Data Management

v2.0 02-Oct-2020

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Case Report Forms (CRFs)

CRFs Summary

- Introduction to the CRFs
- Who should complete each CRF
- General CRF completion guideline
- CRF version
- CRF header & footer
- CRF corrections
- Numeral fields
- Tick boxes
- Guidance text
- Adding additional comments – CRF99
- How to complete logs - **CRF09,** CRF10, CRF11a
- CRF storage

Introduction

- 18 CRFs in total.

- All CRFs:
  - Have been designed and produced by the MRC CTU
  - Have been reviewed and approved by the TMT, TMG and where required the PMG
  - Will be supplied to each site electronically in PDF format prior to site activation
  - Are written in English, expected to be completed and entered onto the database in English
  - Have guidelines on how they should be completed. CRF Completion Guidelines will also be supplied to each site prior to site activation

CRF completion

- All site staff completing CRFs must be listed correctly on the 'Signature List and Delegation of Responsibilities' Log with 'Complete CRFs' listed within the study tasks.

CRF number	CRF name	Completed by
01	Screening	Site staff – DM, RN
02	Baseline	Site staff – DM, RN
03	Randomisation	Site staff – Clinician e.g. PI
04	Clinical Investigations	Site staff – DM, RN
05	Follow-up In-Hospital	Site staff – DM, RN
06	Follow-up Post Discharge	Site staff – DM, RN
07	Antibiotic Acceptability	Site staff – DM, RN
08a	SAE	Site staff – Clinician e.g. PI
08b	Medical Review	MRC CTU staff
09	Doses of antibiotics during admission	Site staff – DM, RN

CRF completion (continued…)

CRF number	CRF name	Completed by
10	Concomitant Medications	Site staff – DM, RN
11a	Adverse Event Log	Site staff – DM, RN
11b	Adverse Event Log – MedDRA Coding	MRC CTU staff
12	PK Substudy Sampling	Site staff – DM, RN
13	PK Storage Log	Site staff – DM, RN
14	Microbiology Storage	Site staff – DM, RN
15	Household Socioeconomic	Site staff – DM, RN
16	Cost to Families for Care and Treatment	Site staff – DM, RN
17	Early Stopping of Trial Participation	Site staff – DM, RN
99	Additional Information	Site staff – DM, RN

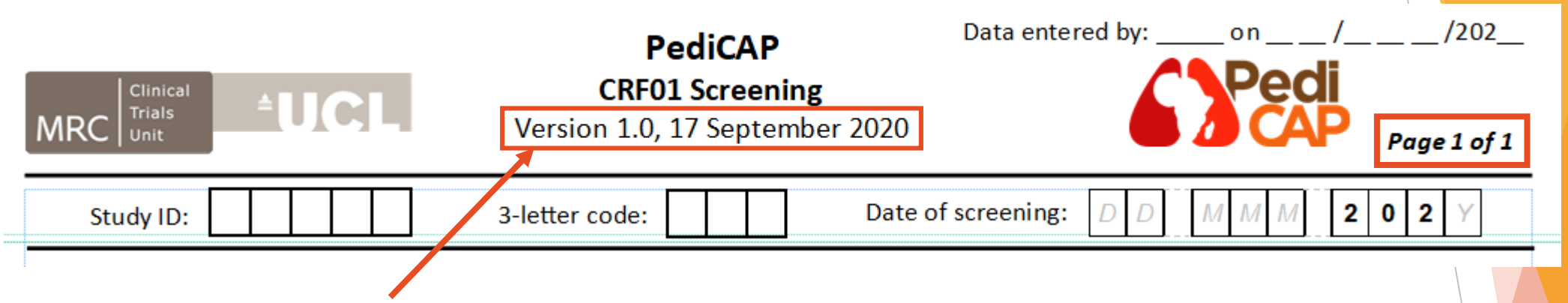
General CRF completion guidelines

- The following slides will provide information on how to complete each CRF, with the use of screenshots and guidance text.

- CRFs should be completed in blue or black ink and in English.
- Erasable pens and pencils should not be used to complete CRFs.

- CRFs should be completed in a legible way in order to avoid any data entry errors and subsequent queries.
- Joined up writing should be avoided as much as possible when writing in free text fields.

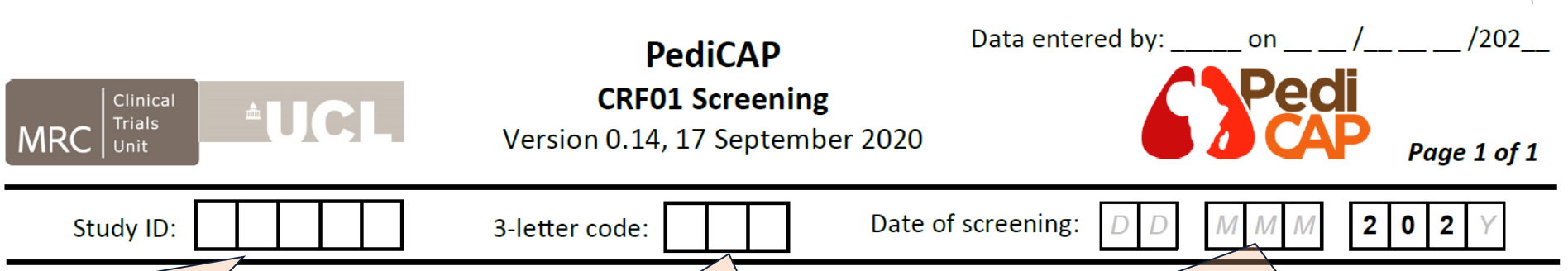
CRF versions



- Please ensure the most up to date version of the CRF is being completed.
- Zambia will start on version 1.0
- Should updated CRF versions be required during the trial, e.g. due to a protocol amendment, they will be made by the MRC CTU and sent to all sites as a PDF via email and will supersede any previous version. Sites will be informed that they must use the new CRF version from a provided effective date. After this date has passed, all superseded CRF versions will not be accepted.
- All versions and differences between each version can be found in the CRF Version History section of the CRF Completion Guidelines document.
- Check how many pages the CRF has and that all pages are completed.

CRF headers

- PediCAP CRF headers contain boxes for providing the following information:



The **Study ID is** a five-digit number.

- The first digit of this is the site number, assigned by the MRC CTU.
- And the second four digits are allocated sequentially per site, in the order participants are randomised (i.e. the first participant receives digits 1001, the second receives 1002 and so on)

3-letter code
This is a randomly generated 3-letter code that is associated with a specific study ID.

Date Fields
Date fields should be written in the format dd-mmm-yyyy

- The day should be 2 numerical digits. If the day is less than 10 it should be prefixed by a 0, e.g. 09.
- The month should be 3 letters e.g. Jan.
- The year should be written in full 4 digit form e.g. 2020

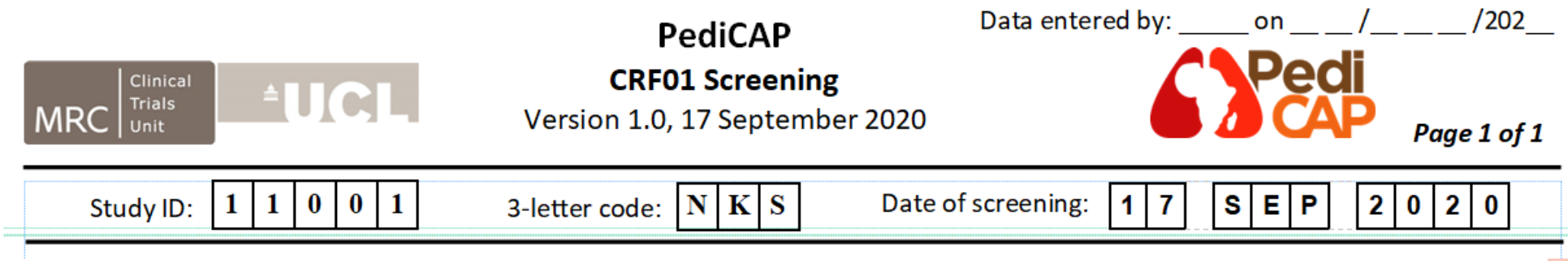
- Once consent for screening has been obtained, the patient should be added to the Trial Register and assigned a Study ID and 3-letter code.
- The Trial Register will provided prior to site activation.

CRF headers

- The list provided to sites in the Trial Register would look like this (this example is for Site 1)

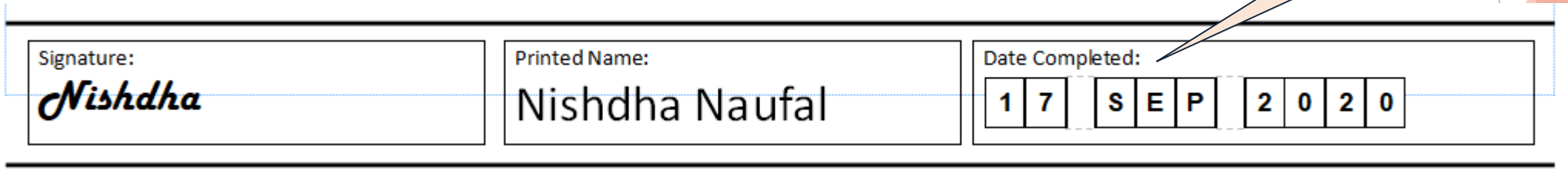
Study ID	3-letter code
11001	NKS
11002	YJT
11003	ENU
11004	RMO
11005	KMZ
11006	CAG
11007	RKR

- The header for the first patient to be screened in PediCAP at Site 1 would look like this:



CRF footers

- At the bottom of each CRF there are fields to sign off the CRF
- The person completing the CRF must print their name, sign and date the footer on **each page** of the CRF
- All site staff completing CRFs must be listed correctly on the 'Signature List and Delegation of Responsibilities' Log with 'Complete CRFs' listed within the study tasks

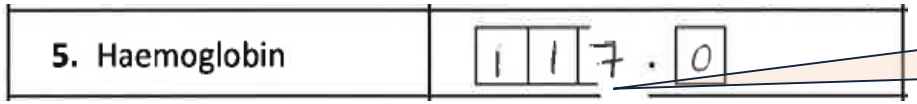


The date of CRF completion is always the date the CRF was signed and filled in.

