **safely stored**;
- Ensure **no** patient identifiers are entered in the eCRF
- **Communicate participant number** to Sponsor in correspondence and / or ensure patient information is **redacted** if documents are shared with Sponsor
- Consult your **Data Protection Officer** in case of queries

Additional information:

- Pseudonymized participant data is processed in countries **outside of the European Union**:
  - eCRF server in Australia;
  - Data management in the United Kingdom;
  - Statistical analysis in the United States.
- Data transfer and processing is according to GDPR

GDPR: PERSONAL DATA BREACH

- A **Personal Data Breach** (*PDB*) is a type of security breach leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to, personal data transmitted, stored or otherwise processed.
- **Reporting of a PDB to the applicable authorities is the responsibility of the data controller's Data Protection Officer (DPO).**
- Investigator sites are the controller of the patient dossier. The patient dossier may be paper-based, electronic, or a combination and includes information about medical history, concomitant medication, signed PIS/CFs and data collected during trial visits.
- Report a potential PDB to the TM team / Sponsor without delay after becoming aware.

Examples of PDBs

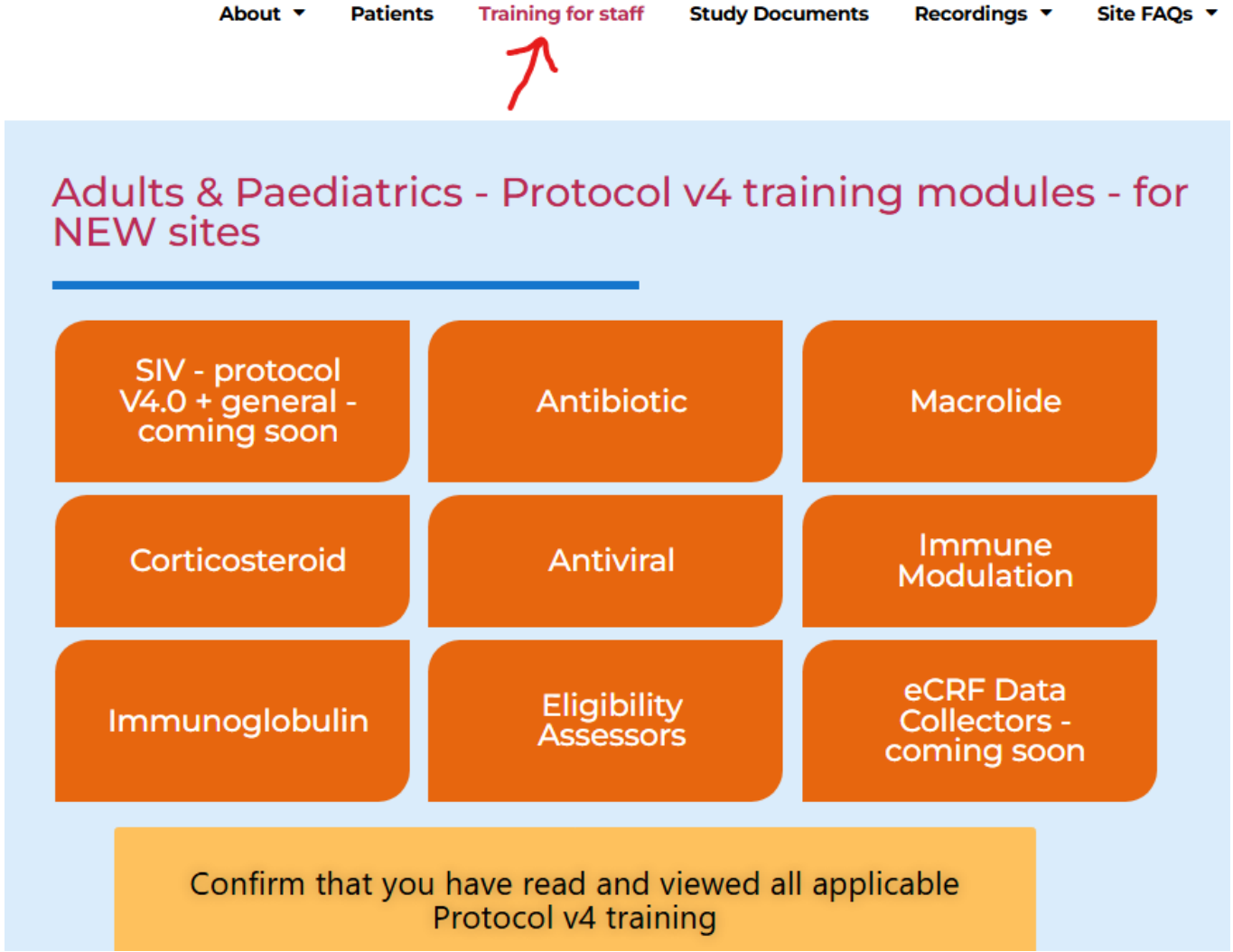
- Trial data from the study database were provided to the wrong recipient
- An email with personal identifiable information was sent to the wrong recipient
- Participant identification log / screening log was shared with the Sponsor
- PIS/CF is misfiled / lost

