PediCAP

Protocol Deviations, ISF and Monitoring

v1.0 24-Sep-2020

EDCTP

PediCAP is part of the EDCTP2 programme supported by the European Union under Grant Agreement RIA2017MC - 2023.

Protocol Deviations

Protocol Deviation Definition

A protocol deviation is defined as any change, divergence, or departure from study design or procedures as described in the approved study protocol.

Identifying Protocol Deviations

- In PediCAP, protocol deviations may be identified:
  - by the site
  - by monitoring
  - by the MRC CTU through central monitoring

Site Protocol Deviation Log

- All protocol deviations should be recorded on the PediCAP Site Protocol Deviation Log.
- The deviation should be classified as either critical, major or minor.
- You will be requested to send MRC CTU a copy of the log approximately every 3 months.

Site Protocol Deviation Log

Site name:	Principal Investigator:

Site protocol deviation number	Study ID	Details of deviation	Classification (Critical, Major, Minor)	Actions taken	Date Investigator aware of deviation	If critical or major, date reported to MRC CTU	If critical or major, date CAP report completed	Initials

Protocol Deviation Classification

Classification	Definition
Critical	Significantly impacts the completeness, accuracy and/or reliability of study results, or significantly impacts the subjects' rights, safety and/or well-being.
Major	Could potentially significantly impact the completeness, accuracy and/or reliability of study results, or the subjects' rights, safety and/or well-being.
Minor	Does not impact the completeness, accuracy and/or reliability of study results, or the subjects' rights, safety and/or well-being.

- Example PediCAP protocol deviations and classifications are listed in the Manual of Operations.

Notifying MRC CTU

- Sites should notify MRC CTU of all critical or major deviations by emailing a PediCAP Protocol Deviation Notification Form.
- Critical deviations should be reported within 1 working day of the investigator becoming aware of the deviation.
- Major deviations should be reported within 1 week.
- If you are unsure of the classification, please contact MRC CTU as soon as possible so that they can advise on the appropriate classification.

PediCAP Protocol Deviation Notification Form

Study Title	PediCAP
Site Name	
Site PI	
Date of Protocol Deviation	
Date Protocol Deviation Identified	
Date sent to MRC CTU	
Protocol Version	

Site's grading assessment	Major/Critical
Protocol Deviation Description	
Please provide a description of the deviation:	

Name of site staff member reporting the deviation:	
Signature:	
Date:	

Corrective Action Plan (CAP) Report

- Upon receipt of a Protocol Deviation Notification Form, MRC CTU will work with your site to complete a CAP report.
- This will include any corrective actions to prevent a re-occurrence of the deviation.
- CAP reports should be completed and signed by the individual with the most knowledge of the deviation, and signed the PI.

PediCAP Corrective Action Plan (CAP) Report

Study Name	PediCAP		
Sponsor	PENTA		
Chief Investigator	Prof Michael Sharland		
Trial Site			
Principal Investigator			
Product name	*If applicable*		
Batch number	*If applicable*		
Expiry date	*If applicable*		
Key issue/reason for report			
Classification of deviation	Critical ☐ Major ☐		
Date deviation occurred		**Site Deviation Number**	

Summary: For Details of deviation. Describe in chronological sequence, start at the most appropriate point in relation to the event. Use factual statements and descriptions; include dates, times and names as appropriate. Continue on a separate sheet as necessary and staple to this copy.

1. **Details of Deviation**
2. **Immediate Actions Completed**
3. **Root Cause Analysis**
4. **Action Plan**
5. **When will the corrective actions highlighted in the action plan be implemented?**

Outcome:

Investigator Site File (ISF)

Creating an ISF

- Following the Site Initiation Visit, MRC CTU will email a site initiation pack containing essential documents for site opening.
- These documents should be printed and used to create an Investigator Site File (ISF).
- You will be sent an ISF Index template, which should be used to form the structure of the file.
- The ISF should be maintained from site opening to site closure, when it will be archived.

Initial ISF Self-Assessment Form

- An Initial Investigator Site File Self-Assessment Form will be sent in the induction pack.
- This form acts as a checklist for all the documentation that should be on file prior to site opening.
- MRC CTU will require copies of many of these documents after they have been completed. A list of these documents will be sent with the induction pack.

