HOW TO REPORT ADVERSE EVENTS

Protocol number: ISRCTN62396133
Version 1.0; date 05 April 2019

ASSESSING PARTICIPANTS FOR ADVERSE EVENTS

- The medical records should be checked daily for any reported medical problems
- Additionally, participants should be asked an open question e.g. Have you had any new problem since yesterday?
- Any event reported by the participants should be checked against the Protocol to see if onward reporting is needed

DEFINITIONS

Adverse event (AE)	Any untoward medical occurrence in a participant to whom a medicinal product has been administered, including occurrences which are not necessarily caused by or related to that product. An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of an investigational medicinal product (IMP).
Serious Adverse Event (SAE)	A serious adverse event is any untoward medical occurrence that: results in death; • is life-threatening; • requires inpatient hospitalisation or prolongation of existing hospitalisation; • results in persistent or significant disability/incapacity • other 'important medical events' may also be considered serious if they jeopardise the participant or require an intervention to prevent one of the above consequences.

DEFINITIONS

Adverse Reaction (AR)	Any untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant. The phrase “response to an investigational medicinal product” means that a causal relationship between a trial medication and an AE is at least a reasonable possibility, i.e. the relationship cannot be ruled out.
Serious Adverse Reaction (SAR)	An adverse event that is both serious and, in the opinion of the reporting investigator, believed with reasonable probability to be due to the trial treatments, based on the information provided.
Suspected Unexpected Serious Adverse Reaction (SUSAR)	A serious adverse reaction, the nature and severity of which is not consistent with the information about the medicinal product in question set out in the in the Investigator’s Brochure (IB).

WHAT SHOULD BE REPORTED?

1. WHILE THE PARTICPANT IS IN HOSPITAL:

✓ Any untoward medical event that occurs **up to 42 days** after randomisation and **NOT** collected on the outcome form

✗ **What does not need to be reported :**

- Data already collected on the outcome form
- Events that are part of the natural history of anaemia, PPH or childbirth, or expected complications of these
- Events relating to a pre-existing condition or any planned hospitalisations for elective treatment of a pre-existing condition

If in doubt: Please call the
24-hour helpline for advice or email woman2@lshtm.ac.uk

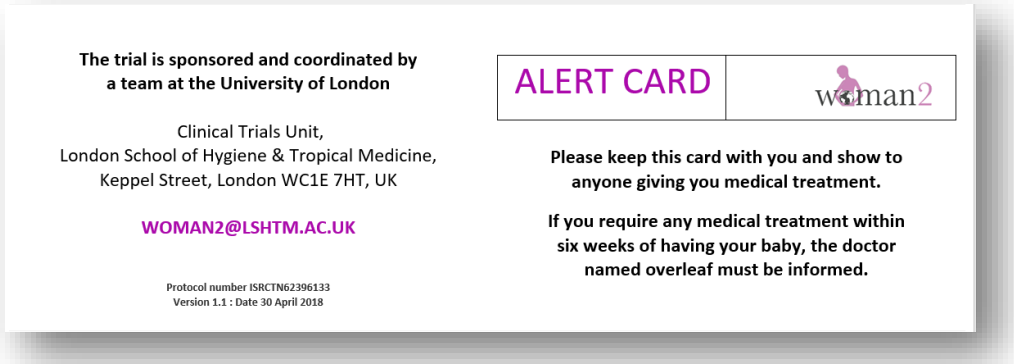
WHAT SHOULD BE REPORTED?