REMAP-CAP

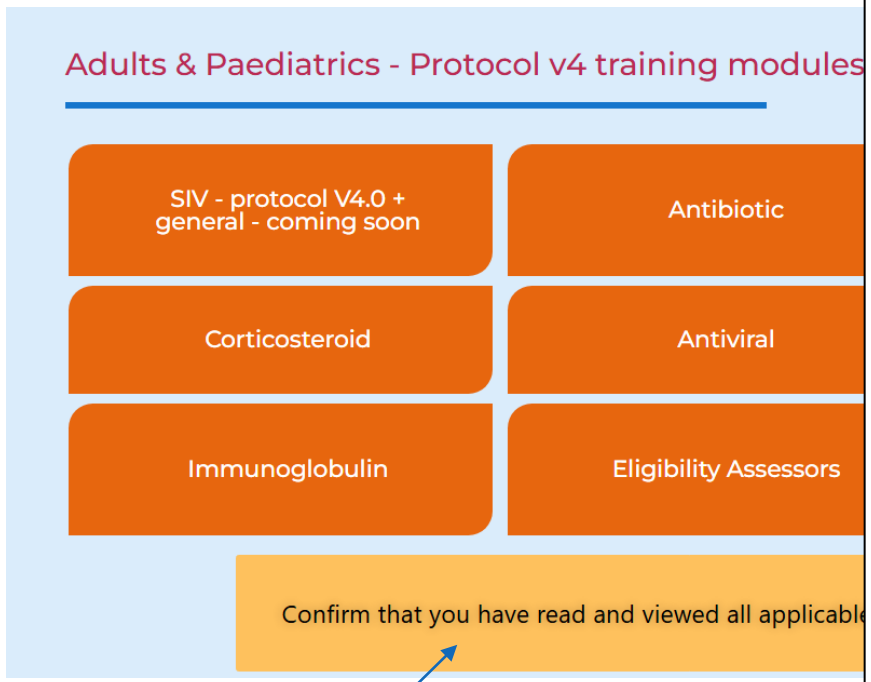
SITE SETUP & ACTIVATION

SITE STAFF TRAINING (INCL. ECRF)

