IMPACCT Trials Coordination Centre (ITCC)

Standard Operating Procedure

5.17 Adverse Event Reporting

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Introduction/Background

Good Clinical Practice clarifies the responsibilities of research sponsors and investigators with regards to research related adverse events in an attempt to forestall adverse events and to ensure when they occur that systems are in place to accurately report, record, and investigate them.

It is important to record adverse events for both Investigational drug and non-drug studies (such as trials that involve surgery, radiotherapy or are observational).

Objective

This SOP describes the procedure by which adverse and serious adverse events and pregnancies are recorded, reported and evaluated as required by Hospital Research Ethics Committees (HRECs) and the International Conference on Harmonisation of Good Clinical Practice (ICH GCP) guidelines.

Scope

This SOP is to be used for any study where adverse and serious adverse events are to be reported. It applies to all staff involved in clinical studies conducted by the IMPACCT Trials Coordination Centre (ITCC) irrespective of individual organisational employment, role or position.

Ownership and Responsibility

All clinical staff in contact with participants are responsible for noting adverse and serious adverse events and pregnancies that are reported by the participant or observed and making them known to the study team caring for the participant in a particular study.

It is the responsibility of the Principal Investigator to ensure that all adverse and serious adverse events and pregnancies are accurately assessed, recorded and reported. While this task can be delegated to other suitably trained and qualified study members and should be recorded in the Staff Signature and Delegation Log (*refer* SOP 4.2.4 Delegation of Duties), overall supervision and responsibility remains with the Principal Investigator.

Procedure

1. Identification of possible adverse events

- The Principal Investigator, site investigators and site staff will be provided with adverse event training at the site initiation visit. There is also an additional 'Adverse Event Training for Sites' PowerPoint presentation that will be provided for reference.
- At each assessment and/or visit the participant should be assessed for the following:

  1) Have there been any problems since the last assessment?

  2) Have there been any new medications, or changes to other medications?

- If the answer is "yes" to either of those two questions, further assessment is needed to determine if the change constitutes an adverse event.
- In addition, each protocol may specify specific symptoms that need to be assessed.

2. Assessing the severity of adverse events

- All problems/symptoms that meet the criteria of an adverse event are to be assessed using the NCI CTCAE criteria
  - Accessible at https://ctep.cancer.gov/protocolDevelopment/electronic_applications/ctc.htm
- The severity is to be a grade between 1 and 5.
- All adverse events are to be discussed with the Principal Investigator.

3. Assessing the causality of adverse events

- Each adverse event must be assessed for relationship and causality of the intervention and the event
- The relationship between an adverse event and study intervention is assigned to be either unrelated, unlikely related, possibly related, probably related or definitely related to the intervention.
- The causality of an adverse event must be assigned as being caused by the underlying disease, another underlying disease, a concomitant medication or non-drug therapy or other specified cause.
- Relationship and Causality must be assessed by the PI or a delegated Investigator.

4. Recording adverse events

- All adverse events are to be fully recorded in the patient clinical record and within the study specific Adverse Event Log (Template 14) and electronic Case Report Form (eCRF).
- All adverse events are to be followed to resolution.
- All adverse events are to be clearly recorded within the participant's medical record.

5. Assessing the seriousness of adverse events

- All adverse events must be assessed to determine if the event also meets the criteria of a serious adverse event.
- This will be a “yes” or “no” response on the Adverse Event Log or eCRF.
- The expected patient population of the study must be taken into consideration when assessing the seriousness of an event.
- In addition, each protocol may specify specific conditions that may be exempt from recording as a Serious Adverse Event.