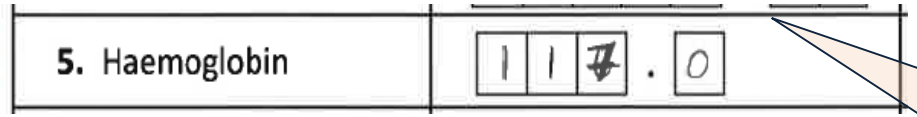
- Signing off the logs will be different – to be discussed later
- CRFs should always be signed and dated on the day of completion. The CRF should not be entered on to the database without a valid signature.

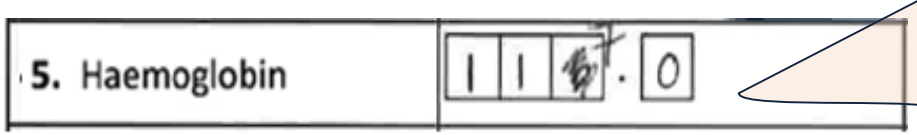
CRF corrections

- Here are some examples of correct ✓ and incorrect ✗ ways to correct or amend a CRF.

✗ 

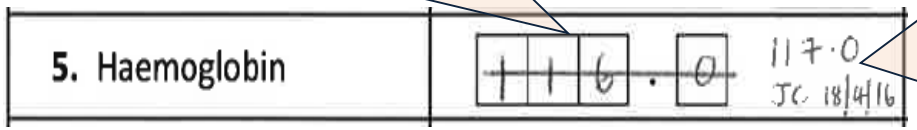
Do not use correcting fluid

✗ 

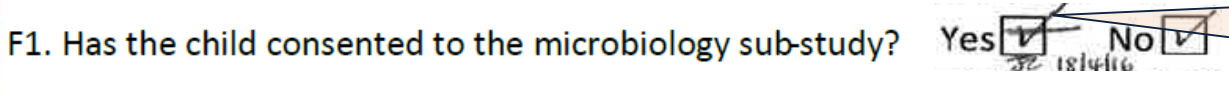
✗ 

Data should not be erased from the CRF by obscuring or overwriting the original answer

Mistakes should be crossed through with a single line, so the original data is not obscured.

✓ 

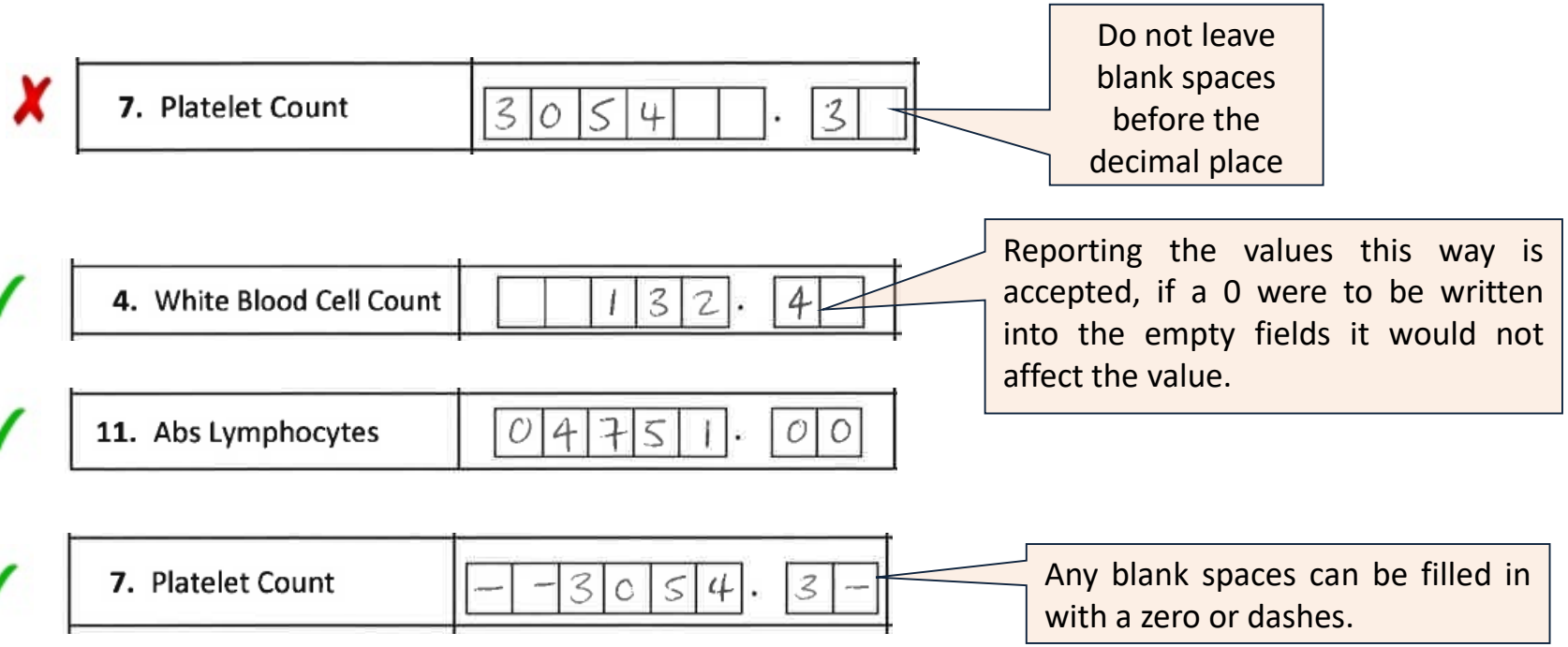
Corrections should be placed as near to the CRF question as possible e.g.. directly next to, or above if space does not permit. This change must be initialled and dated in line with GCP guidelines.

✓ 

When a mistake is made in a tick box, cross through the incorrect tick with a single line, then tick the correct option and initial and date the correction in line with GCP guidelines

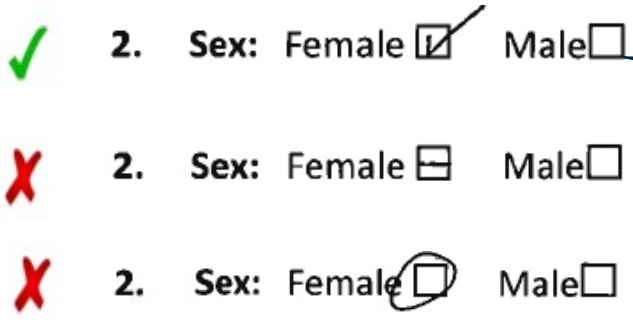
Numerical fields

- This guidance applies to numerical fields including laboratory results and measurements e.g. weight



Tick boxes

- The CRFs will contain tick boxes for data collection.



Tick boxes should be completed with a clear **tick** or a **small cross** as opposed to a line or other form of marking.

Guidance text

- During completion of the CRF's, there will always be guidance text informing whoever is completing the CRF which questions should be completed or omitted based on their responses to the lead question. This text will appear in *italic* font.
- Here are a few examples of how the guidance text will work:

SECTION G: ASSESSMENT	YES	NO
G1. Has any haematology been performed? *If 'Yes', please complete CRF04 (Clinical Investigations Form) with the most recent results when available*	☐	☐
G2. Has any biochemistry been performed? *If 'Yes', please complete CRF04 (Clinical Investigations Form) with the most recent results when available*	☐	☐
G3. Have any specimens been sent for routine microbiology culture or routine respiratory testing? *If 'Yes', please complete CRF04 (Clinical Investigations Form) with the most recent results when available*	☐	☐
G4. Has a chest x-ray been done? *If 'Yes', please complete CRF04 (Clinical Investigations Form) with the most recent results when available*	☐	☐

In this instance, the guidance text prompts you to complete a different CRF if the answer is 'Yes'.

A3. HIV status (*Please tick ONE*): Infected ☐ Exposed, uninfected ☐ Uninfected ☐ Unknown ☐

This example reminds you that you must only select one box to tick from the options.

SECTION F: MICROBIOLOGICAL SUB-STUDY

F1. Has the child consented to the microbiology sub-study? Yes ☐ No ☐ *If 'Yes', complete questions below. If 'No', go to section G.*

F1a. If 'Yes', was a peri-rectal swab taken? Yes ☐ No ☐ F1b. If taken, time: H H : M M (use 24 hour clock)

F1c. If 'No', provide reason: _____ ***Record samples taken on CRF14 Microbiology Storage***