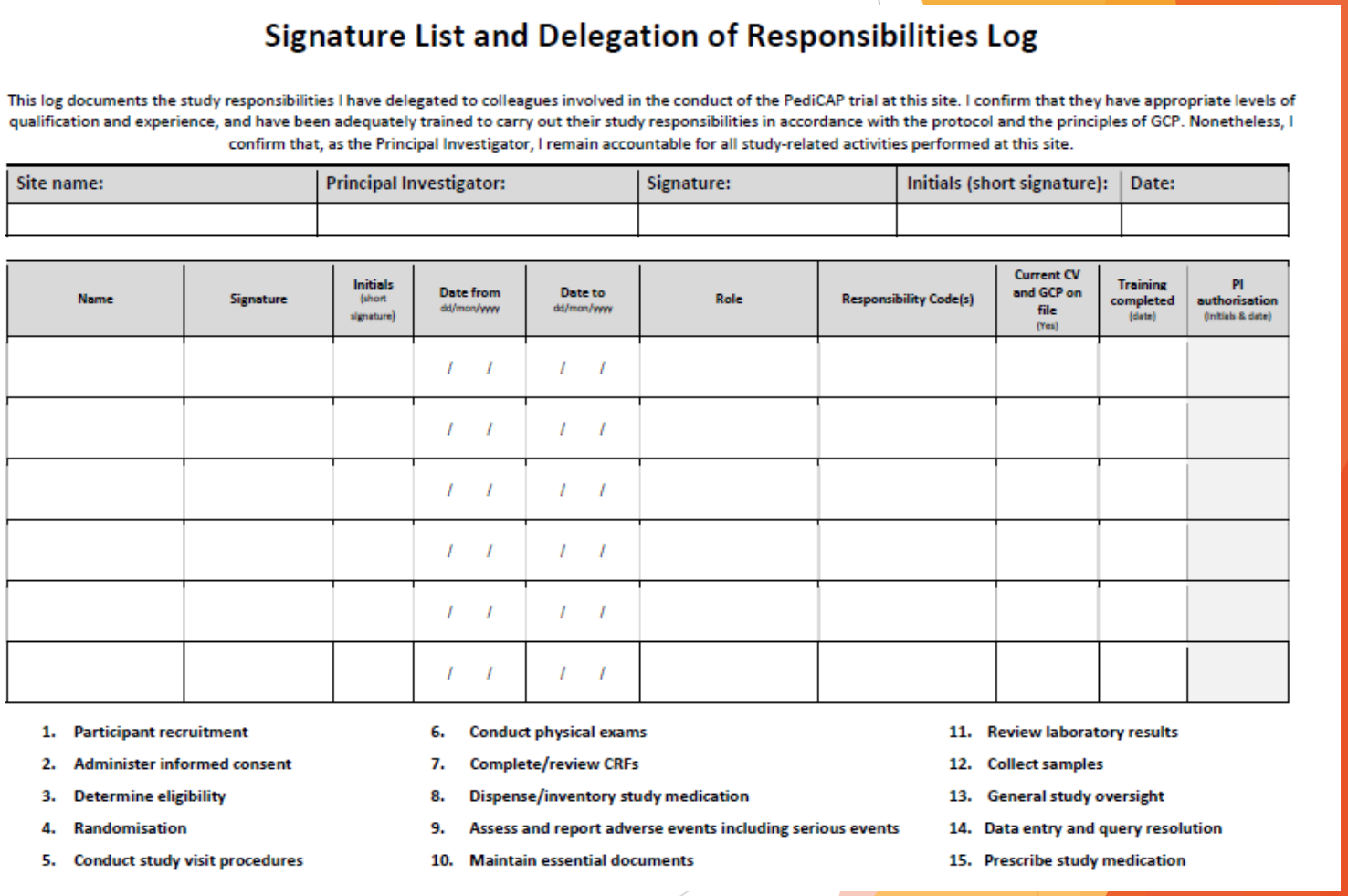
Document	Current version	Tick box to confirm as filed
Signature List and Delegation of Responsibilities Log		☐
Personnel Log		☐
Training Log		☐
CVs and GCP certificates of all staff listed on delegation log (dated within 2 years)		☐
Protocol		☐
Manual of Operations		☐
CRF Completion Guidelines		☐
Data Entry Guidelines		☐
Clinical Trial Agreement		☐
Sponsor Insurance		☐
Local ethics submission documents		☐
Local ethics approval		☐
National ethics submission documents		☐
National ethics approval		☐
Regulatory submission documents		☐
Regulatory approval		☐
Confirmation of National and Local approvals form		☐
Site Event Log template		☐
Trial Register		☐
PediCAP-A Sample Patient Information Sheet and Consent Form		☐
PediCAP-B Sample Patient Information Sheet and Consent Form		☐
Sample CRFs		☐
SmPC - Amoxicillin 250 mg		☐
SmPC - Co-amoxiclav 7:1		☐
SmPC - Co-amoxiclav 4:1		☐
SmPC - Co-amoxiclav 14:1		☐
Contact/appointment card		☐
Drug Information Leaflet		☐
Monitoring Visit Log		☐
Site Protocol Deviation Log		☐
COVID-19 Checklist		☐
Site Facilities Self-Assessment		☐

