Protocol Deviation Instructions

1 What constitutes a protocol deviation?

The STEPCARE trial is pragmatic. This permits a certain margin of error with regard to the interventions. STEPCARE is a trial of targets, so when clinical reasons require a change in the sedation, temperature or blood pressure target this does not constitute a protocol deviation. Monitoring of the interventions is performed within the main eCRF so additional protocol deviations do NOT need to be reported if targets change.

As a general rule: Continue the assigned interventions if this is possible. Collect as much data as possible.

1.1 What not to report

- **Intervention target not achieved**. For example, if a patient randomized to continuous sedation but sedation is not feasible and the patient wakes up, this will be monitored in the main CRF and reported separately.
- **Neuroprognostication prior to 72h**. The time of prognostication and reasons for WLST is monitored separately. A protocol deviation report does not need to be completed.
- **Short periods of non-adherence to target**
  - Examples might include a pause in fever control for an emergency CT-scan.
- **Ineligibility becomes known after randomisation**
  - **Prior limitations in care become known**
    This does not constitute a protocol violation.
  - **A traumatic cause of arrest becomes apparent** - If possible the interventions should continue. A protocol deviation form does not need to be completed.
  - **A minor bleed is seen on a head CT**- This is not a protocol deviation.

1.2 What to report

- **Intervention cannot be delivered**
  - A **Temperature control device not available** If a patient is randomized to early treatment of fever, develops a fever but a temperature management device is not available. (Devices have run out or are broken)
  - Patient **randomised despite being awake and following commands**. In this case the patient should receive regular care. A protocol deviation form should be completed no matter what groups the patient has been randomised to
- **No documented cardiac arrest** - If a patient is randomised, but there has been no documented cardiac arrest. Regular care should continue. As no interventions are performed this constitutes a protocol deviation and should be reported.

- **Erroneous randomisation** - a patient who is known to be ineligible is randomised by mistake (example known pregnancy, but this option not selected in the eCRF). Report as a protocol deviation and **contact the sponsor** so that this patient can be be withdrawn from the database

2 How to report a deviation

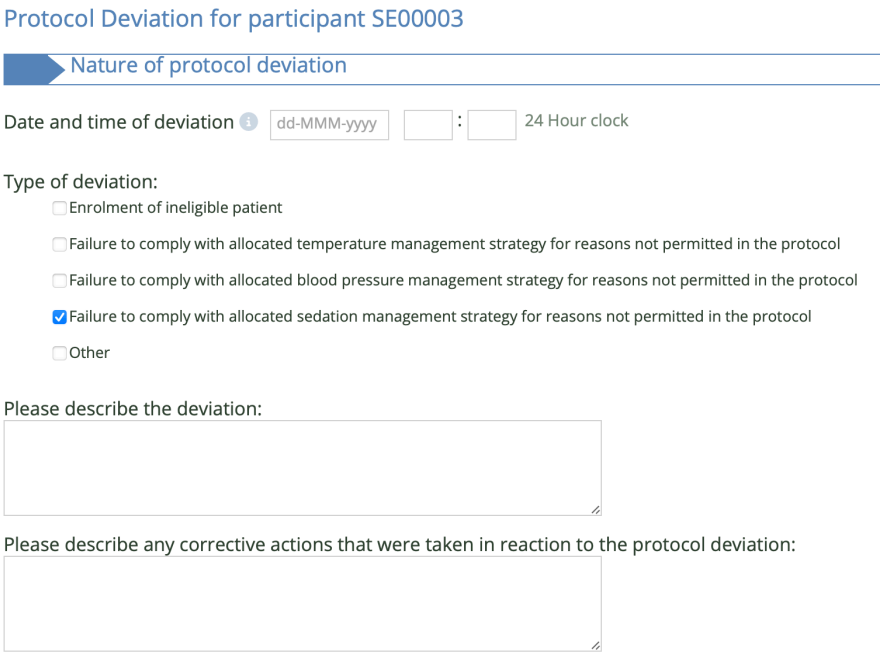
Protocol deviations should be entered in the eCRF and categorised as one of the following:

1. Enrolment of ineligible patient
2. Failure to comply with allocated temperature management strategy for reasons not permitted in the protocol
3. Failure to comply with allocated blood pressure management strategy for reasons not permitted in the protocol
4. Failure to comply with allocated sedation management strategy for reasons not permitted in the protocol
5. Other

2.1 Examples from Section 1.2

- A pregnant patient was randomised by mistake - option *Enrolment of ineligible patient* should be selected.
- A traumatic cause of arrest, participant awake, or no cardiac arrest (known before randomization) - option *Enrolment of ineligible patient* should be selected as the intervention isn't performed (option *three* if conenrolled).
- A patient receives continuous sedation for 36h despite being randomized to minimal sedation. The wrong sedation intervention is performed, select option *four*
- A patient is cooled to 33°C or temperature system malfunction - option *three* should be selected.
- A target MAP is not used at all- option *three* should be selected.

After selecting the appropriate category a description of the event should be entered and any corrective action should be described.



3 Test-cases

If a randomisation process is completed for a test patient on the live eCRF - please contact the info@stepcare.org so that the case can be removed.

In the opposite case, if a real patient is randomized in the test database, please randomize the patient on the live site as soon as possible within the screening window of 240 minutes.

4 Difficult cases

Initial care after cardiac arrest may be chaotic, and information about the arrest or regarding the patient can be lacking. Borderline cases regarding eligibility and protocol deviations are unavoidable. When possible the intervention should be completed if there aren't ethical or medical reasons for discontinuation. When in doubt about reporting a protocol deviation please contact info@stepcare.org.