

# Guidelines for Completion of SAE reports



## Introduction

This document is intended to explain how to complete the form to report an SAE in the STOP-ACEi trial. It does not go into the detail of what constitutes an SAE, or the pharmacovigilance arrangements for STOP-ACEi, but will help with completion of the reports with minimal queries arising.

A copy of the current SAE form and event coding guidance is available to download from the trial website: [www.birmingham.ac.uk/stopacei/docs](http://www.birmingham.ac.uk/stopacei/docs)

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## General guidance

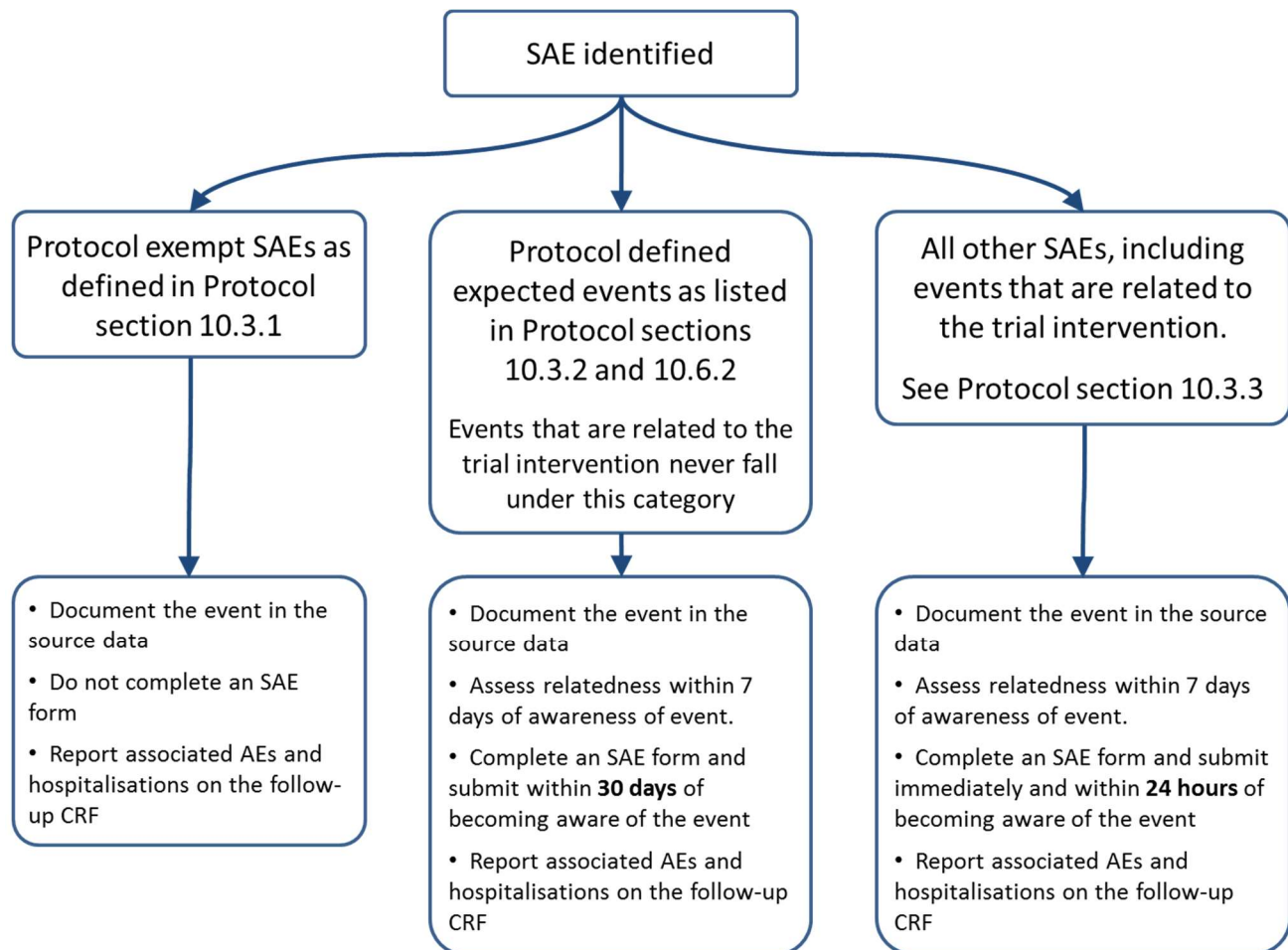
### What constitutes an SAE

For detailed guidance on SAE reporting for STOP-ACEi, see the STOP-ACEi Protocol and relevant regulations.