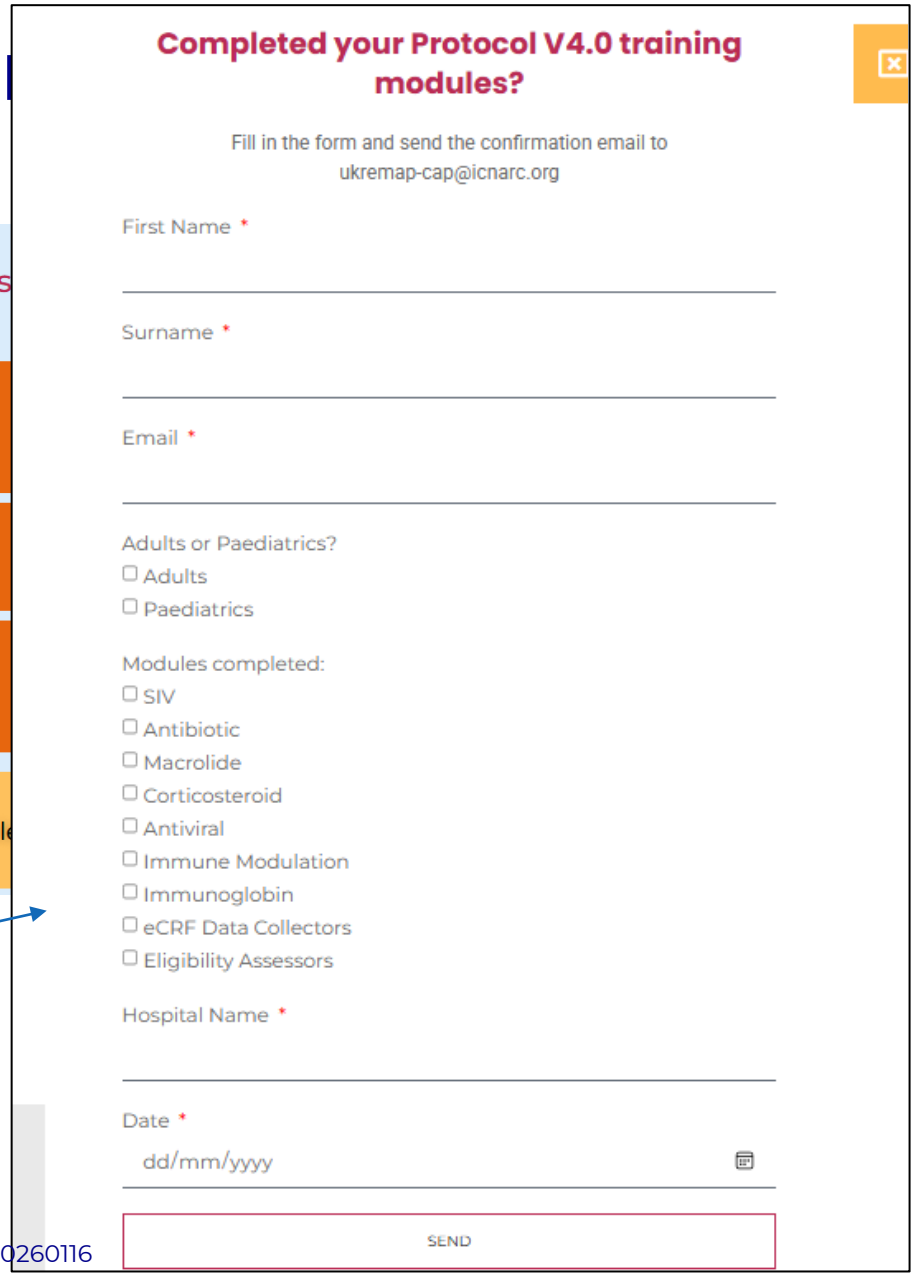
https://remapcap.co.uk/



SITE STAFF TRAINING (INCL. ECI



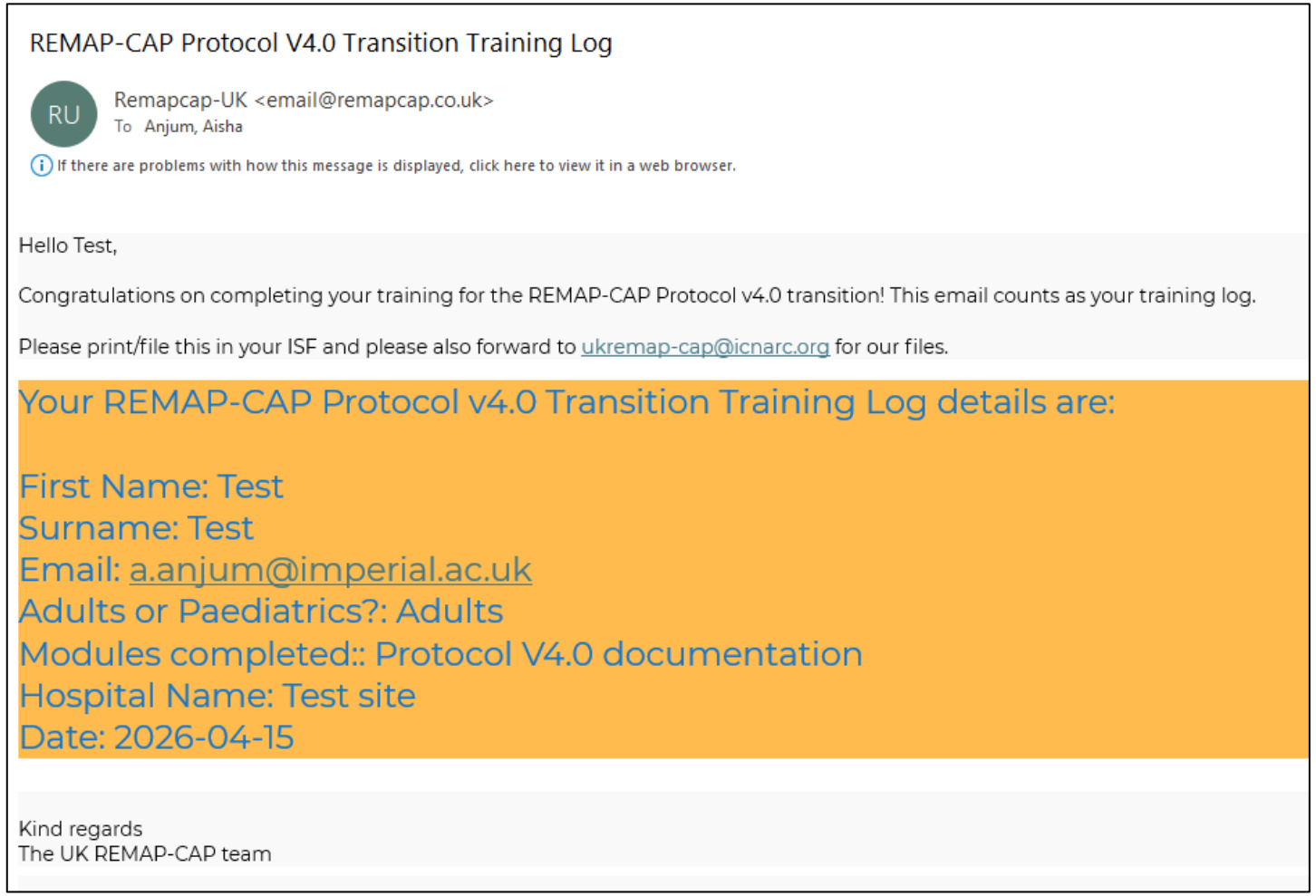
Single training log to complete



SITE STAFF TRAINING (INCL. ECRF)

You will receive an email which counts as a **training log.**

Please print/file in your ISF and fwd to UKREMAP-CAP@icnarc.org



REMAP-CAP Protocol V4.0 Transition Training Log

RU Remapcap-UK <email@remapcap.co.uk>
To Anjum, Aisha

If there are problems with how this message is displayed, click here to view it in a web browser.

Hello Test,

Congratulations on completing your training for the REMAP-CAP Protocol v4.0 transition! This email counts as your training log.

Please print/file this in your ISF and please also forward to ukremap-cap@icnarc.org for our files.