2. AFTER PARTICIPANT DISCHARGE

✓ After discharge, <u>any</u> untoward medical event, which develops **up to 42 days** after randomisation **(including those listed on the outcome forms)**

- All participants should be given an ALERT CARD at discharge which contains information on who to contact if they develop any problems

If in doubt: Please report or call the 24-hour helpline for advice



The trial is sponsored and coordinated by a team at the University of London

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Protocol number ISRCTN62396133
Version 1.1 : Date 30 April 2018

ALERT CARD

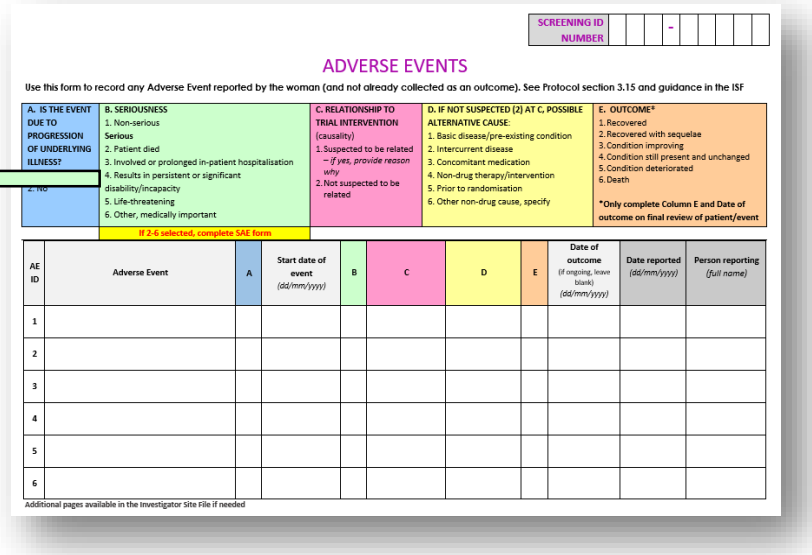
woman2

Please keep this card with you and show to anyone giving you medical treatment.

If you require any medical treatment within six weeks of having your baby, the doctor named overleaf must be informed.

REPORTING EVENTS

- Record **all Adverse Events (AEs)** in the Case Report Form (CRF) Booklet
- The report can be completed by any clinical member of staff and should be completed at first knowledge of the event



SCREENING ID NUMBER

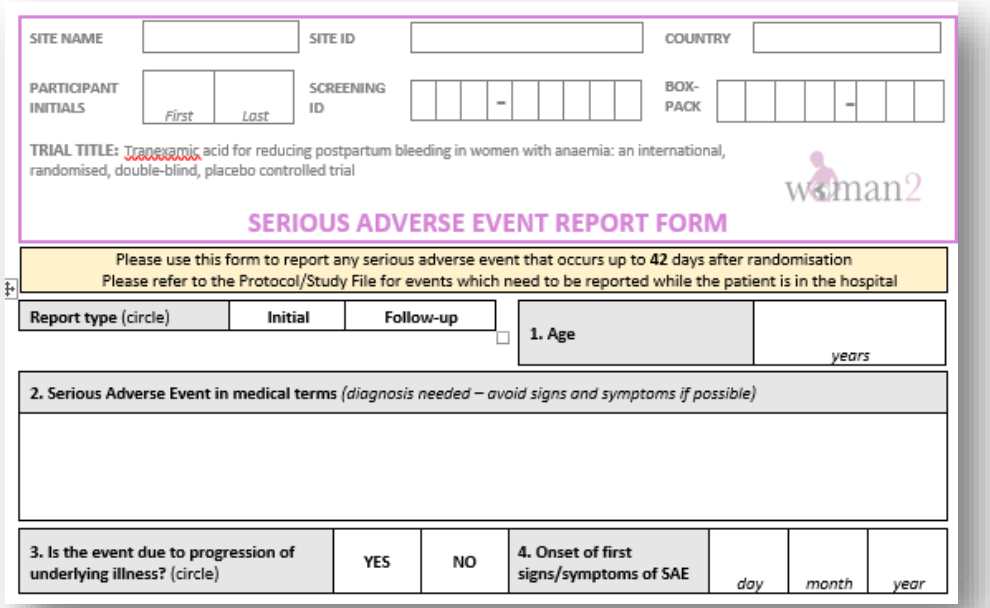
ADVERSE EVENTS

Use this form to record any Adverse Event reported by the woman (and not already collected as an outcome). See Protocol section 3.15 and guidance in the ISF