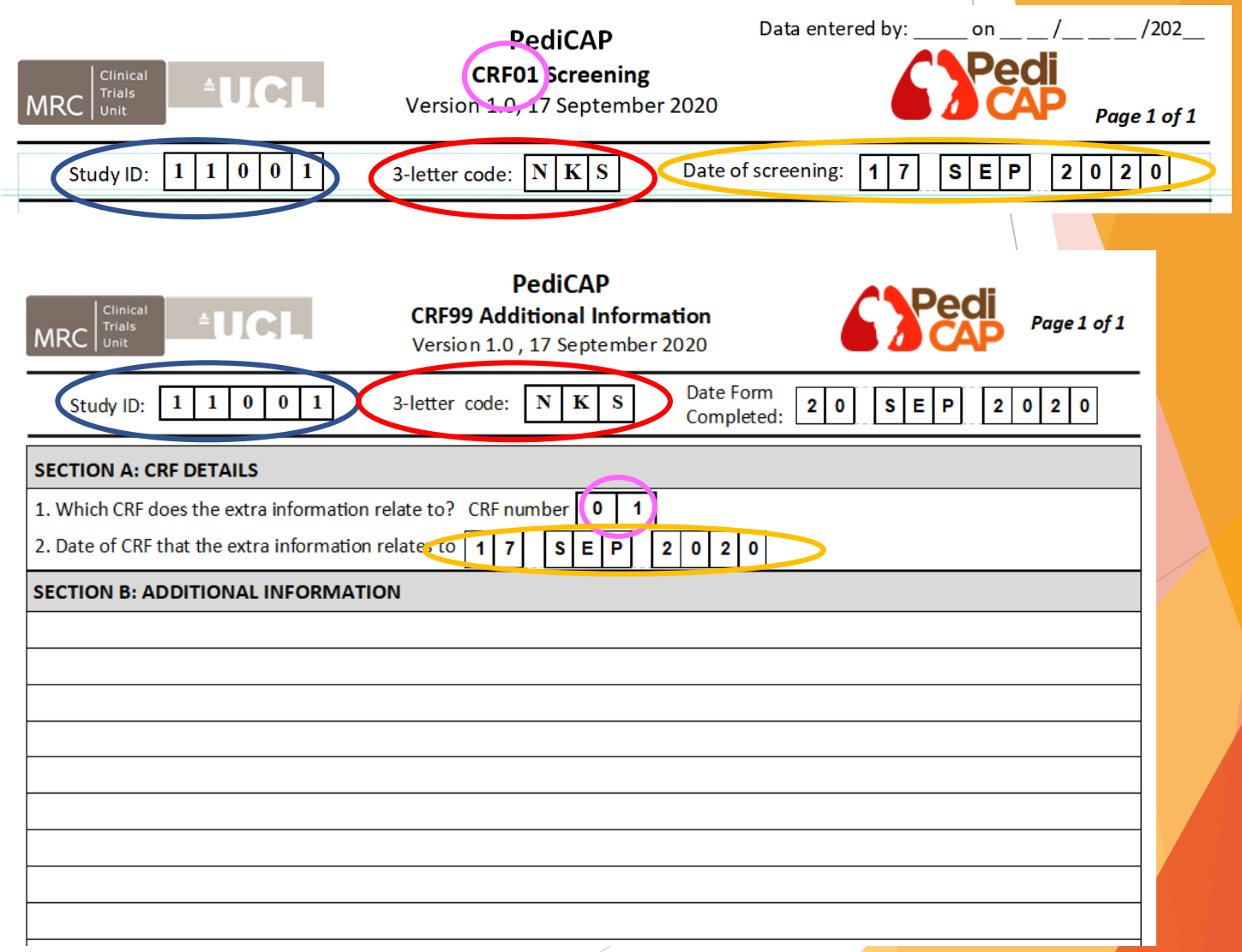
F2a. If 'Yes', was a nasopharyngeal swab taken? Yes ☐ No ☐ F2b. If taken, time: H H : M M (use 24 hour clock)

F2c. If 'No', provide reason: _____ ***Record samples taken on CRF14 Microbiology Storage***

This guidance text is there to remind you that when answering 'NO' to Question F1, a lead question, would mean you could move directly to Section G. This will help complete the CRFs in a quick and timely manner.

Additional Information – CRF 99

- If additional space for comments is required, use CRF 99 – Additional Information. This should also be added to the database.
- Complete the header on CRF 99 to indicate which CRF you are referring to.
- For example, if you would like to add additional comments about something on CRF01 Screening, you would use CRF 99 – Additional Information by completing it like this:



PediCAP
CRF01 Screening
Version 1.0, 17 September 2020

Data entered by: _____ on __ __/__ __ __/202__

Page 1 of 1

Study ID: 1 1 0 0 1 | 3-letter code: N K S | Date of screening: 1 7 S E P 2 0 2 0

PediCAP
CRF99 Additional Information
Version 1.0 , 17 September 2020

Page 1 of 1

Study ID: 1 1 0 0 1 | 3-letter code: N K S | Date Form Completed: 2 0 S E P 2 0 2 0

SECTION A: CRF DETAILS

1. Which CRF does the extra information relate to? CRF number 0 1
2. Date of CRF that the extra information relates to 1 7 S E P 2 0 2 0

SECTION B: ADDITIONAL INFORMATION

How to complete the logs

- CRF09 - Doses of Antibiotics During Admission (Trial and Non-trial)
- CRF10 - Concomitant Medications
- CRF11a - Adverse Event Log

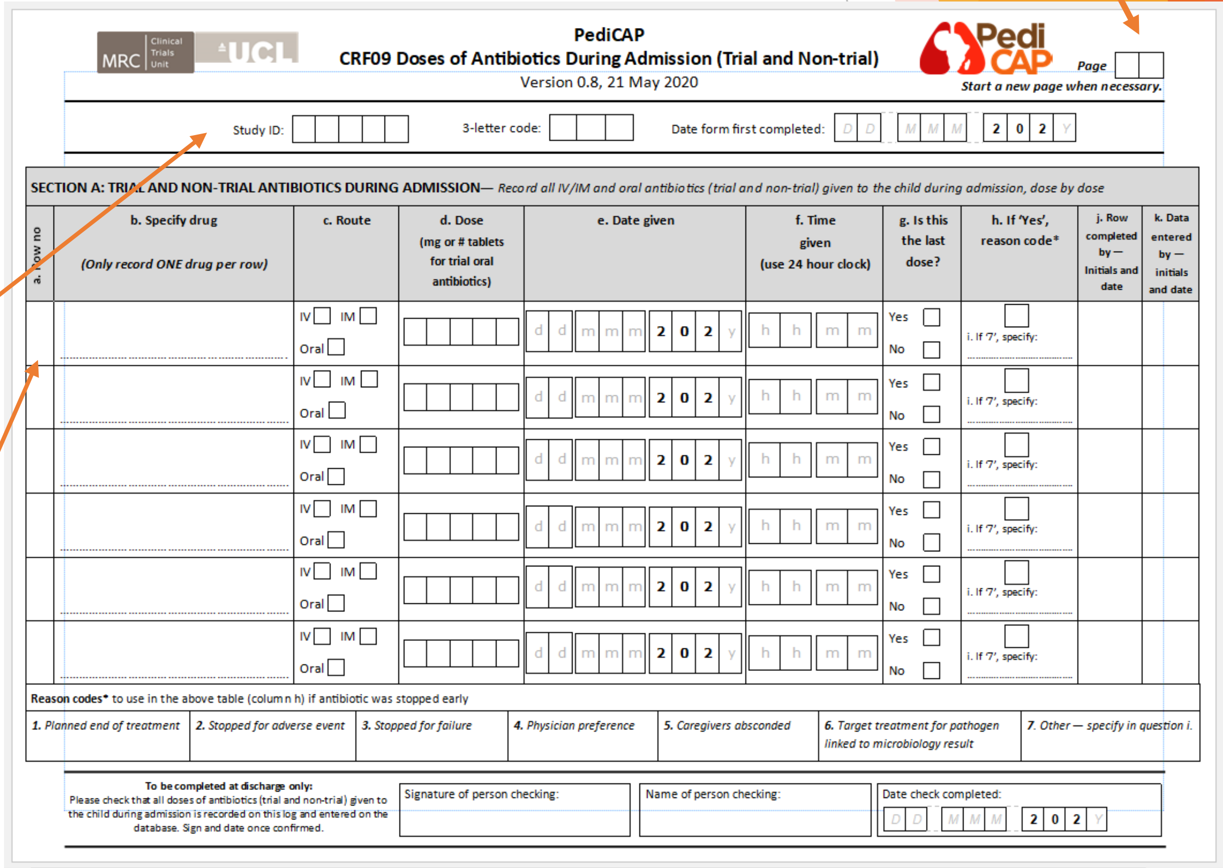
CRF09 Doses of Antibiotics During Admission (Trial and Non-trial) Completion

- **CRF09 Doses of Antibiotics During Admission (Trial and Non-trial)** should be used to record all IV/IM and oral antibiotics (trial and non-trial) given to the child during admission, dose by dose.
- This includes: **start of drug, changes to drug dose, frequency or route** and **stop of drug**

1. Complete page number (e.g. 01)

2. Complete header:
- Study ID
- 3-letter code
- Date first completed

3. In column a, enter a row number, this should be consecutive starting with row number 1.



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PediCAP
CRF09 Doses of Antibiotics During Admission (Trial and Non-trial)
Version 0.8, 21 May 2020

PediCAP | Page
Start a new page when necessary.

Study ID: | 3-letter code: | Date form first completed: D D M M M 2 0 2 Y

SECTION A: TRIAL AND NON-TRIAL ANTIBIOTICS DURING ADMISSION— *Record all IV/IM and oral antibiotics (trial and non-trial) given to the child during admission, dose by dose*

a. Row no	b. Specify drug (*Only record ONE drug per row*)	c. Route	d. Dose (mg or # tablets for trial oral antibiotics)	e. Date given	f. Time given (use 24 hour clock)	g. Is this the last dose?	h. If 'Yes', reason code*	j. Row completed by — Initials and date	k. Data entered by — initials and date
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		

Reason codes* to use in the above table (column h) if antibiotic was stopped early

1. Planned end of treatment | *2. Stopped for adverse event* | *3. Stopped for failure* | *4. Physician preference* | *5. Caregivers absconded* | *6. Target treatment for pathogen linked to microbiology result* | *7. Other — specify in question i.*

To be completed at discharge only:
Please check that all doses of antibiotics (trial and non-trial) given to the child during admission is recorded on this log and entered on the database. Sign and date once confirmed.

Signature of person checking: | Name of person checking: | Date check completed: D D M M M 2 0 2 Y

CRF09 Doses of Antibiotics During Admission (Trial and Non-trial) Completion

4. In column b, write the name of the drug e.g. amoxicillin. Only <u>**one**</u> drug per row.

5. In column c, tick the route of administration. Tick only one.

6. In column d, specify the dose. If 'IV' or 'IM' has been ticked in column c, dose should be recorded in mg. But if 'oral' has been ticked, number of tablets is sufficient.

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CRF09 Doses of Antibiotics During Admission (Trial and Non-trial)

Version 0.8, 21 May 2020

PediCAP

Page

Start a new page when necessary.

Study ID: | 3-letter code: | Date form first completed: D D M M M 2 0 2 Y

SECTION A: TRIAL AND NON-TRIAL ANTIBIOTICS DURING ADMISSION— *Record all IV/IM and oral antibiotics (trial and non-trial) given to the child during admission, dose by dose*

a. Row no	b. Specify drug *(Only record ONE drug per row)*	c. Route	d. Dose (mg or # tablets for trial oral antibiotics)	e. Date given	f. Time given (use 24 hour clock)	g. Is this the last dose?	h. If 'Yes', reason code*	j. Row completed by — Initials and date	k. Data entered by — initials and date
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		

Reason codes* to use in the above table (column h) if antibiotic was stopped early

1. Planned end of treatment	*2. Stopped for adverse event*	*3. Stopped for failure*	*4. Physician preference*	*5. Caregivers absconded*	*6. Target treatment for pathogen linked to microbiology result*	*7. Other — specify in question i.*

To be completed at discharge only:
Please check that all doses of antibiotics (trial and non-trial) given to the child during admission is recorded on this log and entered on the database. Sign and date once confirmed.

