



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)	<p>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.</p> <p>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).</p>
Serious Adverse Event (SAE)	<p>A serious adverse event is any untoward medical occurrence that:</p> <ul style="list-style-type: none">• 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)	<p>Any untoward and unintended response in a participant to an investigational medicinal product which is related to any dose administered to that participant.</p> <p>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.</p>
Serious Adverse Reaction (SAR)	<p>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.</p>
Suspected Unexpected Serious Adverse Reaction (SUSAR)	<p>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 Investigator’s Brochure (IB).</p>

WHAT SHOULD BE REPORTED?

1. WHILE THE PARTICIPANT 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, any 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

<p>The trial is sponsored and coordinated by a team at the University of London</p> <p>Clinical Trials Unit, London School of Hygiene & Tropical Medicine, Keppel Street, London WC1E 7HT, UK</p> <p>WOMAN2@LSHTM.AC.UK</p> <p><small>Protocol number ISRCTN62396133 Version 1.1 : Date 30 April 2018</small></p>	<p>ALERT CARD</p> <p></p> <p>Please keep this card with you and show to anyone giving you medical treatment.</p> <p>If you require any medical treatment within six weeks of having your baby, the doctor named overleaf must be informed.</p>
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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	C. RELATIONSHIP TO TRIAL INTERVENTION (causality)	D. IF NOT SUSPECTED (2) AT C, POSSIBLE ALTERNATIVE CAUSE	E. OUTCOME*
1. No 2. Yes	1. Non-serious 2. Serious 3. Patient died 4. Involved or prolonged in-patient hospitalisation 5. Results in persistent or significant disability/incapacity 6. Life-threatening 7. Other, medically important	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				

If 2-6 selected, complete SAE form


AE ID	Adverse Event	A	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 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 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

SITE NAME	<input type="text"/>	SITE ID	<input type="text"/>	COUNTRY	<input type="text"/>	
PARTICIPANT INITIALS	<input type="text"/> <small>First</small>	<input type="text"/> <small>Last</small>	SCREENING ID	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>	BOX-PACK	<input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/>
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	<input type="checkbox"/>	1. Age	<input type="text"/> years	
2. Serious Adverse Event in medical terms (<i>diagnosis needed – avoid signs and symptoms if possible</i>)						
<input type="text"/>						
3. Is the event due to progression of underlying illness? (circle)	YES	NO	4. Onset of first signs/symptoms of SAE	<input type="text"/> day	<input type="text"/> month	<input type="text"/> year

FORM COMPLETION TIPS

- Please write **clearly** on all paper forms
- **All fields must be completed – do not leave any 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 24 hours 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

Home > Patient > View

Patients

Database entry #	5
Screening ID	100-00004
Randomisation status	Randomised
Box-pack	2010-202
Site Country	Sunnyside Hospital United Kingdom
Source of data	Online
Patient initials	AA
Date of randomisation	29/11/2018
Patient outcome	

Baseline Outcome Queries **Adverse Events**

+ Add Adverse Event

SAR #2 Nausea

Query ID 2 hello

SAR #3 Pneumonia View PI Certification

SAE #8 Allergic reaction

Find patient record and adverse event to certify

Home > Adverse Events > View

To patient

AE ID #8 - Patient Trial ID: 2010-202

Patient Details

Country	United Kingdom
Site & Site ID	Sunnyside Hospital, #10
Patient Initials	AA
Patient Trial ID (Participant ID)	2010-202
DOB or Age	(age 25)
Patient Start Date	29/11/2018
Patient Start Time	
Patient Outcome	
Patient Outcome Date	

Adverse Event Report Form **PI Certification** Queries

Add

Click on PI Certification tab and 'add'

Home > CrfPICertification > Add

Adverse Event Adverse Events

Add Pi Certification

1. PI certification provided as confirmation that all information present is accurate and representative of the event as a whole:

PI certified
 Not certified

2. Comments

2a. A final version of this adverse event and all correspondence regarding any data amendments must be stored in the site Study File. Please confirm that you have printed all forms and correspondence and stored these in your Study File

Yes
 No

Pin

By entering my pin I declare that the information presented in this Case Record Form accurately reflects the medical records, including the results of tests and evaluations performed on the dates specified

*Note: does not apply when LSHTM staff are only changing validation status of form

Submit

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)