- An adverse event that meets the seriousness criteria is counted as an SAE. A single event can meet several of the criteria or cause multiple admissions. Likewise, a single admission could relate to multiple SAEs if more than one of the adverse events meets the criteria for seriousness.
- STOP-ACEi patients have heavy disease burden and so experience a high number of SAEs, mostly hospitalisations. The majority of events reported for STOP-ACEi do not relate to the trial intervention, but to the patient's existing morbidities. These events usually still need to be reported but there may be more generous timeframes for reporting – see How to submit an SAE report and general reporting guidance.
- There are some SAEs that are excluded from reporting in STOP-ACEi – see the trial Protocol for details. These are predominantly for planned hospitalisations.
- Deaths should always be reported as an SAE.
- If in doubt, report the event as an SAE and seek guidance from the PI or BCTU.

### How to submit an SAE report and general reporting guidance

- The reporting time-frame for SAEs in STOP-ACEi depends on the nature of the SAE. The timeframes are summarised in the flowchart below (Figure 1) but please see section 10 of the current Protocol for details. If there is any doubt, please submit a report as soon as you become aware of an SAE for a STOP-ACEi participant, and within 24 hours of becoming aware.



**Figure 1: Flowchart for reporting of SAEs in STOP-ACEi**

- SAE reports are submitted and managed on paper, rather than the information being entered directly online. The data are entered from the paper form into the trial system by staff at BCTU. SAE reports and the consent form are the only forms managed like this for STOP-ACEi.
- Initial SAE reports should be submitted by fax or scanned and sent by e-mail. Where initial SAE reports are submitted via e-mail, they should be accompanied by a phone call to ensure the report is picked up by a member of staff at BCTU promptly, e.g. in case the STOP-ACEi staff are not available.
- With reports submitted by e-mail, care must be taken to remove patient identifiable information such as the patient name, full date of birth etc. The SAE form contains minimal identifiers – the participant's trial ID number, partial DoB, gender, recruiting hospital. Particular care is needed with clinical reports or discharge summaries which can contain many identifiers, including within narrative text. Transfer via the normal STOP-ACEi mailbox ([stopacei@trial.bham.ac.uk](mailto:stopacei@trial.bham.ac.uk)) is NOT secure. However, transfer to the @NHS.net account ([STOP.ACE@nhs.net](mailto:STOP.ACE@nhs.net)) from another @NHS.net account is secure.
- The initial report may be scant if it is not possible to gather all the information. If this is the case, submit a report with as much detail as you have. If you do not have some of the details immediately available or the PI is unavailable to sign a report, leave those sections blank for later completion and ensure you meet the relevant deadline for reporting. Further detail can be completed in follow-up reports or as form queries are resolved. It is expected that 30-day reports will generally be well completed due to the generous reporting timeframe.
- Receipt of new initial SAE reports is confirmed by BCTU via e-mail. If you do not receive a confirmation e-mail within 1 working day of reporting an event, please contact BCTU to check the report has been transferred successfully.