Your REMAP-CAP Protocol v4.0 Transition Training Log details are:

First Name: Test
Surname: Test
Email: a.anjum@imperial.ac.uk
Adults or Paediatrics?: Adults
Modules completed:: Protocol V4.0 documentation
Hospital Name: Test site
Date: 2026-04-15

Kind regards
The UK REMAP-CAP team

SITE ACTIVATION

Required files

- Regulatory approvals
- Named PI
- Fully signed Clinical Trial Agreement
- Local R&D approval
- Participant insurance
- Lab normal ranges
- CV/GCP certificates
- (e)ISF at site

Documents for completion

- Protocol sign. page
- Domain choice pages
- Delegation log
- Spiral database form
- Source document location log
- Retention of records statement
- Self-training logs (DSAs)
- SIV training & attendance Log
- Site visit log for SIV
- IMP receipt (if externally supplied)

Site activation

- Green Light letter sent
- Site-specific PIS/CF shared
- Site staff eCRF accounts activated
- Domains and interventions switched on, in eCRF

✓ Enrolment can start!

REMAP-CAP

SITE MONITORING

MONITORING, AUDITS & INSPECTIONS

- An assigned monitor will be available for contact moments to discuss study and recruitment status and reach out to arrange for regular monitoring visits.
- Notify the Sponsor **immediately** when audits/inspections are announced at your site.

First monitoring visit

- After 3 participants enrolled, or
- Within 6 months of first patient inclusion

Next monitoring visit(s)

Depending on site performance:

- Every 6 months, or
- Every year, or
- Every 2 years

E-SYSTEMS

- It is the site's responsibility to ensure their electronic systems (e.g. Electronic Health Record Systems) are compliant to clinical research regulations.
- If systems are changed, all previous trial data must be available in case of monitoring, audit or inspection.
- Sponsor will share an eSource-Readiness Assessment Tool (*eSRA*), which sites can complete to demonstrate compliance.
- Requirements for electronic patient records include (not limited to):
  - Access rights regulated;
  - Security systems in place;
  - Audit trail;
  - Read-only monitor account.*

* If read-only monitor account is not possible: Arrange for printed certified copies.

SITE CLOSE-OUT

- In theory REMAP-CAP will run indefinitely, with the following limiting factors:
  - Funding;
  - Poor site performance;
  - Site request to stop recruitment;
  - All scientific questions have been answered.
- Sites may be **'paused'** for a season or two (e.g. for capacity reasons) or are encouraged to go into **'dormant'** state if they no longer wish to participate long term, in which case a temporary close-out visit would be undertaken.
- The 'dormant' state means the site agreement is still active, therefore the site can be reactivated for recruitment immediately should there be a **pandemic**.
- In case a permanent site close-out is required / requested, a monitor will reach out to arrange this.*

* Site documents should be retained at site for 25 years!

REMAP-CAP

PUBLICATION POLICY

PLATFORM CONCLUSIONS & PUBLICATIONS

- Platform conclusions can lead to domain (intervention) changes.
- Sites will be notified about platform conclusion(s) and the consequences.
- If a platform conclusion is relevant to public health:
  - Results will be shared, e.g. at conferences and/or in publications.
  - Site staff will be listed as collaborators on the publication.
- Site staff may **not** publish or present any interim results from REMAP-CAP themselves.
- Refer to the REMAP-CAP Authorship and Publication Policy

CONTACT & STAY UP TO DATE

Find us online!