Signature of person checking: | Name of person checking: | Date check completed: D D M M M 2 0 2 Y

7. In column e and f, record the date and time the action was carried out. This may be the date and time of change, start or stop.

8. Column h requires a code to be selected from the "reason codes" below. If 'other' is selected, question i should be completed.

CRF09 Doses of Antibiotics During Admission (Trial and Non-trial) Completion

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PediCAP
CRF09 Doses of Antibiotics During Admission (Trial and Non-trial)
Version 0.8, 21 May 2020

Page ☐☐
Start a new page when necessary.

Study ID: ☐☐☐☐☐ 3-letter code: ☐☐☐ Date form first completed: D D / M M M / 2 0 2 Y

SECTION A: TRIAL AND NON-TRIAL ANTIBIOTICS DURING ADMISSION— *Record all IV/IM and oral antibiotics (trial and non-trial) given to the child during admission, dose by dose*

a. Row no	b. Specify drug (*Only record ONE drug per row*)	c. Route	d. Dose (mg or # tablets for trial oral antibiotics)	e. Date given	f. Time given (use 24 hour clock)	g. Is this the last dose?	h. If 'Yes', reason code*	j. Row completed by — Initials and date	k. Data entered by — initials and date
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		
		IV ☐ IM ☐ Oral ☐		d d m m m 2 0 2 y	h h m m	Yes ☐ No ☐	☐ i. If '7', specify:		

Reason codes* to use in the above table (column h) if antibiotic was stopped early

1. Planned end of treatment | *2. Stopped for adverse event* | *3. Stopped for failure* | *4. Physician preference* | *5. Caregivers absconded* | *6. Target treatment for pathogen linked to microbiology result* | *7. Other — specify in question i.*

To be completed at discharge only:
Please check that all doses of antibiotics (trial and non-trial) given to the child during admission is recorded on this log and entered on the database. Sign and date once confirmed.

Signature of person checking: | Name of person checking: | Date check completed: D D / M M M / 2 0 2 Y

9. Column j should be initialled and dated by the individual who completed a-h. And column k should be initialled and dated by the person completing data entry.

10. Once all the rows on page 1 has been completed, it should be checked that all rows have been completed fully and correctly and the footer should be completed before starting page 2 (if necessary)

11. Begin a new form with the page number entered as 02 and so on. On the new page, continue the row numbers from the first page e.g. if page 1 has rows 1-6 then page 2 starts with row number 7 (in column a)

CRF10 – Concomitant Medications

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PediCAP
CRF10 Concomitant Medications
Version 0.7, 20 May 2020

PediCAP

Page: ☐☐
Start a new page when necessary.

Study ID: ☐☐☐☐☐ 3-letter code: ☐☐☐ Date form first completed: D D / M M M / 2 0 2 Y

SECTION A: CONCOMITANT MEDICATIONS

Record all non-trial antibiotics outside of hospital and concomitant medication given inside and outside of hospital to the child during the study.
Do not record in-hospital antibiotics on this form.

a. Row no.	b. Specify drug *(Only record ONE drug per row)*	c. Route	d. Start date	f. Initials &date for b,c,d/e	g. Stop date	h. Still ongoing at Day 29? YES	NO	i. Initials and date for g/h	j. Data entered by – initials and date
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		
	....	IV ☐ Oral ☐ IM ☐ Other ☐	D D / M M M / 2 0 2 Y *Or e.* Unknown ☐		D D / M M M / 2 0 2 Y	☐	☐		

Please check this page is fully completed and entered on the database. Sign and date once confirmed.	Signature of person checking:	Name of person checking:	Date check completed: D D / M M M / 2 0 2 Y

CRF11a – Adverse Event Log

PediCAP
CRF11a Adverse Event Log
Version 0.11, 22 May 2020

MRC Clinical Trials Unit | UCL | PediCAP

Page ☐☐

Start a new page when necessary.

Study ID: ☐☐☐☐☐ 3-letter code: ☐☐☐ Date form first completed: D D M M M 2 0 2 Y

SECTION A: ADVERSE EVENT LOG

Details of Adverse Event

a. Row no.	b. Adverse Event (*Only record ONE AE per row*)	c. Date of onset of symptoms	d. worst grade *DAIDS v2.1 (1—5)*	e. Related-ness to antibiotics *1=Related 2=Unrelated*	f. If '1' provide antibiotic code* *Add antibiotic reason code ONLY if column e. Relatedness to antibiotics is 1*	h. Action taken *0=None 1-Dose reduction 2=Treatment delayed 3=Treatment reduction & delayed 4=Treatment stopped*	i. Is this an SAE or part of an SAE? *(If 'Yes, complete CRF08a SAE)*	j. Was a concomitant medication given to treat the AE? *(If 'Yes', complete CRF10 Concomitant Medications)*	k. Status *1 = Resolved 2 = Resolving 3 = Not Resolved 4 = Resolved with sequaele 5 = Chronic/ Stable 6 = Fatal 7= Unknown*	l. Date of resolution *Add a Date of resolution ONLY if column k. Status was 1, 4, 5 or 6*	m. Row completed by - Initials and date	n. Data entered by - initials and date
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		
		D D M M M 2 0 Y Y	☐	☐	☐ *g. If '8' specify:*	☐	Yes ☐ No ☐	Yes ☐ No ☐	☐	D D M M M 2 0 Y Y		

Antibiotic reason codes* to use in the above table (column f) if event is related to antibiotics

1. Amoxicillin	*2. Co-amoxiclav*	*3. Benzylpenicillin*	*4. Ampicillin*	*5. Gentamicin*	*6. Ceftriaxone*	*7. Cefotaxime*	*8. Other — specify in question g.*

Please check this page is fully completed and entered on the database. Sign and date once confirmed.	Signature of person checking:	Name of person checking:	Date check completed: D D M M M 2 0 2 Y

CRF storage

- All CRFs must be kept locked away at all times when not in use.
- The cabinets where the CRFs are stored must have restricted access. Rooms where the cabinets are stored should have restricted access wherever possible.
- Each patient should have a folder where the original CRFs should be filed.
- Copies of the CRFs should be filed in the medical notes (where this is not possible it must be discussed with the MRC CTU trial team in advance).

Database

Database Summary

- Database Overview
- Database Release Phases
- Phase 1 Deliverables
- Phase 2 Deliverables
- Database Access
- Data Entry and Query Training
- Database Role
- Database Log-In Screen
- Switchboard
- Randomisation of an ineligible patient
- Randomisation of an eligible patient
- Data Entry Timelines
- Query Module
- Viewing Queries
- Managing Queries

Database Overview

- PediCAP will be using the **CACTUS** (Collaborative Academic Clinical Trials User System) database developed by MRC CTU.
- PediCAP trial is **remote data capture (rDC)** i.e. all sites perform their own randomisation, data entry and query resolution.

Except Form 08b and 11b

- **Internet Explorer**  is the preferred browser as it has optimal compatibility for using the database.
- MRC CTU staff will also be able to randomise participants if a site is unable to do so e.g. poor internet connection at site preventing access to the database.

Database Release Phases

- Three main phases planned:
- **Phase 1** – estimated delivery date is mid-October 2020.
- **Phase 2** – still to be scheduled for programming.

Phase 1 Deliverables

- CRF01 Screening
- CRF02 Baseline
- CRF03 Randomisation
- CRF04 Clinical Investigations
- CRF05 Follow-Up In-hospital
- CRF06 Follow-Up Post Discharge
- CRF07 Antibiotic Acceptability
- CRF08a SAE
- CRF08b Medical Review
- CRF09 Doses of Antibiotics During Admission (Trial and Non-Trial)
- CRF10 Concomitant Medications
- CRF11a Adverse Event Log
- CRF11b Adverse Event Log – MedDRA Coding
- CRF17 Early Stopping of Trial Participation

- Randomisation System
- Individual Visit Schedule Report

Phase 2 Deliverables

- CRF12 PK Sub-Study Sampling
- CRF13 PK Storage Log
- CRF14 Microbiology Storage Form
- CRF15 Household Socioeconomic
- CRF16 Cost to Families for Care and Treatment
- CRF99 Additional Information

- Accrual Report
- Individual Patient Monitoring Report
- Entered CRFs Report

Database Access

- Access to the PediCAP CACTUS Database is only granted to authorised members of site staff, once database training has been completed. There are two stages to database training:
  - CACTUS Database Training
  - PediCAP Data Entry & Query Training
- If a site staff is required to perform data entry and/or resolve queries, the ‘Complete CRFs’ and/or ‘Query completion’ must be listed as delegated task for that staff member on the PediCAP Delegation Log
- A completed copy of the PediCAP Delegation Log should be returned to the MRC CTU electronically via email following the SIV, and every time a new member of data entry staff joins the site.
- The PediCAP DM at MRC CTU will then contact the relevant site staff to organise their database training.

PediCAP Data Entry & Query Training

- Before receiving access to the live PediCAP database, all users must complete database/data entry training. The training process will ensure users are familiar with how to enter and manage data in the PediCAP database, and will identify if there are any outstanding training needs.
- User accounts are assigned externally by the PediCAP DM or TM at MRC CTU
- During the training you will:
  - Enter data for two different dummy patients
  - Experience automated data validations that the database will perform (e.g. missing form)
  - Respond to data queries raised by the MRC CTU team
- The entered data is then checked by the PediCAP DM to make sure the data has been entered correctly and the queries have been dealt with as described in the training document.