#### What happens to an SAE report once submitted?

- Initial processing of an SAE report aims to determine whether the event is an SAE, SAR or potential SUSAR, based on the causality and (where applicable) the expectedness assessments. SUSARs must be reported by BCTU to the MHRA very quickly. Therefore, it is essential that we receive the causality assessment as soon as possible. All SAE reports must be reviewed, signed and dated by the Principal Investigator (or delegate) within 7 days of site's awareness of the SAE.
- All SAE reports are checked by BCTU to make sure the data are complete, makes sense, and is consistent with the other information in the patient's trial record. If there are any issues, these can be resolved with queries. There are generally more queries for SAE reports than normal CRFs, e.g. if the situation is unclear when the event is first reported, and the forms need to be completed and submitted very quickly.
- In addition to the local PI reviewing the event, the Chief Investigator (or delegate) will perform a central clinical review of all SAE reports submitted. This is so we can detect any potential safety concerns, and potentially up-escalate a report, e.g. if the event needs to be reported urgently to MHRA.
- The second reviewer can potentially ask additional questions if they need more information to make their assessment. These would be handled as extra form queries.

#### Follow-up reports: What to do when you have new information or the situation changes after an SAE report has been submitted

- When an SAE is ongoing, you must be vigilant for any new information, especially anything that might change the causality assessment, how the event was clinically coded, or additional SAEs.
- If new information could alter the causality assessment, submit a follow-up report with the new information as soon as possible.

- If a new SAE is detected, report this within the appropriate timeframes as normal.
- If new information is merely to resolve data queries or has no impact on how the event would be categorised, it is not necessary to submit an immediate follow-up report. For example, it is fine to resolve all data queries with one follow-up report if there is no change to the event or causality. If in doubt, it is best to submit a follow-up report or seek advice from the PI or BCTU.
- When submitting follow-up information:
  - It is best to amend the original report to add the new information or correct any previously submitted data. This will mean that when the event is resolved, you will have a single complete and final report for the event. When information for an event is spread across multiple forms, it can potentially be unclear what information forms the final report.
  - You must be careful to initial and date changes or corrections so the audit trail is clear. An auditor or inspector will expect to be able to re-create the various versions of the report from your records.
  - BCTU keeps copies of all versions of all SAE reports received.
  - If amending the form will make the record unclear (e.g. lots of changes to one aspect of the form), you can supersede a report with an entirely new version. If you do this, make sure the previous report is marked superseded. Information in the new report will replace anything in the previous report. Be careful when transcribing information onto a new report to avoid new queries.

#### How and why are SAEs clinically coded?

- STOP-ACEi uses the Clinical Trials Common Adverse Events (CTCAE) coding system, version 5.0.
- Using a coding system assists with the reporting and monitoring of SAEs for the trial. For example, so that oversight committees can detect an increase in a particular type of clinical event in one arm of the trial.
- The 'Codes for STOP-ACEi SAE Reporting' document should be used to complete the clinical coding and grade sections of the SAE report. This can be found on the trial website: [www.birmingham.ac.uk/STOPACEi/CTCAE](http://www.birmingham.ac.uk/STOPACEi/CTCAE)
- Tips for coding events:
  - Use the 'find' function to help navigate the coding document by clicking Ctrl+f on your keyboard then searching for the patient's symptoms or condition.
  - The coding document includes navigation notes to help distinguish between similar events, e.g. the navigation note for bacteraemia prompts you to consider sepsis.
  - All events are graded, with grades 1-5 generally correlating to mild, moderate, severe, life-threatening or fatal severities, respectively.
  - Not all grades are available for all events. For example, grade 1 myocardial infarction is not available; neither is grade 5 dysuria.
  - Semicolons in the grading descriptions should be interpreted as 'OR'. Therefore, it is not necessary for all the elements of the grade to be present for the event to be graded. If the patient exhibits elements of several grades, assign the highest grade.
  - A code is provided for each event in a 3-letter and 3-digit format. It is this code that should be entered on the SAE report. The 3 letters correspond to the system order class and the 3 digits to the specific type of event. For example, chronic kidney disease is given the code, REN004.
- The PI should review the coding assigned and authorises it as part of signing off the SAE report.