6. Recording serious adverse events

- If an adverse event is determined to be a Serious Adverse Event (SAE), the details are to be recorded on a Serious Adverse Event Report (Template 40) and emailed to the IMPACCT Trials Coordination Centre **within 24 hours** of becoming aware of the event.
- The SAE must also be entered into the database within 24 hours.
    - Once the SAE form has been received and the SAE entered in the database, the IMPACCT Trials Coordination Centre will check the SAE report and seek clarification when required. Follow-up up reports may be required to be submitted by the site to respond to any request for clarification or to provide updated information related to the SAE that may not be known at the time the site staff became aware of the event.
    - The SAE will be reported to HREC if indicated by the initial assessment (as outlined above), and in accordance with the approving HREC requirements, and will also be reported to:
        - The Joint PaCCSC/CST Trials Management Committee
        - The Data Safety Monitoring Committee/Medical Monitor
        - The regulatory authorities when the adverse events are both **serious and unexpected drug reactions OR serious and expected drug reactions** or when the SAE may affect the conduct of the trial, the safety of the participants or their willingness to continue participation in the trial using the standard form for Adverse Drug Reactions Advisory Committee (ADRAC) by the PaCCSC National Manager only.
- The adverse event reporting requirements of the approving HREC and local research governance office are to be followed **at all times**.

7. Follow-up of serious adverse events

- The serious adverse event is to be followed up to resolution, death, or where further information is no longer possible to obtain.

8. Pregnancy Safety reporting

Although not an adverse event, study Participant pregnancy must be reported following first dose of study drug until study completion (reporting period).

During the reporting period, the Principal Investigator (or his/her designee) must report pregnancy using the Serious Adverse Event Report (Template 40); the same process for reporting serious adverse events (as described above) must be followed.

Pregnancy will be monitored and followed up to term for study Participants. Partners of study Participants who become pregnant during the reporting period, will be asked to give consent to have their pregnancy reported and monitored. Long term follow-up of the baby may be required.

Pregnancy data collected will be used for study safety reporting and analysis.

Related SOPs

4.2.4 Delegation of Duties
5.5.5 Allocation of Participant ID Number
5.5.1 Electronic Data Handling
5.17.1 Medical Monitor
6.0 Protocol Development
8.0 Essential Documents

Other related documents

Template 14: Adverse Event Log
Template 40: Serious Adverse Event Report
Adverse Event Training for Sites PowerPoint Presentation

References

Therapeutic Goods Administration. Pharmacovigilance responsibilities of medicine sponsors-Australian recommendations and requirements, version 2.1. June 2018 (accessed 14/02/2020) https://www.tga.gov.au/publication/pharmacovigilance-responsibilities-medicine-sponsors

Cancer Therapy Evaluation Program, Common Terminology Criteria for Adverse Events, V4.0, DCTD, NCI, NIH, DHHS, May 28, 2009.

International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH). Integrated Addendum to ICH E6(R1): Guideline for Good Clinical Practice E6(R2). November 2016 (accessed 23/10/2017)

https://www.ich.org/fileadmin/Public_Web_Site/ICH_Products/Guidelines/Efficacy/E6/E6_R2__Step_4.pdf

National Statement on Ethical Conduct in Human Research (2007)- Updated 2018- (accessed 07/02/2020)

https://www.nhmrc.gov.au/about-us/publications/national-statement-ethical-conduct-human-research-2007-updated-2018

Note for Guidance on Clinical Safety Data Management: Definitions and Standards for Expedited Reporting. 2000 (accessed 12/11/2017)

https://www.tga.gov.au/sites/default/files/ich37795.pdf

Note for Guidance on Good Clinical Practice (CPMP/ICH/135/95). Annotated with TGA comments 2000 (accessed 17/10/2017)

https://www.tga.gov.au/sites/default/files/ich13595an.pdf

Acknowledgments

Praxis Australia

History			
Version	Date	Author	Reason
1.1	10/01/2006	Contributing authors	New procedure
1.2	25/02/2007	S Whicker	Administrative update
1.3	11/07/2007	B Fazekas	Update prior to MAB review
1.4	18/08/2007	B Fazekas	Changes ratified by MAB and external review
1.5	16/10/2007	B Fazekas	Update after David Currow review
1.6	21/01/2008	B Fazekas	Administrative update following new reference material
1.7	9/09/2010	B Fazekas, T Shelby-James	Periodic review
2.0	3/02/2011	B Fazekas	Changes ratified by MAB
2.1	19/05/2015	C Hope	Periodic review
2.2	28/02/2018	B Fazekas, S Kochovska	Periodic review Publication of the ICH GCP E6 (R2)
2.3	16/03/2020	C Strauss	Periodic review Publication of TGA Pharmacovigilance responsibilities of medicine sponsors V2.1 (June 2018)

Approval		
Version	Approval Name	Approval Signature
2.3	David Currow