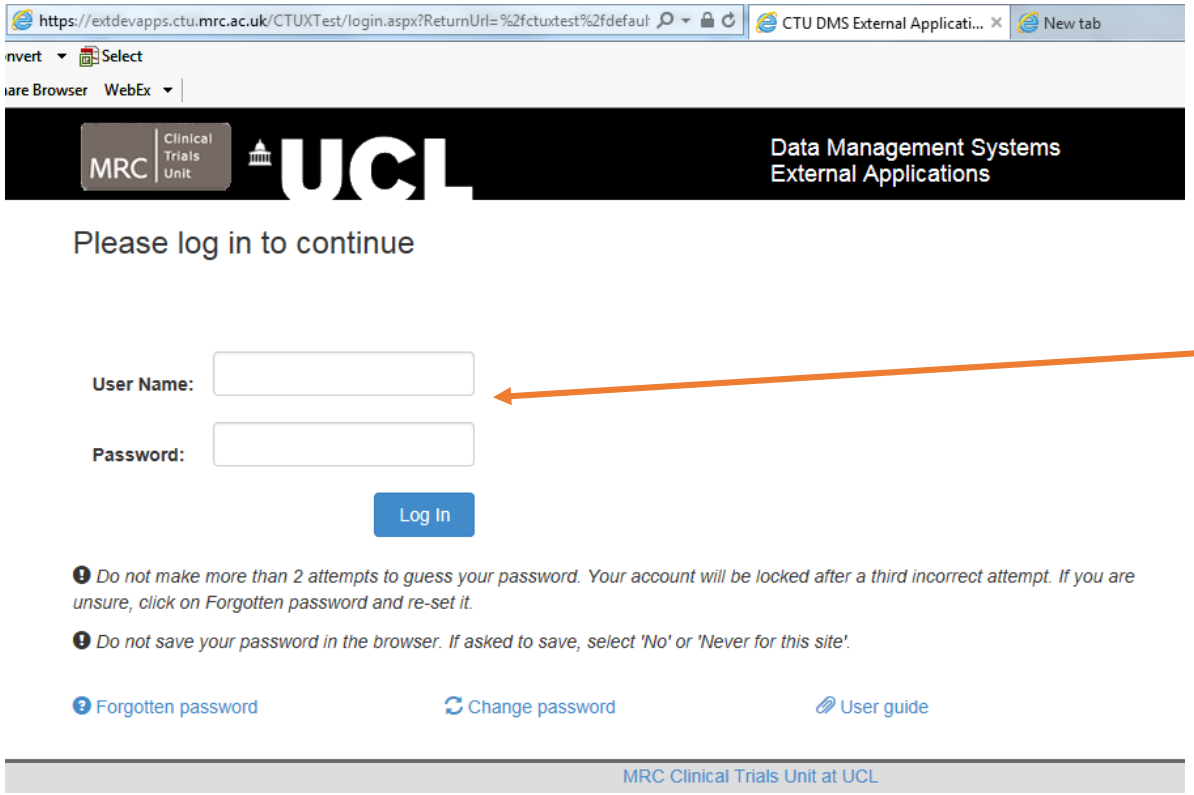
Database Role

- All data entry staff will be assigned a “Data Manager” role once database training has been completed successfully

  - Data Manager: Can view, add, edit all CRFs except Form08b and Form11b. Add, edit queries; randomise. This role is intended for site staff, and will normally only be granted with access to data for that site.

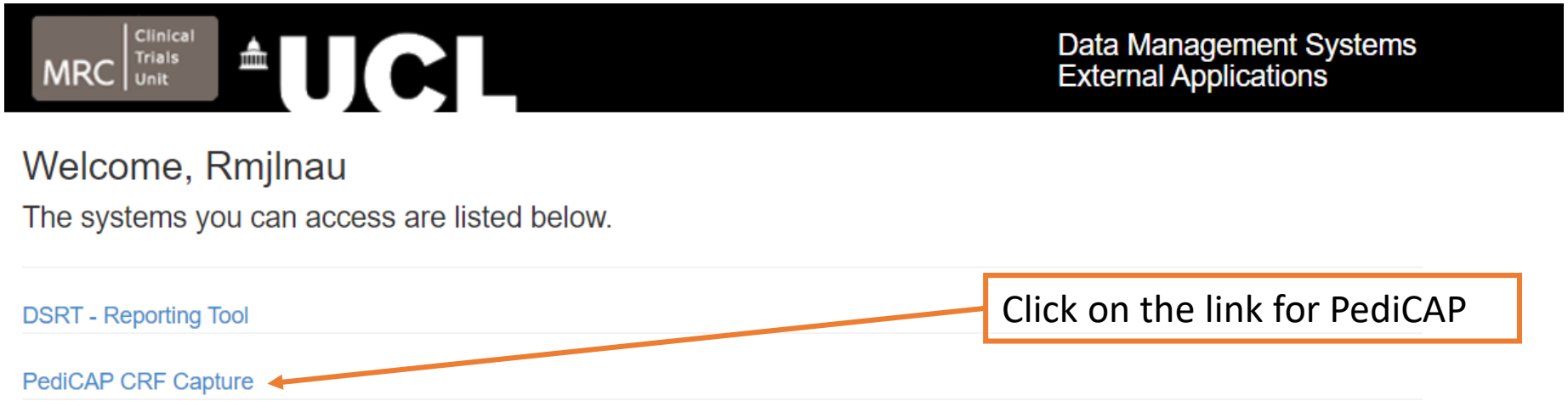
Database Log-In Screen

- https://extdevapps.ctu.mrc.ac.uk/ctuxtest/Login.aspx

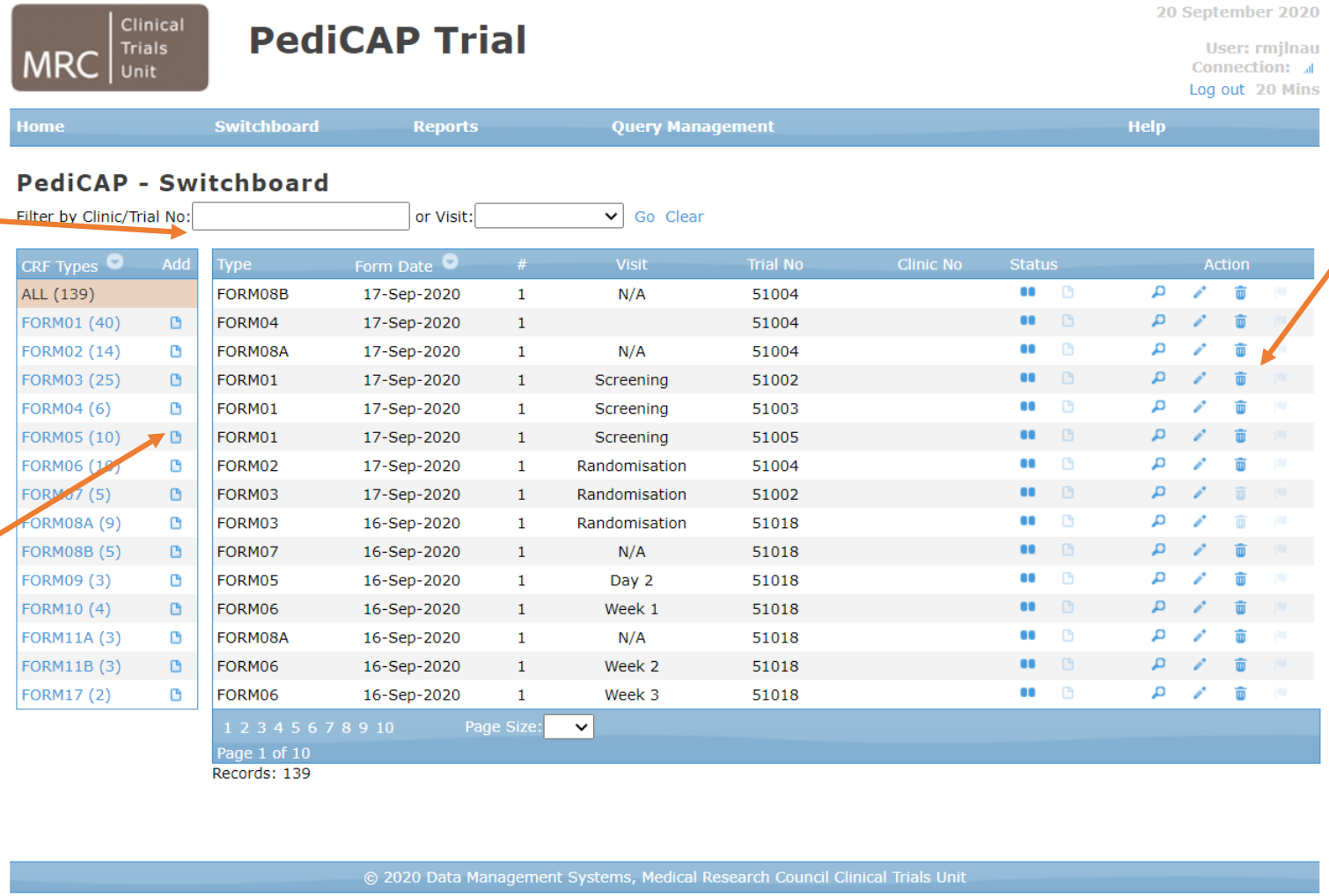


Temporary password received via email is provided for the first entry only and will expire after initial entry.

Database Log-In Screen



Switchboard



Search for specific Study ID using this field

List of all forms available shown by form number and name. They can be added by clicking on the 'Add' icon

'View, edit and delete' Forms (depending on user's profile)

View a CRF by selecting the 'magnifying glass' symbol.

Edit a verified CRF by selecting the 'pencil' symbol.

Delete a CRF by selecting the 'trash' symbol

Randomisation of an ineligible patient

- Form 01 Screening and Form 03 Randomisation should be completed on the database in order to randomise a patient.
- Form 01 Screening must be completed before Form 03 Randomisation.
- Validation checks at randomisation will cross check with Form 01 Screening and if this form is not entered or any eligibility criteria on this Form or on Form 03 is not met, the computer will not randomise this patient.
- Example - a patient who has a CRP level of <10 is randomised. This makes them ineligible to join the study. The database should **NOT** allow this randomisation to take place.