## Guidance for SAE form completion

### Page 1: Identifiers

STOP-ACEi Trial Number:	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	Month & year of Birth:	<input type="text"/> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Responsible study clinician:		Hospital Name:	
Participant Gender:	Female <input type="checkbox"/> Male <input type="checkbox"/>	Trial arm:	Continue <input type="checkbox"/> Discontinue <input type="checkbox"/>
Report type:	Initial Report <input type="checkbox"/>	Follow-up Report <input type="checkbox"/>	Final Report <input type="checkbox"/>

- This section should be completed fully so we can identify which patient the report relates to. Remember that for reports submitted by fax, we will not know which centre the report has come from.
- The responsible study clinician is usually the PI.
- The hospital name is the hospital where the patient is seen for trial follow-up, regardless of whether the SAE actually occurred within that hospital.
- The trial arm should be reported in line with the patient's randomised treatment allocation, regardless of whether the patient is currently compliant with this.
- Report type:
  - The first report submitted for an event should be marked as the initial report.
  - For follow-up reports, you can amend the report type by crossing through the tick for initial report and ticking the follow-up report box. Remember to initial and date changes.
  - A report is not final until BCTU have confirmed that all queries are resolved. BCTU will advise you to mark a report as final once an event is resolved.

### Page 1: Report Type

<b>Report Type</b> Please refer to Protocol section 10	
<input type="checkbox"/> SAE that is expected for the trial population and is listed in Protocol section 10.6.2. <b>Report within 30 days.</b>	→ For 30 day reports, please give the event code from Protocol section 10.6.2: <input type="text"/> <input type="text"/>
<input type="checkbox"/> SAE that is related to the trial intervention, or any reportable SAE that is not listed in Protocol section 10.6.2. <b>Report within 24 hours.</b>	

- Every SAE should be classed as either a 30 day or 24 hour report according to section 10 of the trial Protocol.
- Events that are expected for the trial population and are listed in Protocol section 10.6.2 must be reported within 30 days of the site's awareness of the event. If the event is listed in section 10.6.2, the code from the Protocol should also be provided.
- Events that are not listed in section 10.6.2 of the Protocol, or if this is unclear, should be reported within 24 hours of the site's awareness of the event.
- A protocol deviation will be recorded for any events reported outside the appropriate timeframe.



Page 1: Seriousness

Seriousness of event (provide a response to each question)	No	Yes	Details
Death	<input type="checkbox"/>	<input type="checkbox"/>	→If Yes, date of death (DD/MMM/YYYY, e.g. 01-Jun-2018) <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> Cause of death category: <input type="checkbox"/> 1 – Cancer, 2 – Cardiovascular, 3 – Cerebrovascular, 4 – Renal, 5 – Hepatic, 6 – Respiratory, 7 – Neurodegenerative, 8 – Accidental (death not caused by disease), 9 – Other, please specify: .....
Life threatening event	<input type="checkbox"/>	<input type="checkbox"/>	
In-patient hospitalisation or prolongation of existing hospitalisation	<input type="checkbox"/>	<input type="checkbox"/>	→If Yes, <input type="checkbox"/> Initial <input type="checkbox"/> Prolonged →If Yes, number of days spent in hospital as result of the SAE <input type="text"/> <input type="text"/> <input type="text"/>
Persistent or significant disability/incapacity	<input type="checkbox"/>	<input type="checkbox"/>	
Congenital abnormality or birth defect	<input type="checkbox"/>	<input type="checkbox"/>	
Other pertinent medical reason for reporting?	<input type="checkbox"/>	<input type="checkbox"/>	→If Yes, please specify: ..... .....

- All options for seriousness must be ticked, either yes or no. It is possible for more than one option to be ticked as 'yes'.
- For SAE reporting, "life-threatening" refers to an event in which the patient was at risk of death at the time of the event. It does not refer to an event which hypothetically might have caused death if it were more severe.
- Initial and prolonged hospitalisations:
  - If the event caused an existing inpatient admission to be prolonged (without the patient first being discharged) then this would be a prolongation.
  - For example, if a patient was admitted for stroke and then their hospitalisation was prolonged due to a hospital-acquired infection, then the stroke would be the initial admission and the infection would be the prolongation of hospitalisation.
  - All events must meet the criteria for seriousness to be classed as SAEs. Incidental findings during an admission which do not warrant hospitalisation themselves (e.g. those that will be followed-up in outpatients) are not classed as SAEs.
  - For SAEs due to prolongation of existing hospitalisation, the patient must have been initially admitted for a different reason.
  - A long period of hospitalisation does not necessarily mean that an SAE is due to a prolonged hospitalisation.
- A newly identified congenital abnormality or birth defect would be very unusual for the trial population.
- A PI or trial clinician always has the option to report an event as an SAE if they see a pertinent medical reason for reporting even if the event does not meet any of the listed criteria.