A. IS THE EVENT DUE TO PROGRESSION OF UNDERLYING ILLNESS?	B. SERIOUSNESS 1. Non-serious Serious 2. Patient died 3. Involved or prolonged in-patient hospitalisation 4. Results in persistent or significant disability/incapacity 5. Life-threatening 6. Other, medically important	C. RELATIONSHIP TO TRIAL INTERVENTION (causality) 1. Suspected to be related – *if yes, provide reason why* 2. Not suspected to be related	D. IF NOT SUSPECTED (2) AT C, POSSIBLE ALTERNATIVE CAUSE: 1. Basic disease/pre-existing condition 2. Intercurrent disease 3. Concomitant medication 4. Non-drug therapy/intervention 5. Prior to randomisation 6. Other non-drug cause, specify	E. OUTCOME* 1. Recovered 2. Recovered with sequelae 3. Condition improving 4. Condition still present and unchanged 5. Condition deteriorated 6. Death *Only complete Column E and Date of outcome on final review of patient/event
2. No	If 2-6 selected, complete SAE form			

AE ID	Adverse Event	A	Start date of event (dd/mm/yyyy)	B	C	D	E	Date of outcome (if ongoing, leave blank) (dd/mm/yyyy)	Date reported (dd/mm/yyyy)	Person reporting (full name)
1										
2										
3										
4										
5										
6										

Additional pages available in the Investigator Site File if needed



SITE NAME | SITE ID | COUNTRY

PARTICIPANT INITIALS (First / Last) | SCREENING ID | BOX-PACK

TRIAL TITLE: Tranexamic acid for reducing postpartum bleeding in women with anaemia: an international, randomised, double-blind, placebo controlled trial

SERIOUS ADVERSE EVENT REPORT FORM

Please use this form to report any serious adverse event that occurs up to **42** days after randomisation
Please refer to the Protocol/Study File for events which need to be reported while the patient is in the hospital

Report type (circle)	Initial	Follow-up	1. Age	years

2. Serious Adverse Event in medical terms *(diagnosis needed – avoid signs and symptoms if possible)*

3. Is the event due to progression of underlying illness? (circle)	YES	NO	4. Onset of first signs/symptoms of SAE	day	month	year

- If the event meets **ANY** of the 'seriousness' criteria, a Serious Adverse Event (SAE) report form should also be completed
- Copies of the SAE report form can be found in the Investigator Site File, Section 4

REPORTING EVENTS

Event Medical Term and Seriousness Criteria

Adverse event medical term

- Record only one diagnosis per event/form
- Multiple diagnoses needed to be reported separately
- Signs and symptoms should be avoided unless diagnosis/cause is unknown

Seriousness criteria

- Indicate ALL that apply – can be more than one
- Should be an assessment of the seriousness in relation to the specific event only, not the participant status as a whole

REPORTING EVENTS

Causality

Assessment of causality

- The site PI or medical delegate must assign a causality using the definitions in the table below:

Relationship	Description
Suspected to be related	There is evidence to suggest a causal relationship with administration of the trial treatment and the influence of other factors is unlikely.
Not suspected to be related	There is little or no evidence to suggest there is a causal relationship (e.g. the event did not occur within a reasonable time after administration of the trial treatment). There is another reasonable explanation for the event (e.g. the participant's clinical condition, other concomitant treatment).

REPORTING EVENTS

Event follow up and outcome

- Some serious events may take longer to resolve and the final outcome may not be available at discharge
- Events will require follow-up until the event has stabilised or resolved
- A **follow-up** report (new SAE form but follow-up/indicated at Q2 - ‘Report type’) should be completed when any additional/new information becomes available e.g. change in the patients status from ‘condition improving’ to ‘resolved’
- There may be more than one follow up form between the initial report and resolution of the event
- All changes between initial and follow up should be reflected on the follow up form. E.g. if patient has received additional treatment for the adverse event, Q12 ‘Action taken’ should be updated in line with this

COMPLETING THE ADVERSE EVENT FORM (IN CRF BOOKLET)