Randomisation of an ineligible patient

MRC Clinical Trials Unit

PediCAP Trial

Home | Switchboard | Reports | Query Management

FORM01: Screening (verified)

Page 1

Study ID* 21015 | 3-letter code* TTN | Date of screening* 20-Sep-2020

SECTION A: ADMISSION AND SCREENING

A1. Time of screening (Hours) 02 (Minutes) 02

A2. Date of admission 20-Sep-2020

A3. Time of admission (Hours) 01 (Minutes) 00

A4. Date of Birth 07-Apr-2020

SECTION B: DIAGNOSIS

Does the child have

B1. Severe pneumonia judged to require at least 24h of intravenous antibiotics by the treating physician Yes

SECTION C: SYMPTOMS AND SIGNS

C1. Difficulty breathing Yes

C2. Chest indrawing Yes

STEP 1: Form 01 questions completed correctly so far

SECTION E: CONSENT AND CRP TEST

E1. Signed parent/carer consent for CRP test Yes

E2. C-reactive protein (CRP) test >10mg/l at screening Yes

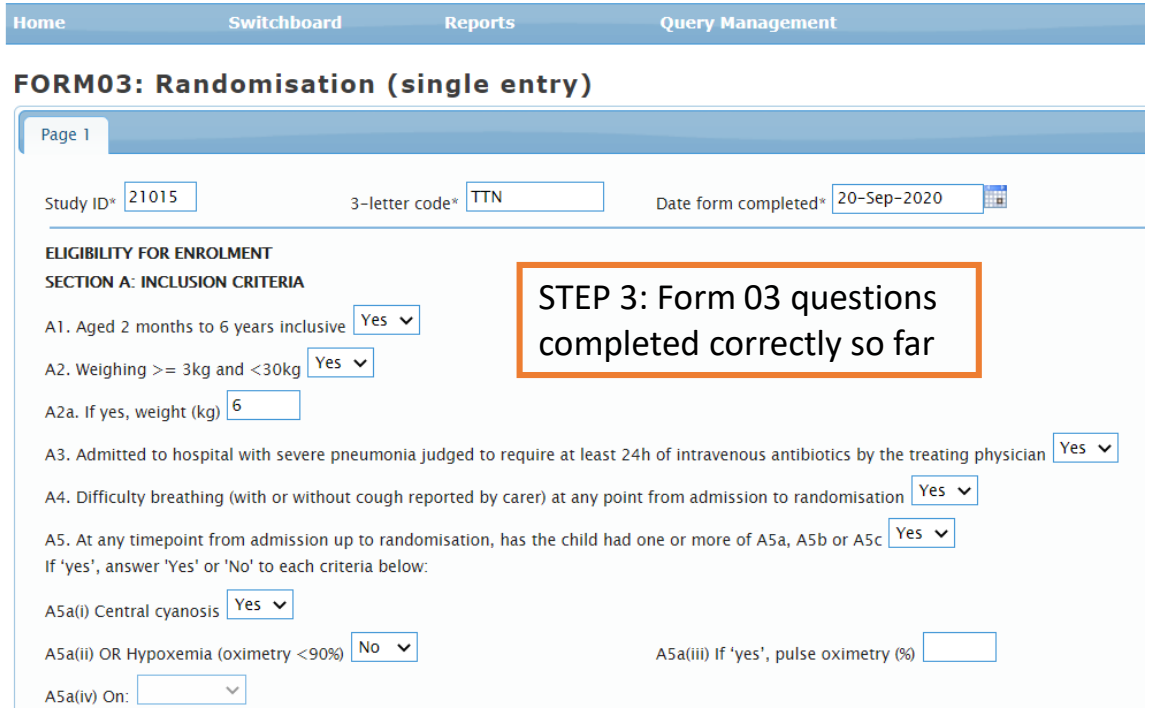
E2a. Time of test (Hours) 02 (Minutes) 01

E2b. Result (mg/l) <10

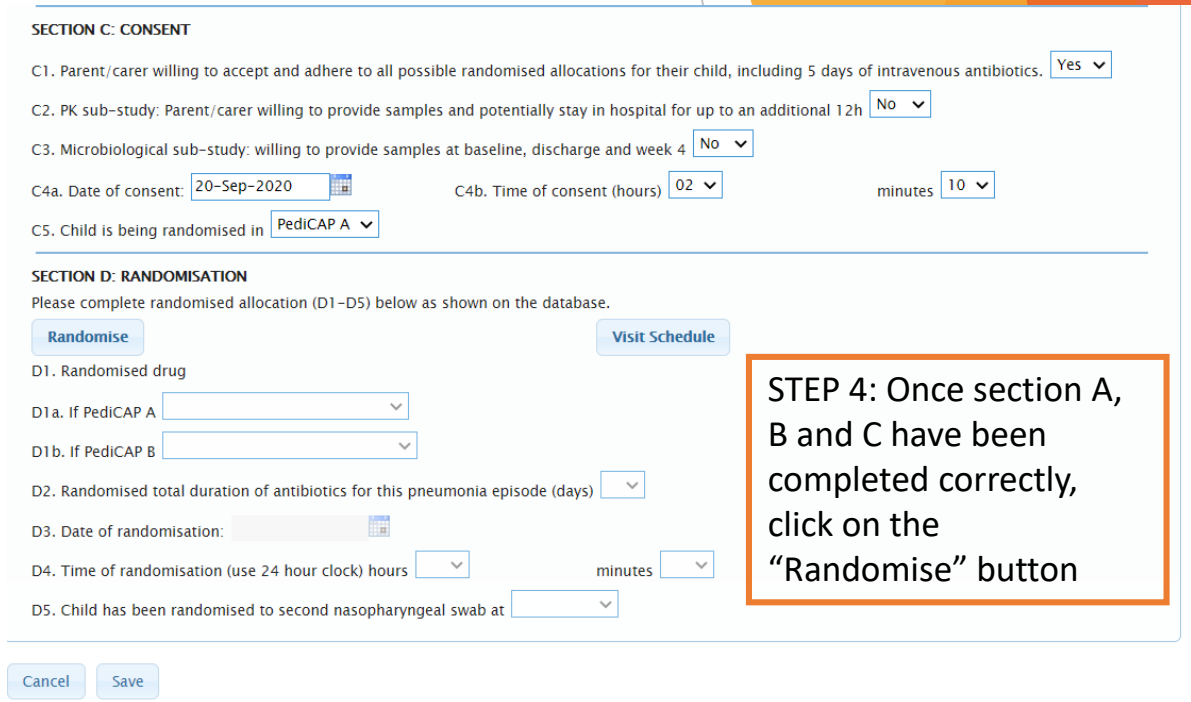
Cancel Save

STEP 2: E2b collects CRP result, and <10 is selected.
Click "Save".
Form 01 should save.

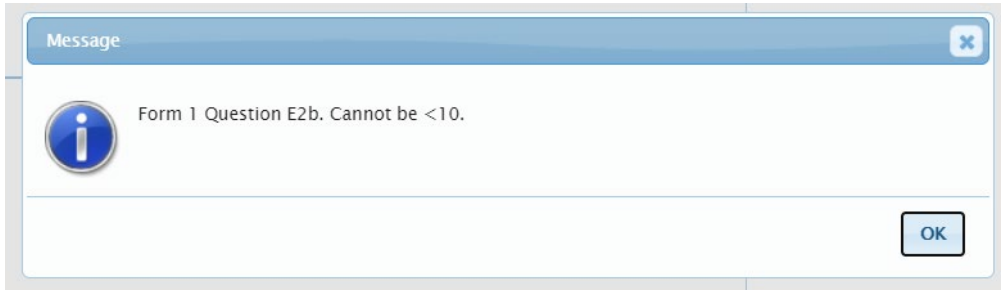
Randomisation of an ineligible patient



STEP 3: Form 03 questions completed correctly so far



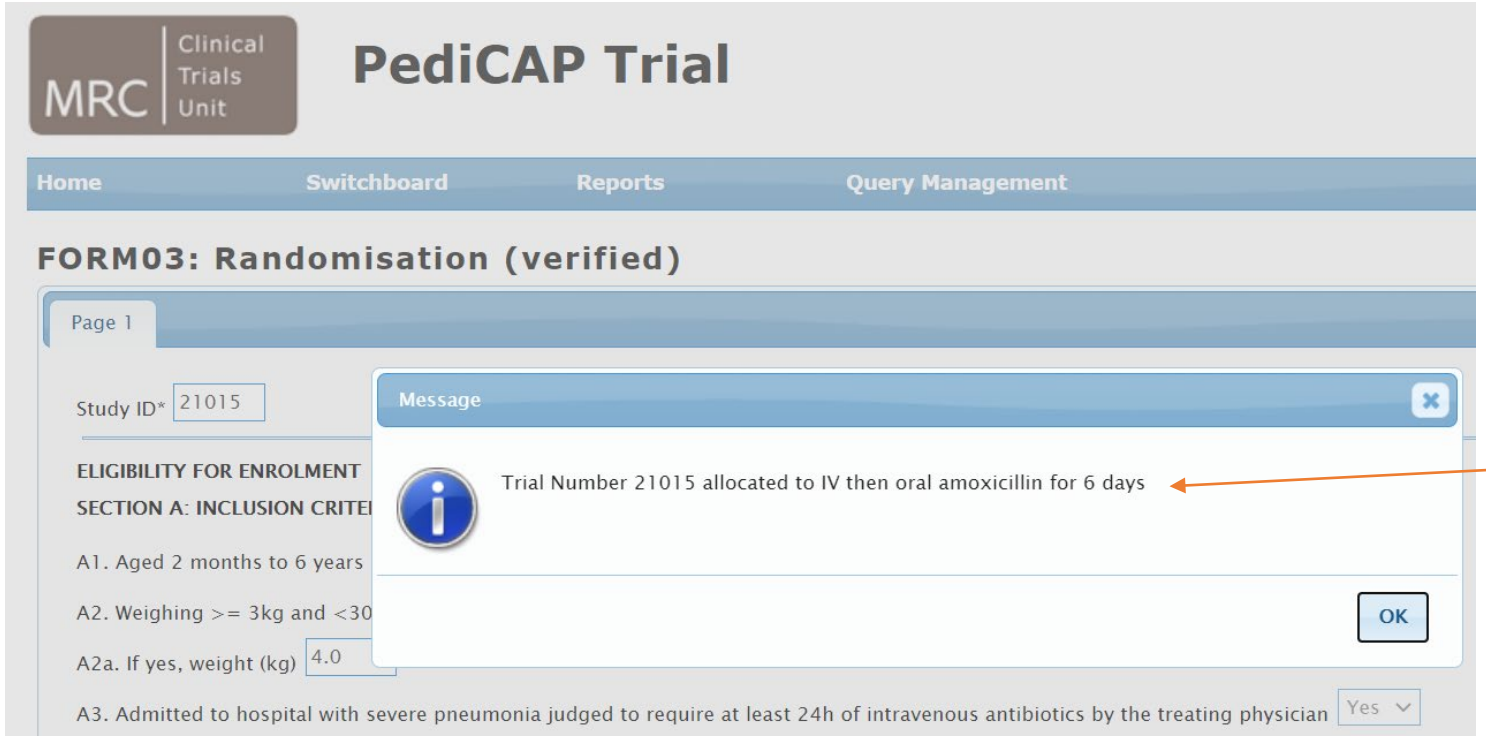
STEP 4: Once section A, B and C have been completed correctly, click on the "Randomise" button



STEP 5: Error message will pop up, and patient will **NOT** be randomised.