The image shows two overlapping documents related to adverse event reporting for the WOMAN-2 trial. The top document is 'GUIDANCE NUMBER 8.1 ADVERSE EVENT REPORTING FLOWCHART'. It is a flowchart that starts with the question 'Is the event already captured on the outcome form?'. If 'NO', it instructs to 'Record on the paper Adverse Event form in the CRF booklet' and 'Report this to the CTU by entering into the WOMAN-2 database within 24 hours'. If 'YES', it states 'Event does not require reporting as an Adverse Event'. Below this, it asks 'Does the event fulfil any of the following serious' criteria: results in death, life threatening, requires in-patient hospitalisation or prolongation of stay, results in persistent or significant disability/incapacity, or other, medically important. If 'YES', it defines a 'Serious Adverse Event (SAE)' and instructs to 'Complete a paper Serious Adverse Event report form' and 'Report this to the CTU by entering into the WOMAN-2 database'. If 'NO', it asks 'Does the investigator / CTU suspect that the SAE is possibly linked to the trial drug?'. If 'NO', it defines a 'Serious Adverse Reaction (SAR)' and instructs 'CTU to assess against Reference Safety Information'. If 'YES', it asks 'Is the SAR expected?'. If 'NO', it instructs 'CTU to assess against Reference Safety Information'. If 'YES', it instructs 'All SAEs, SARs and SUSARs are reported through an annual report to the relevant Regulatory Authorities and Ethics Committees'. It also lists what the report includes: list of SAEs, SARs and SUSARs; Data Monitoring Committee report; and annual reporting on the anniversary of the first Regulatory agency approval. The bottom document is 'GUIDANCE NUMBER 8.2 GUIDANCE ON ADVERSE EVENT REPORTING'. It lists 'REPORTING - POINTS TO CONSIDER' and 'WHAT TO REPORT'. It includes a table for 'ADVERSE EVENTS' and a 'Serious Adverse Event Report Form'.

GUIDANCE NUMBER 8.1 ADVERSE EVENT REPORTING FLOWCHART

Adverse Event (AE): Any untoward medical occurrence affecting a trial participant during the course of a clinical trial.

Is the event already captured on the outcome form?

- NO: Record on the paper Adverse Event form in the CRF booklet. Report this to the CTU by entering into the WOMAN-2 database within 24 hours.
- YES: Event does not require reporting as an Adverse Event.

Does the event fulfil any of the following serious

- results in death
- is life threatening
- requires in-patient hospitalisation or prolongation of stay
- results in persistent or significant disability/incapacity
- other, medically important

YES: Serious Adverse Event (SAE). Complete a paper Serious Adverse Event report form. Report this to the CTU by entering into the WOMAN-2 database.

NO: Does the investigator / CTU suspect that the SAE is possibly linked to the trial drug?

- NO: Serious Adverse Reaction (SAR). CTU to assess against Reference Safety Information.
- YES: Is the SAR expected? If NO, CTU to assess against Reference Safety Information. If YES, All SAEs, SARs and SUSARs are reported through an annual report to the relevant Regulatory Authorities and Ethics Committees.

Report includes:

- List of SAEs, SARs and SUSARs
- Data Monitoring Committee report

Reported annually on the anniversary of the first Regulatory agency approval.

The Site File contains:

- Guidance on AE Reporting for the WOMAN-2 trial (Trial)
- Additional copies of AE CRF (from CRF booklet) and SAE
- Completed AE forms and SAE report forms should be box file 1

CTU will coordinate the reporting to all relevant Ethics Committees. URGENT ADVICE REQUIRED: CTU emergency number 444 444

GUIDANCE NUMBER 8.2 GUIDANCE ON ADVERSE EVENT REPORTING

REPORTING - POINTS TO CONSIDER

- Ensure the participant is assessed daily for any untoward medical events
- If there is an untoward medical event, assess if this meets the adverse event reporting criteria

WHAT TO REPORT

- Any adverse event as defined in the Trial Protocol that occurs up to 42 days after randomisation
- See Protocol Page 20 for full adverse event definitions

Consider:

- Is the event untoward for that participant or the natural history of the primary trial disease under investigation i.e. anaemia > low haemoglobin?
- Is it a new medical occurrence, not present prior to randomisation?
- Has a pre-existing chronic condition appeared to worsen post-randomisation?
- Is it an event that is NOT already reported on the outcome form e.g. PPH, anaemia, vomiting etc.?

IF YES - REPORT

- Record all Adverse Events (AEs) in the Case Report Form (CRF) Booklet. Complete one row per Adverse Event

ADVERSE EVENTS

AE ID	AE Description	AE Type	AE Severity	AE Date	AE Status	AE Reported	AE Reported Date	AE Reported By	AE Reported To

SERIOUS ADVERSE EVENT REPORT FORM

WOMAN-2 Guidance on Adverse Events Reporting
Final v1.0, 07 January 2010
Protocol Number: (SACT)02/06/13
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LONDON
SCHOOL of
HYGIENE
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MEDICINE