- Complete one line per event reported
- For questions A-E, use the coloured key to find the correct response and enter the corresponding number into the table
- If the event meets any of the seriousness criteria, i.e. if B is any of 2-6, a Serious Adverse Event form needs to be completed **in addition to the AE form**

SCREENING ID NUMBER				-					

ADVERSE EVENTS

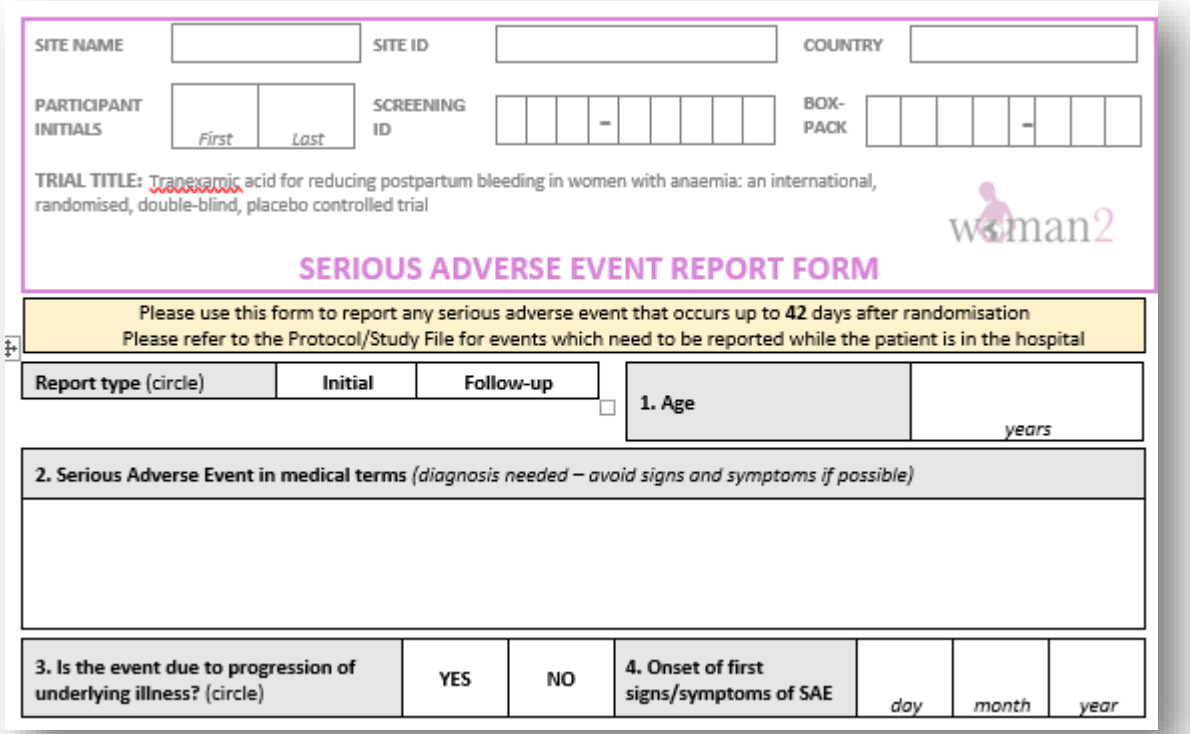
Use this form to record any Adverse Event reported by the woman (and not already collected as an outcome). See Protocol section 3.15 and guidance in the ISF

A. IS THE EVENT DUE TO PROGRESSION OF UNDERLYING ILLNESS?	B. SERIOUSNESS	C. RELATIONSHIP TO TRIAL INTERVENTION (causality)	D. IF NOT SUSPECTED (2) AT C, POSSIBLE ALTERNATIVE CAUSE:	E. OUTCOME*
1. Yes 2. No	1. Non-serious **Serious** 2. Patient died 3. Involved or prolonged in-patient hospitalisation 4. Results in persistent or significant disability/incapacity 5. Life-threatening 6. Other, medically important **If 2-6 selected, complete SAE form**	1. Suspected to be related – *if yes, provide reason why* 2. Not suspected to be related	1. Basic disease/pre-existing condition 2. Intercurrent disease 3. Concomitant medication 4. Non-drug therapy/intervention 5. Prior to randomisation 6. Other non-drug cause, specify	1. Recovered 2. Recovered with sequelae 3. Condition improving 4. Condition still present and unchanged 5. Condition deteriorated 6. Death ***Only complete Column E and Date of outcome on final review of patient/event**