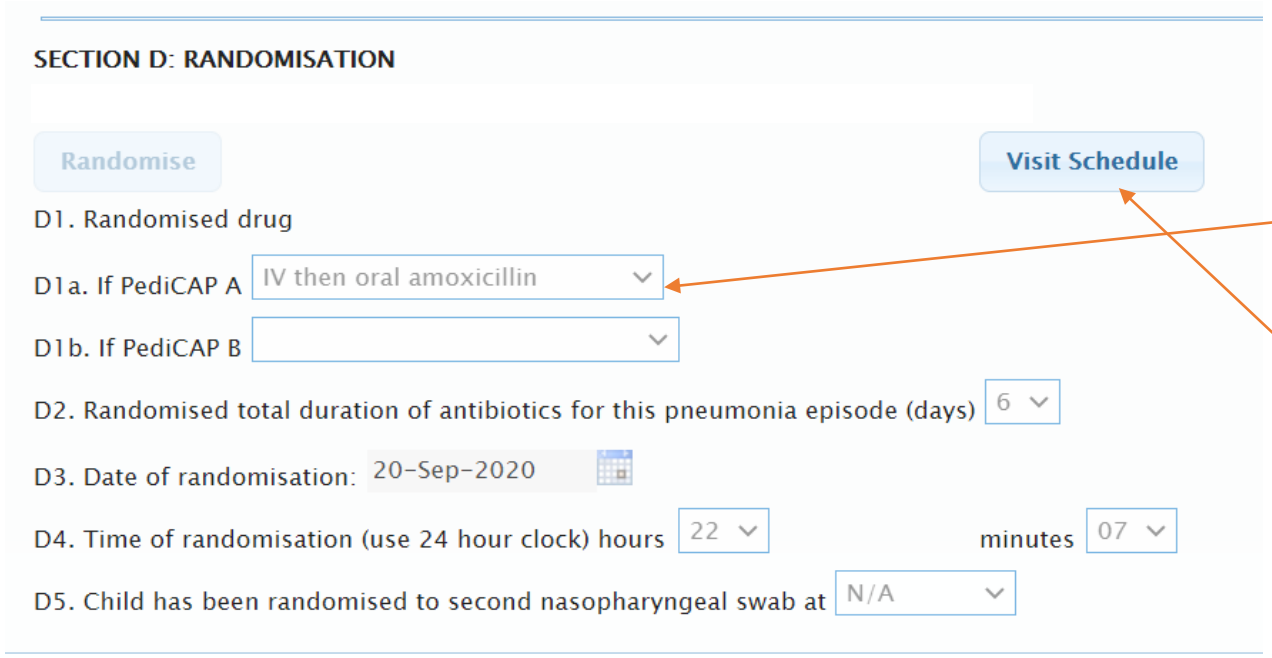
Randomisation of an eligible patient

- A patient meeting all inclusion criteria and none of the exclusion criteria is randomised.



Patient successfully randomised and trial allocation shown on screen.

Randomisation of an eligible patient



Section D automatically completed by the database if a patient is successfully randomised.

An Individual Visit Schedule will be generated at randomisation.

SECTION D: RANDOMISATION

☞ ***Please complete randomised allocation (D1-D5) below as shown on the database.***

D1. Randomised drug: *D1a. If PediCAP A:* IV only ☐ IV then oral amoxicillin ☑ IV then oral co-amoxiclav 7:1 ☐

D1b. If PediCAP B: IV then oral co-amoxiclav 4:1 ☐ IV then oral co-amoxiclav 14:1 ☐

D2. Randomised total duration of antibiotics for this pneumonia episode *(days):* 4 ☐ 5 ☐ 6 ☑ 7 ☐ 8 ☐

D3. Date of randomisation: 2 0 S E P 2 0 2 0 D4. Time of randomisation: 2 2 : 0 7 (use 24 hour clock)

D5. Child has been randomised to second nasopharyngeal swab at: Discharge ☐ Week 4 ☐ N/A ☑

The individual performing the randomisation should complete Section D of CRF03 Randomisation as shown on the database

Individual Visit Schedule

- An Individual Visit Schedule will be generated at randomisation. This can be downloaded and printed.
- The schedule should be used to plan the patient's visits with the parent/carer.

PediCAP Individual Visit Schedule

rmjlnau 20-Sep-2020 21:24

Study ID: 21015

3-Letter Code: TTN

Centre : King Edward VIII Hospital (Durban)

Date of First IV dose: 20 September 2020

Randomisation Date: 20 September 2020

Patient has been randomised to: IV then oral amoxicillin for 6 days

Visit	Target Date
Day 1	20 September 2020
Day 2	21 September 2020
Day 3	22 September 2020
Day 4	23 September 2020
Day 5	24 September 2020
Day 6	25 September 2020
Day 7	26 September 2020
Day 8	27 September 2020
Day 9	28 September 2020

Week Number	Window Open	Window Closed
Week 1	27 September 2020	29 September 2020
Week 2	04 October 2020	06 October 2020
Week 3	11 October 2020	13 October 2020
Week 4	16 October 2020	23 October 2020

Data Entry Timelines – CRFs completed at each study visit

Visit	Day	CRF Number	CRF Name	Submission Timeline
Screening	1	CRF01	Screening	Immediately
Randomisation	1	CRF02 CRF03 CRF04 CRF15	Baseline Randomisation Clinical Investigations Household Socioeconomic	CRF03 must be entered immediately to randomise a participant. CRF02, CRF04 and CRF15 must be entered within 3 working days
In-Hospital Follow-Up Visits	Daily until discharge	CRF05 CRF04 CRF09	Follow-up – In hospital Clinical Investigations Doses of Antibiotics During Admission	Within 1 working week of the study visit
Discharge	Day of discharge	CRF05 CRF07	Follow-up – In hospital Antibiotic Acceptability^	Within 1 working week of the study visit
Week 1	8-10	CRF06 CRF04 CRF07	Follow-up - Post Discharge Clinical Investigations Antibiotic Acceptability^	Within 1 working week of the study visit
Week 2	15-17	CRF06 CRF04 CRF07	Follow-up - Post Discharge Clinical Investigations Antibiotic Acceptability^	Within 1 working week of the study visit
Week 3	22-24	CRF06 CRF04	Follow-up - Post Discharge Clinical Investigations	Within 1 working week of the study visit
Week 4	27-34	CRF06 CRF04 CRF16	Follow-up - Post Discharge Clinical Investigations Cost to Families for Care and Treatment	Within 1 working week of the study visit

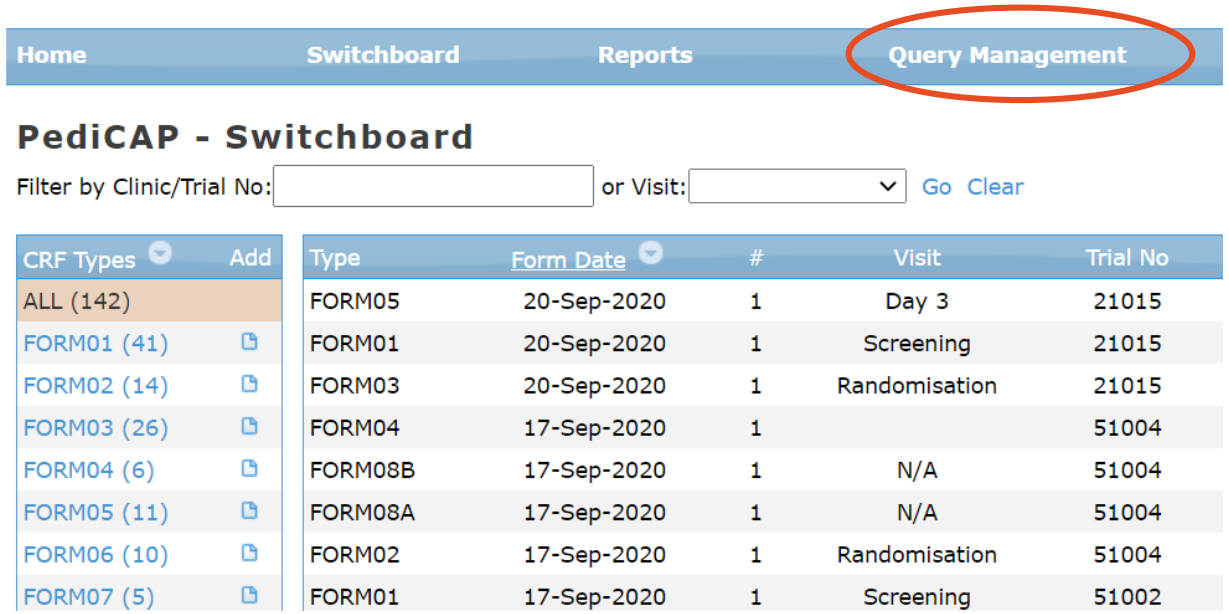
^Antibiotic Acceptability should be completed for patients who have stepped down to oral medication. Only complete at week 2 if they had not finished their treatment at the last assessment.