Page 1: Date of event and date of site awareness

Date Event Started (DD/MMM/YYYY, e.g. 01-Mar-2018)	<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	
Date site became aware of event (DD/MMM/YYYY)	<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	<input type="text"/>	/	<input type="text"/>	<input type="text"/>	<input type="text"/>	<b>PTO</b>

- Event start date:
  - This relates to the Serious AE, so if an event does not initially require hospitalisation but progresses to require hospitalisation, the start date is when the event developed such that it required hospitalisation. For example, if a patient has a history of shortness of breath which is usually managed successfully in the community, but has an episode of shortness of breath that requires hospitalisation, the start date is when this particular episode started, rather than the date that shortness of breath was first observed in the patient.
  - This is often the date of admission for a hospitalisation.
- Date site became aware of event
  - Enter the first date on which the local trial team became aware of the SAE.

### Page 2: Identifiers

STOP-ACEi Trial Number:	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>	<input type="text"/>
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- Complete the patient's Trial ID number at the top of pages 2 and 3 to ensure the report can be clearly identified. This is especially helpful when multiple reports are submitted at the same time, partial reports are submitted or for reports submitted by fax.

### Page 2: SAE description

**Serious adverse event description: narrative / signs and symptoms.** Please attach copies of relevant reports. Where investigations or lab tests are appended, please ensure patient identifiers are replaced with trial number only.

- Provide a narrative description of the event, as might appear in the patient's clinical records. This might include details of the patient's symptoms, treatments, investigation results and identified conditions.
- If full details are not known at the time of submitting the initial report, further details can be added in subsequent follow-up reports.
- Submitting relevant reports:
  - Clinical reports or a discharge summary can be submitted to support the description, e.g. a test report that confirms a diagnosis. Please do not simply refer to clinical reports in the description, e.g. "see MRI report". The SAE report should be a standalone record of the event for the trial. Only information from the SAE report itself can be recorded on the trial database. If there is anything relevant in a clinical report, please include the details in the SAE report.
  - Reports are only useful for relevant results, e.g. those that confirm the diagnosis. It is not necessary to submit irrelevant results or results from general patient monitoring unless these show something relevant for the event. For example, you do not need to submit every lab report relating to patient monitoring during a long admission. However, an ECG that confirms a previously unknown arrhythmia could potentially be useful, e.g. for the CI's central review.
  - Be careful to fully anonymise clinical reports. Replace any patient identifiable information with the STOP-ACEi ID number. Please do not include the patient's hospital ID number, full name, full date of birth, discharge address, next of kin details, GP name, etc. If we receive excessive patient identifiers which we do not have permission to hold, we will ask you to report this internally and will treat it as a GCP deviation.
  - Staff at BCTU are not clinically trained so cannot interpret clinical reports. If there are relevant results in the clinical reports, please include some detail of these on the SAE report itself.

## Page 2: Relevant medical history

**Details of relevant medical history. If none, please indicate 'nil relevant'.**

- It is not necessary to state irrelevant medical history, i.e. it is not necessary to list all known medical history. However, anything relevant to the event should be reported.
- The SAE report acts as a standalone record of the event so it may be necessary to list items here that have already been reported elsewhere. Remember the clinician performing the central review may not have immediate access to the CRFs submitted for the patient.
- If the event relates to exacerbation of existing/recurrent conditions or symptoms, these should be described.
- If the patient has known risk factors for the event, these should be described here.
- If there have been recent medication/treatment changes that are relevant to event, these should be listed here.
- If there is no relevant medical history, please complete this section as 'nil relevant'.