AE ID	Adverse Event	A	Start date of event *(dd/mm/yyyy)*	B	C	D	E	Date of outcome (if ongoing, leave blank) *(dd/mm/yyyy)*	Date reported *(dd/mm/yyyy)*	Person reporting *(full name)*
1										

COMPLETING THE SERIOUS ADVERSE EVENT FORM

- Any event that meets any of the seriousness criteria should be recorded on the SAE form **in addition to** the AE form
- All 3 pages must be completed per serious adverse event



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TRIAL TITLE: Tranexamic acid for reducing postpartum bleeding in women with anaemia: an international, randomised, double-blind, placebo controlled trial

WOMAN2

SERIOUS ADVERSE EVENT REPORT FORM

Please use this form to report any serious adverse event that occurs up to **42** days after randomisation
Please refer to the Protocol/Study File for events which need to be reported while the patient is in the hospital

Report type (circle)	**Initial**	**Follow-up**	**1. Age**	*years*

2. Serious Adverse Event in medical terms *(diagnosis needed – avoid signs and symptoms if possible)*

3. Is the event due to progression of underlying illness? (circle)	**YES**	**NO**	**4. Onset of first signs/symptoms of SAE**	*day*	*month*	*year*

FORM COMPLETION TIPS

- Please write **clearly** on all paper forms
- **All fields must be completed – do not leave <u>any</u> fields blank.**
  - If there is no information to record, write NK (not known) or NA (not applicable)
- The information supplied must be consistent and fully representative of the data recorded on the source data i.e. medical records and other data forms
- Guidance for completing the questions is provided in Trial Procedures File, 8.2

Once the initial paper report is complete, enter into the database within <u>24 hours</u> of notification of event:

https://ctu-auth.lshtm.ac.uk/woman2/

See presentation 'The Trial Database and Online Data Queries' for guidance on database entry

IF YOU NEED URGENT ADVICE ABOUT REPORTING AN ADVERSE EVENT PLEASE CALL +44(0)7768 707500

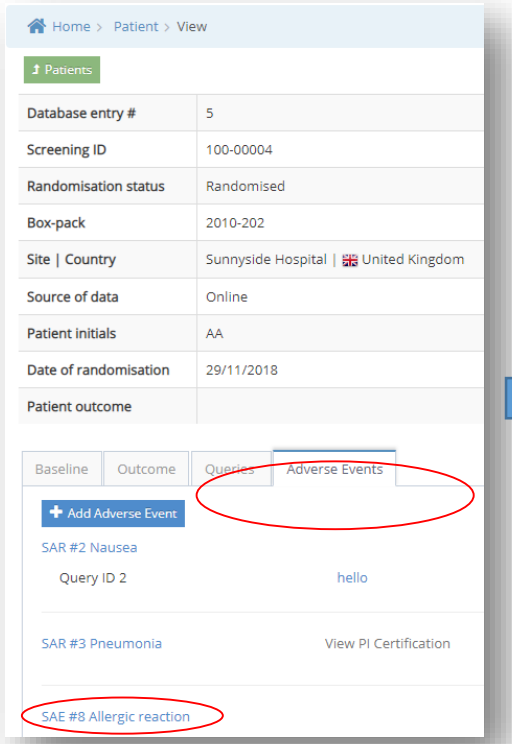
PRINCIPAL INVESTIGATOR CERTIFICATION

- When an event is resolved, and the final follow-up form received, there will be a request for Principal Investigator (PI) certification