Confirmation of Receipt Forms

- Confirmation of Receipt Forms may be created during the trial for any new essential documents that are sent to you that require filing, for example documents for a substantial amendment.
- Separate Confirmation of Receipt forms will be created for the ISF and Pharmacy File.

Signature List and Delegation of Responsibilities Log

- All site staff members working on the PediCAP study should sign the Delegation Log.
- The responsibilities of each individual should be specified on the log using the list provided.
- The PI should sign the final column for each individual to confirm that study training has been completed and to authorise the listed responsibilities.
- It should be confirmed that a current CV and GCP certificate is filed in the ISF.



Signature List and Delegation of Responsibilities Log

This log documents the study responsibilities I have delegated to colleagues involved in the conduct of the PediCAP trial at this site. I confirm that they have appropriate levels of qualification and experience, and have been adequately trained to carry out their study responsibilities in accordance with the protocol and the principles of GCP. Nonetheless, I confirm that, as the Principal Investigator, I remain accountable for all study-related activities performed at this site.

Site name:	Principal Investigator:	Signature:	Initials (short signature):	Date:

Name	Signature	Initials (short signature)	Date from dd/mon/yyyy	Date to dd/mon/yyyy	Role	Responsibility Code(s)	Current CV and GCP on file (Yes)	Training completed (date)	PI authorisation (initials & date)
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			/ /	/ /					
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1. Participant recruitment
2. Administer informed consent
3. Determine eligibility
4. Randomisation
5. Conduct study visit procedures
6. Conduct physical exams
7. Complete/review CRFs
8. Dispense/inventory study medication
9. Assess and report adverse events including serious events
10. Maintain essential documents
11. Review laboratory results
12. Collect samples
13. General study oversight
14. Data entry and query resolution
15. Prescribe study medication

Signature List and Delegation of Responsibilities Log

- The Global Health Network has a free online GCP course which will issue a certificate upon completion. The course can be found at the following link: https://globalhealthtrainingcentre.tghn.org/ich-good-clinical-practice/
- Activities should only be undertaken for the study if the individual has been assigned the appropriate responsibility on the log.
- The Signature and Delegation Log should be updated every time a member of staff leaves, a new member of staff joins, or the responsibility of an individual changes.
- The log should be held in the main ISF and pharmacy staff should sign this copy. A copy should be sent to MRC CTU and Pharmacy each time a change is made to the log.

Monitoring

On-site Monitoring

- Local monitors will conduct on-site monitoring visits every 3 months.
- MRC CTU will aim to visit annually (this may change depending on the coronavirus pandemic).
- Monitors will contact your site to arrange a suitable time for each visit.
- During the visit the monitors may visit the main clinic/ward to review patient notes and the ISF, pharmacy to review the pharmacy files and confirm the participant was dispensed drug corresponding to their randomised allocation, and the laboratory to check the sample management.
- You should ensure that monitors have access to the medical notes of patients selected for review.
- A member of staff should be available to help with any queries or address any findings.

On-site monitoring

- At the end of each visit, monitors will hold a de-brief meeting.
- In this meeting, monitors will highlight key findings and any immediate corrective actions that should be implemented.
- Following the visit, monitors will send a summary report, full report and Action Item Summary (AIS).
- Upon receipt of these documents, the PI should review the summary report and sign to confirm receipt.
- All actions listed on the Action Item Summary should be resolved within 4 weeks. If there are any critical or major findings, these are expected to be resolved first and as soon as possible.

Central Monitoring

- Central monitoring will be conducted regularly by the MRC CTU to monitor data quality.
- Items such as missing forms, number of data queries, common queries and timely submission of CRFs will be reviewed.
- Any issues identified will be raised via email or as a query added to the database.