## Page 2: Concomitant medications

**Concomitant Medication.** Please provide details of medication/s the patient was taking prior to the event which are relevant to the SAE. You do not need to list irrelevant medications:

Drug Name (give generic name)	Start date (DD/MMM/YYYY)	Tick if continuing or specify stop date (DD/MMM/YYYY)	Dose	Unit	Freq- uency	Route
			Please refer to coded list on Page 4			
_____	__/___/___	<input type="checkbox"/> __/___/___				
_____	__/___/___	<input type="checkbox"/> __/___/___				
_____	__/___/___	<input type="checkbox"/> __/___/___				

- This section should list medications **relevant to the event** that the patient was taking at the time of event onset, i.e. prior to the event.
- You do not need to include medications given to treat the SAE, i.e. those started after event onset.
- You do not need to list all medications that the patient was taking.
- If the event was (or might have been) caused by medication/s, the details of the medication/s should be listed. For example, if the patient has an SAE due to hypotension that may have been caused or exacerbated by overtreatment with antihypertensives, please list all the antihypertensive medications the patient was taking at the time of the event. Likewise, if the SAE is a medication side effect, the medication details should be listed.
- If you do not have the details when submitting the initial report, remember it is fine to leave parts of the form blank and submit the additional information in a later follow-up report.
- If information is truly unknown, please report it as such on the form, rather than leaving it blank, to avoid a query.
- If only partial dates are known, these are still helpful.
- If the patient dies, all medications should be reported as stopped.
- Codes:
  - For unit, frequency and route, use the codes on the back of the form.
  - If you use code 97 – other – you must specify what the 'other' is.



- If the dose is variable (e.g. insulin, warfarin), please complete this as 'variable', rather than leaving it blank, to avoid a query.
- The reported con-meds are compared against the other information in the patient's trial records. Inconsistencies will prompt queries.

**Page 2: Event outcome**

What was the final outcome of the event?	
Resolved no sequelae <input type="checkbox"/>	→If Resolved, date of resolution: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Resolved with sequelae <input type="checkbox"/>	→If Resolved, date of resolution: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> →Specific sequelae: .....
Continuing <input type="checkbox"/>	→If Continuing, please provide date of resolution on follow-up/final SAE form
Fatal <input type="checkbox"/>	

- An SAE report cannot be closed until the final event resolution is known.
- An event is resolved if it clinically resolves, ceases to be 'serious' or stabilises.
- For hospitalisations, the date of resolution is often the date of discharge.
- A sequela is a condition which is the consequence of a previous disease. For example, dysphasia could be a sequela of stroke.

**Page 3: Identifiers**

STOP-ACEi Trial Number: <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
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- Complete the patient's Trial ID number at the top of pages 2 and 3 to ensure the report can be clearly identified. This is especially helpful when multiple reports are submitted at the same time, partial reports are submitted or for reports submitted by fax.

**Page 3: Causality assessment**

Trial intervention causality assessment. The assessment of causality <u>must</u> be provided by a clinician.		
For the control arm (continue ACEi/ARB), is the SAE related to the particular ACEi and/or ARB the participant is taking? For the experimental arm (discontinue ACEi/ARB), is the SAE related to the withdrawal of ACEi/ARB treatment?		
Date of randomisation: (DD/MMM/YYYY)	Date last dose of ACEi/ARB taken: (DD/MMM/YYYY)	Causality Assessment. Please tick one option only.
<input type="text"/>	<input type="text"/>	<input type="checkbox"/> Unrelated to trial intervention <input type="checkbox"/> Unlikely to be related to trial intervention <input type="checkbox"/> Possibly related to trial intervention <input type="checkbox"/> Probably related to trial intervention <input type="checkbox"/> Definitely related to trial intervention
		} unrelated } related
Action taken due to SAE. Please tick one option only.		Please give reasons for the causality assessment provided above. If unrelated, please provide an alternative cause: ..... ..... ..... .....
<input type="checkbox"/> ACEi/ARB stopped or (if on discontinue arm) ACEi/ARB re-started. <input type="checkbox"/> ACEi/ARB Dose reduced <input type="checkbox"/> ACEi/ARB Dose increased <input type="checkbox"/> No change to ACEi/ARB use <input type="checkbox"/> Unknown <input type="checkbox"/> N/A, i.e. because participant not on trial treatment or has died.		
If treatment was altered, did the reaction abate after drug changes? No <input type="checkbox"/> Yes <input type="checkbox"/>		