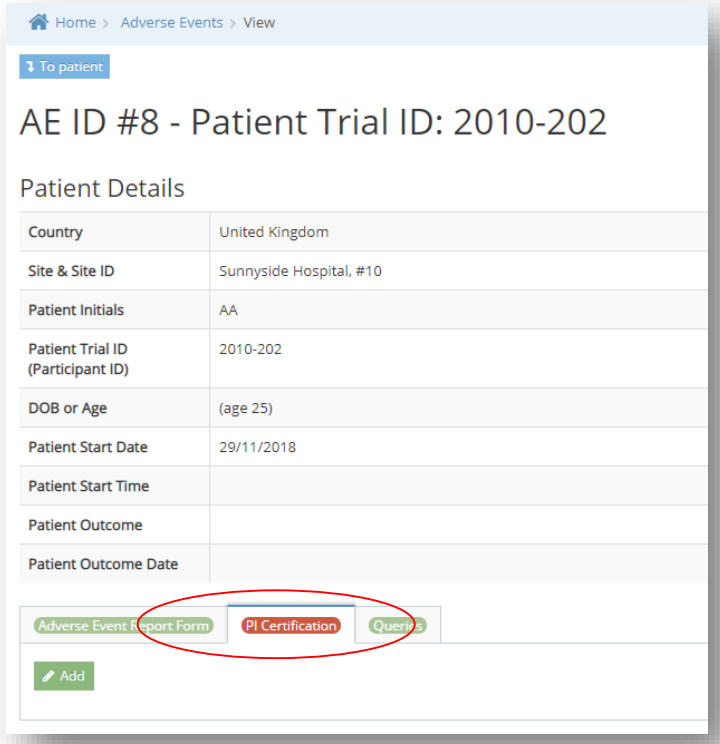
- It is the PI's responsibility to:
  - Review the adverse event in its entirety (initial and any follow-ups)
  - Confirm that the final report form is accurate according to the medical records, and are representative of the whole event
  - Confirm the final diagnosis
  - Record their name, date and signature (Q21 on the paper form for SAE, or page 41 on CRF booklet for AE)
  - Update the PI certification fields on the database

COMPLETING PI CERTIFICATION ON THE DATABASE

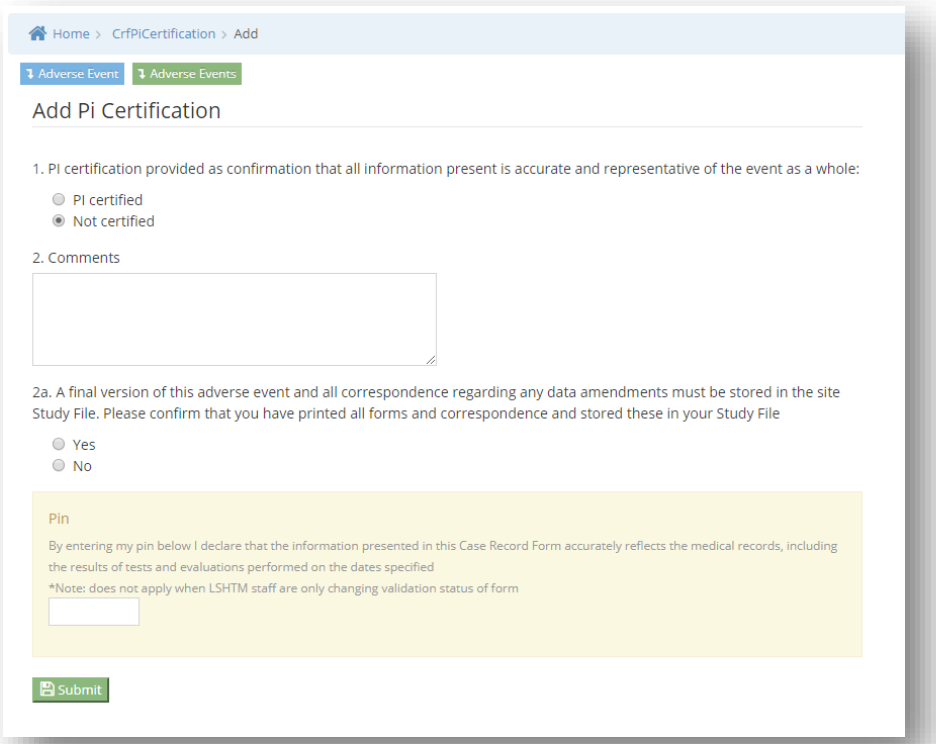
- The PI will receive an email once an event is ready for certification
- The email link will take PI directly to the adverse event
- PI must review Adverse event data and once happy, complete ‘Principal Investigator’ tab