Data Entry Timelines – Other CRFs

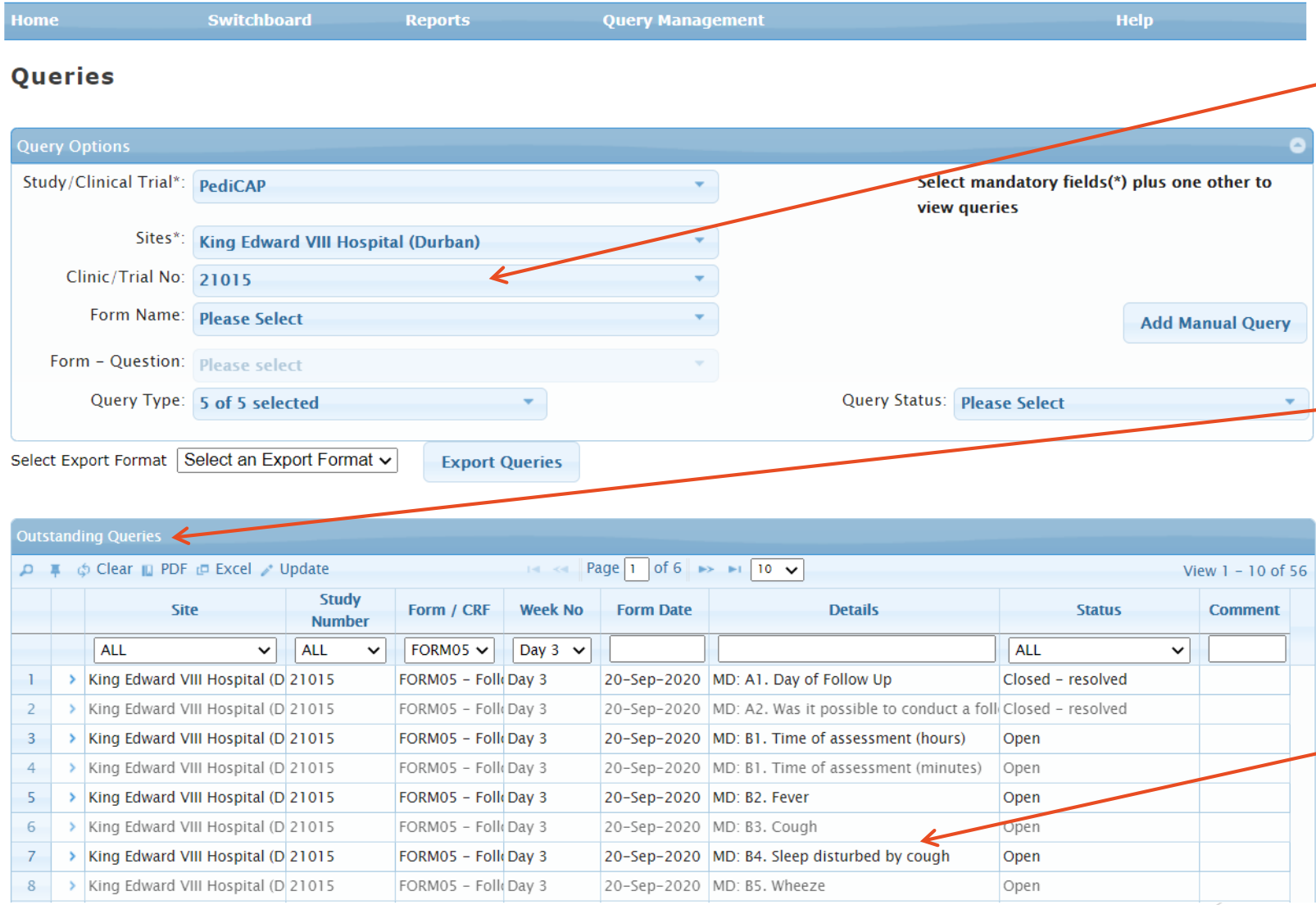
CRF Number	CRF Name	Submission Timeline
CRF08a	Serious Adverse Events and Notable Events	Submit paper CRF via email within 1 working day of site awareness Data entry within 3 working days of paper CRF submission
CRF10	Concomitant Medications	As soon as possible within 1 working week of awareness of a change
CRF11	Adverse Event Log	As soon as possible within 1 working week of site awareness
CRF17	Early Stopping of Trial Participation	As soon as possible within 1 working week
CRF99	Additional Information	At the same time as the CRF the additional information is referring to

Query Module

- The database has been designed to perform programmed data checks on verified forms.
- The database currently checks for missing data (MD) and data inconsistencies (I).
- If errors are found, the database generates queries which are written to a query table in the database.
- Queries can be viewed in the ‘Query Management’ module on the switchboard.



Viewing Queries



Filter data based on 'Clinical/Trial No.', 'Form Name' and one other field in the 'Query Options' section to view existing queries.

Queries which match the specified criteria are displayed in the 'Outstanding Queries' grid. The 'details' field shows query type:

- MD – Missing Data
- MF – Missing Forms
- MV – Missed Visits
- I – Inconsistencies
- MQ – Manual Query

The history of a query selected in the 'Outstanding Queries' section, is displayed in the 'Query History' section. The history can also be viewed by clicking on the > sign to the left of a selected query.

Managing Queries

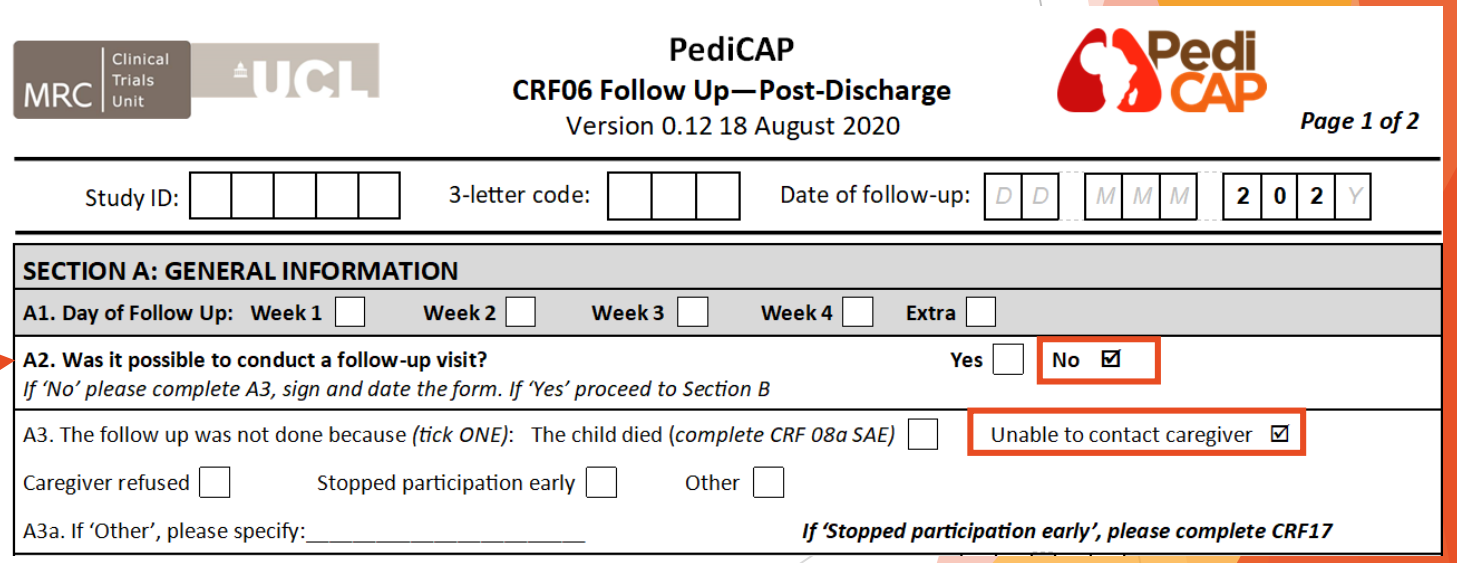
- There are two types of queries:
  - Automatic – generated by the database from verified forms
  - Manual – generated by MRC CTU for obvious data mistakes on forms in the database or queries sent through by trial statistician. These will be sent to site via email.
- When data entry records are updated, the database re-runs the programmed checks and any existing queries are updated accordingly (e.g. if missing data is added to the form, the database will automatically close the query).
- The query management screen can be used to record and track the history of queries from when they open to when they are resolved, whether they are automatic or manual.
- There is an audit trail.

Data Query Report

- The Data Query Report, showing all outstanding data queries, are sent to sites electronically in PDF format every 2 weeks (report generated on a Monday and sent to sites same day)
- Sites are expected to answer the queries on the database and return the completed Data Query Report to the CTU within 10 working days.
- If any queries are unclear, the site should contact MRC CTU via email for clarification. Sites should never ‘guess’ how to resolve a query.
- Some queries may be emailed to sites by MRC CTU rather than added to the database. These will usually be related to a safety event, or from checks performed by the statistician that cannot easily be added to the query module of the database.
- The MRC CTU may also email a site regarding a query on the database that they feel is important, or that they feel needs clarification. Queries highlighted as important or needing an urgent response should always be prioritised over addressing standard queries raised automatically on the database.

Missing Forms Report

- The Missing Forms Report, showing all outstanding forms, are sent to sites electronically in PDF format every 2 weeks (report generated on a Monday and sent to sites same day)
- Missing forms should be added to the database by within 5 working days of the report being sent to sites (i.e. on a Friday)
- If a visit has not been attended, the follow-up CRF should still be submitted, confirming that the visit did not take place in section A.



MRC Clinical Trials Unit | UCL

PediCAP

CRF06 Follow Up—Post-Discharge

Version 0.12 18 August 2020

PediCAP

Page 1 of 2

Study ID: | 3-letter code: | Date of follow-up: D D M M M 2 0 2 Y

SECTION A: GENERAL INFORMATION

A1. Day of Follow Up: **Week 1** ☐ **Week 2** ☐ **Week 3** ☐ **Week 4** ☐ **Extra** ☐

A2. Was it possible to conduct a follow-up visit? **Yes** ☐ **No** ☑

If 'No' please complete A3, sign and date the form. If 'Yes' proceed to Section B

A3. The follow up was not done because *(tick ONE)*: The child died (*complete CRF 08a SAE)* ☐ Unable to contact caregiver ☑

Caregiver refused ☐ Stopped participation early ☐ Other ☐

A3a. If 'Other', please specify:_____ ***If 'Stopped participation early', please complete CRF17***

Key Contacts

- mrcctu.pedicap@ucl.ac.uk
- For all general queries relating to the CRFs and database

- Nishdha Naufal – PediCAP Data Manager
- n.naufal@ucl.ac.uk

- Emily Dennis – PediCAP Trial Manager
- emily.dennis@ucl.ac.uk

Questions?