- Date of randomisation: Including this allows anyone reviewing the report to know how long after joining the trial the event occurred. This can be found in the original email confirmation of randomisation, or in the main patient form in the patient's trial record on the trial database.
- Date last ACEi/ARB taken:
  - This should be the last date an ACEi/ARB was taken prior to the event starting, i.e. this date cannot be later than the event start date.
  - For patients randomised to STOP that are compliant with their randomised treatment allocation, this should be close to the date of randomisation.
  - For patients randomised to continue that are compliant with their randomised treatment allocation, this should be the same as the event start date or shortly beforehand.
- Causality assessment:
  - This must be completed by the PI or a doctor with this responsibility delegated.
  - For patients randomised to the continue arm, this asks whether the event is thought to be related to the patient's continued use of ACEi/ARB. This applies regardless of whether the patient is compliant with the randomised treatment allocation.
  - For patients randomised to the STOP arm, this asks whether the event is thought to be related to withdrawal of ACEi/ARB. This applies regardless of whether the patient is compliant with the randomised treatment allocation.
  - If completed as possibly, probably or definitely related to trial treatment, the event will be treated as a SAR and may therefore require expedited reporting to the MRHA.
- Action taken due to SAE:
  - This relates to action with the use of ACEi/ARBs only and applies for patients in both arms of the trial. Actions could include re-starting ACEi/ARB, stopping ACEi/ARB or dose changes. A change in use of ACEi/ARB could potentially indicate causality.
  - The 'No change to ACEi/ARB use' option should be used to indicate wherever there has been no change to ACEi/ARB use, even if the patient was not on any ACEi/ARB treatment to begin with.
  - The 'N/A' option should be used if the patient has died and treatment changes were therefore not possible, or if the patient was non-compliant with the randomised treatment allocation at the time of event onset.
- Reasons for the causality assessment:
  - This section must be completed for all SAEs, regardless of the causality assessment.
  - If the event is possibly, probably or definitely related to the trial intervention, this should explain why the event is thought to have been caused by either the use or withdrawal of ACEi/ARB treatment.
  - If the event is unrelated or unlikely to be related to the trial intervention, this should provide an alternative cause and explain why the event is not thought to have been caused by either the use or withdrawal of ACEi/ARB treatment.
- Did reaction abate after drug changes: This section must be completed if there were any changes to use of ACEi/ARB, otherwise please leave blank.

### Page 3: Clinical coding and grading

<b>Event Clinical Coding</b>				
Once resolved, the event should be coded using CTCAE v5.0, which can be found at <a href="http://www.birmingham.ac.uk/STOP-ACEi/CTCAE">www.birmingham.ac.uk/STOP-ACEi/CTCAE</a> . The coded event should meet at least one of the criteria for seriousness (see page 1).				
CTCAE term code: <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/>	If other, specify: .....			
CTCAE grade: Please tick one option only				
<input type="checkbox"/> Grade 1	<input type="checkbox"/> Grade 2	<input type="checkbox"/> Grade 3	<input type="checkbox"/> Grade 4	<input type="checkbox"/> Grade 5

- Please also see the above section, How and why are SAEs clinically coded?
- CTCAE term code:
  - The form should be completed with the appropriate code for the event term. This should be taken from the STOP-ACEi SAE coding document available on the trial website: [www.birmingham.ac.uk/stopacei/CTCAE](http://www.birmingham.ac.uk/stopacei/CTCAE)
  - The appropriate term can change over time if the diagnosis was not initially correct or more information alters the assessment. We recommend coding the event once it is resolved or when enough information is known to be confident of its coding.
  - If the SAE is complex and it's unclear what the most appropriate term is, report the main clinical event that forms the SAE or the most severe event. This will be according to the PI's discretion.
  - Please avoid using the 'other' options unless the event cannot be further coded.
- CTCAE grade:
  - All events should be graded as grade 1-5 according to the CTCAE coding system.
  - Not all grades apply to all terms.