Find patient record and adverse event to certify



Click on PI Certification tab and ‘add’



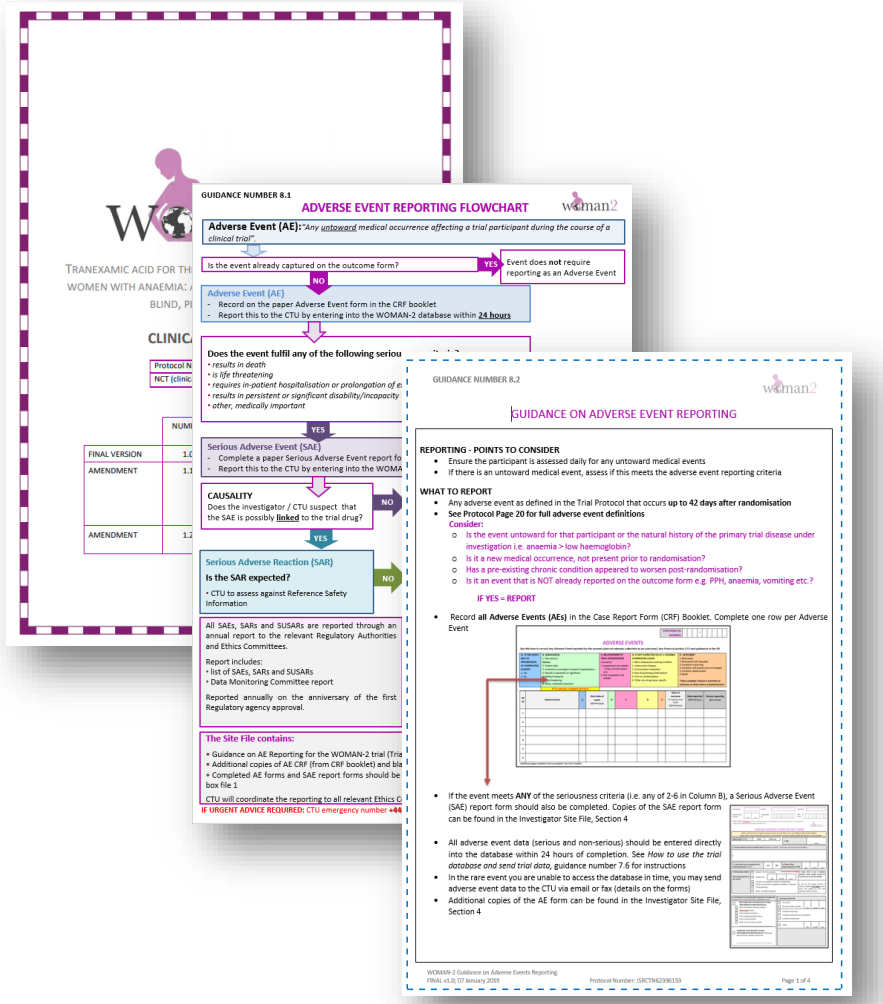
Complete fields and press ‘Submit’

FOR FURTHER GUIDANCE PLEASE SEE:

- **Trial Procedure file, section 8:**

1. Adverse Event reporting flowchart, guidance number 8.1
2. Guidance on Adverse Event Reporting, guidance number 8.2

- **Trial protocol (Section 3.15)**



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