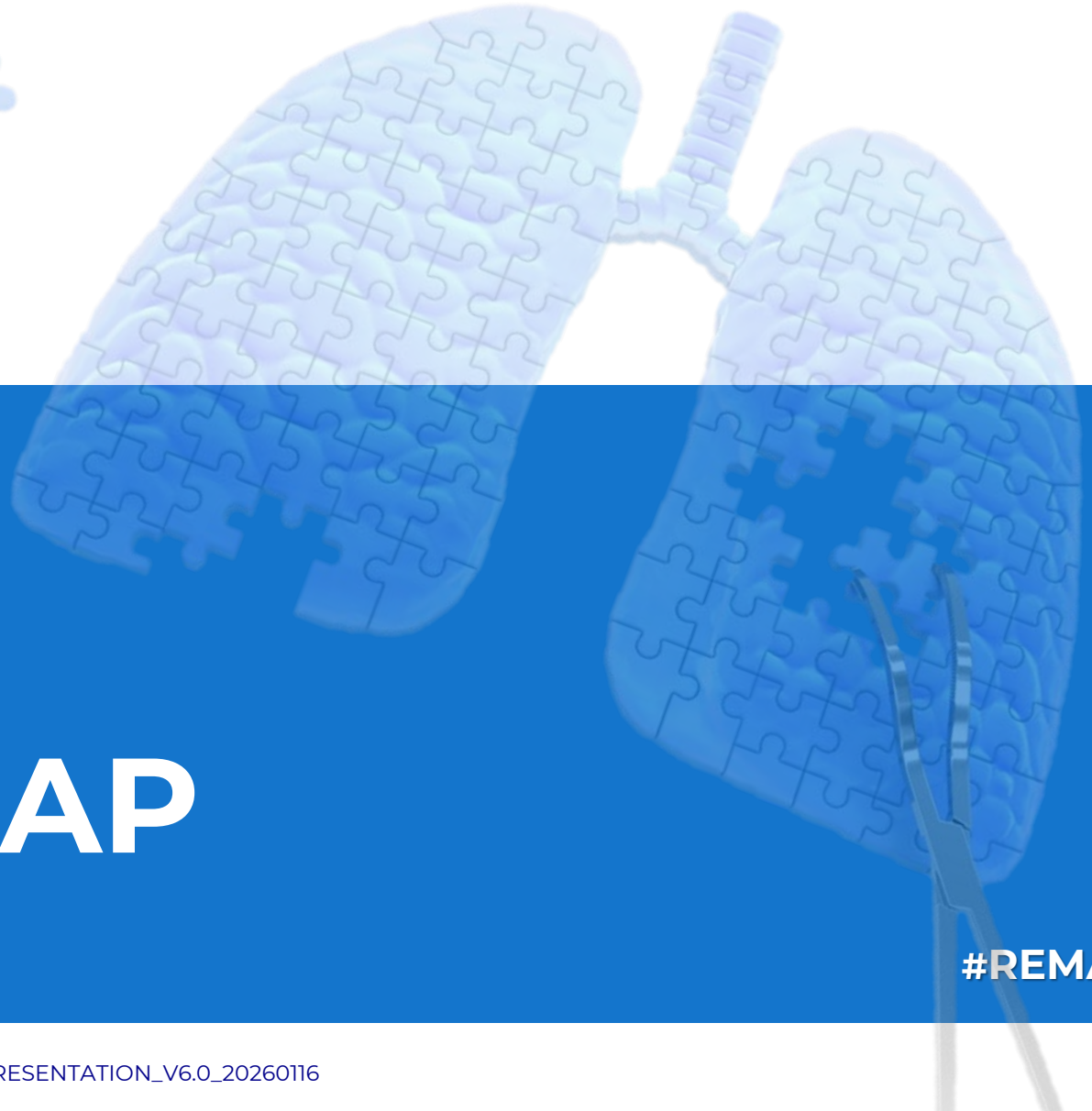
- Global website: www.remapcap.org /European website: www.remapcap.eu
- UK website: www.remapcap.co.uk
- Instagram: https://www.instagram.com/remapcap/
- LinkedIn: https://www.linkedin.com/company/ remap-cap/mycompany/

Contact us!

- Email for UK Trial Management Team: UKREMAP-CAP@icnarc.org
- E-mail address for general questions to sponsor: eu.remapcap@umcutrecht.nl
- E-mail address for **urgent matters outside business hours**: info@remapcap.org

Want to learn more?

Are you a young investigator looking to broaden your expertise in the field? Intrigued by the concept of Adaptive Trial Designs? Or just interested in educational opportunities related to Clinical Trials? Visit https://ecraid.eu/education



REMAP-CAP

THANK YOU!

#REMAPCAPFAMILY