### Page 3: Details of person reporting

<b>Details of person reporting</b> (you must have signed the site delegation log)	
Name of Person Reporting: .....	Signature of Person Reporting: .....
Position: .....	Date of signature: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
Telephone Number:	Email Address:
Fax Number: (state N/A if not used)	Date of first reporting: _____ / _____ / _____

- Although BCTU may have your contact details on file, please complete this section fully. This is partly as a record of who submitted the report, and partly so that anyone at BCTU could contact you urgently if there was an immediate problem.
- If you do not have a fax machine, please complete this as 'N/A' or similar. If blank, this will prompt a query.
- The date of reporting is the date of first notifying BCTU of the event. This does not change, e.g. if new follow-up reports are submitted.


### Page 3: PI signature

<b>Principal Investigator sign off</b>	
I confirm that I have reviewed this report and have assessed the seriousness, causality and clinical coding of this event.	
Signature: .....	Date of signature: <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>

- The PI must review and sign all SAE reports, with particular attention given to the seriousness, causality assessment and clinical coding.
- If the PI is unavailable to sign the report, an unsigned report should be submitted to meet the required reporting timeframes described in Protocol section 10.

### Guidance on the SAE Query Process

- SAE reports are checked by BCTU for missing data and for inconsistencies with data already submitted for the patient from follow-up visits.
- Queries are logged and sent to sites in a Data Clarification Form (DCF). The DCF will be sent as a PDF attachment and will contain all queries that have been identified by BCTU and the Chief Investigator. An example is included below:



## Open SAE Queries by Report

Query number

SAE Number  Participant number

Centre name

Query raised  Raised by

Details of query

1. Seriousness: some options unanswered. Each category (death, life-threatening event etc.) should be answered either yes or no.

2. PI signature: missing. Please ask the PI to sign the report to confirm review

Response from site

Completed by	Date	Signature
PI Name	Date	PI Signature

By signing above, you confirm that you have reviewed the new information and assessed whether it has any impact on the causality assessment for the SAE. If the causality assessment is changed, please update the SAE report accordingly.

### How to process DCFs

- Print the DCF
- Resolve the query:
  - If SAE report data needs to be amended (e.g. to correct a previous error, or add missing information), please update the original SAE report to resolve the query. Remember to initial/date changes to maintain the audit trail.
  - If missing data is not available, make a clear record of this on the original SAE report. For example, if a medication start date is not available in the patient’s records, complete this field as ‘NK’ or ‘Not known’. Remember to initial/date changes to maintain the audit trail.
  - If no data changes are needed (e.g. if the original data was correct), please provide an explanation in the ‘Response from site’ section of the DCF.
- Complete the ‘Response from site’ field of the DCF. This must be completed for the query to be closed.

- If form data was amended, please complete as 'see updated report' or similar. It is not necessary to transcribe the updated information into the DCF.
- If no data changes are needed, please complete the 'Response from site' section of the DCF to resolve the query.
- Sign the 'completed by' section of the DCF. In doing this you are confirming the data provided is correct, and are granting permission for the Renal Trials Team at BCTU to amend the online database accordingly.
- The PI should then sign the PI signature section to confirm:
  - Review of the new information, including whether this impacts the causality assessment.
  - That, if the new information alters the causality assessment, this has been updated on the SAE report.
- Send the completed DCF and updated SAE report to us at BCTU in one of the following ways. Please ensure any documents are fully anonymised prior to sending.
  - Scan and e-mail.
  - Fax.
  - Mail a photocopy, but retain the original at site.
- File the original completed and signed DCF in the patient's trial record, along with any SAE reports and relevant correspondence.
- Further DCFs may be sent for unresolved queries or when updated SAE reports are sent to BCTU. The process for resolving any additional DCFs is the same and still requires PI sign off.
- BCTU will confirm via email when all queries have been resolved and the report can be marked as 'final'.