PV Office Processing for Non-CTIMP Studies

1. Introduction

This guideline outlines the process to be followed when a Serious Adverse Event (SAE) report for a non-CTIMP study is submitted to the Pharmacovigilance (PV) Office for sponsored studies.

The level of support required from the PV Office for a non-CTIMP study will be defined in the protocol or other study-specific documentation prior to recruitment.

According to National Research Ethics Service guidance, only events considered related and unexpected are subject to expedited reporting. For the majority of non-CTIMP studies, the PV Office will be responsible for handling related and unexpected serious adverse events only.

For high-risk non-CTIMP studies, the PV Office may provide full support if detailed in the study protocol, Safety Reporting Plan or other study-specific document.

All related and unexpected SAEs in a non-CTIMP study must be reported to the Sponsor within 24 hours of awareness of the event.

2. Low-risk Non-CTIMP Studies

In low-risk non-CTIMP studies, where the PV Office is required to process related and unexpected SAEs only, the PV and Safety Manager will review all submitted SAEs.

The PV and Safety Manager will acknowledge receipt of the SAE report and review whether the following report fields have been completed:

- Reporter (name, site, email address, phone number)
- Study
- Participant ID
- Diagnosis
- Serious criteria
- Causality and expectedness

Should any of the items above be missing or inconsistent, the PV and Safety Manager will query the information with the site personnel responsible for submitting the SAE.

Where causality and expectedness have been provided, the PV and Safety Manager will check that the event meets the following Sponsor reporting requirements:

- The event is a serious adverse event as defined within SOP 55.004
- The event is related to the study procedures (this could be a drug, a study-specific procedure, a questionnaire, interview etc.)
- The event is considered unexpected by the reporting investigator

Should the event meet the above criteria, the PV and Safety Manager will check the reported SAE against the expected adverse events documented within the study protocol. Where an adverse event is not listed in the study protocol, the SAE should be reviewed by the CI or a delegated member of the study management group.

Should the event not meet the Sponsor reporting requirements, the investigator will be reminded of the requirements and advised that no further action is required. The SAE will be filed within the non-CTIMP section of the Sponsor PV File.

3. High-risk Non-CTIMP Studies

In high-risk non-CTIMP studies, where the PV Office is required to process all SAEs, the following processes will apply.

3.1 SAE Receipt

Initial and follow-up SAE reports can be submitted to the PV Office as follows:

- On a paper SAE form (generic or study-specific) by fax or email
- Verbal report by telephone
- Using reporting procedures built into a study GCTU eCRF application

3.1.1 Paper reports:

a. Completed paper SAE report forms will be emailed to the PV Office or faxed directly to the PV Office fax number (which triggers an automatic email alert to be sent to PV Office personnel).
b. The handwritten report will be saved and reviewed by the PV Office following the processes detailed in sections 3.2 and 3.3.
c. The PV Office will acknowledge receipt of the report by email. The acknowledgement email will include any queries resulting from the initial review by the PV Office and will be saved within the SAE folder as detailed in section 3.2.
d. With regards to studies that use eCRF reporting procedures, the site staff responsible for submitting the report will be instructed to complete an SAE report via the study eCRF.

3.1.2 Verbal reports:

a. Any call received at the GCTU requesting to report a SAE will be directed to the PV Office. Should PV personnel be unavailable, the call should be directed to the Pharmacovigilance and Safety Manager or RCB Senior Management.
b. The reporter will be asked to provide as much information about the SAE as possible, with a minimum of the following details:
    - Reporter (name, site, email address, phone number)
    - Study
    - Participant ID
    - Diagnosis
    - Serious criteria
    - Causality and expectedness
c. The PV Office will acknowledge the report by email. This email will detail the information provided verbally and will be saved within the SAE folder as detailed in section 3.2.
d. With regards to studies that use eCRF reporting procedures, the site staff responsible for submitting the report will be instructed to submit the SAE information to the eCRF within 48 hours of the verbal report. For all other studies, the reporter will be instructed to follow up the verbal report with a written copy within 48 hours of the verbal report.

3.1.3 eCRF reports:

a. Where studies have reporting facilities built into an eCRF application, an automatic email alert will be triggered on input of an SAE report from site. This alert is sent to the PV Office and relevant Sponsor and study personnel.

b. The PV Office will download a copy of the .pdf report from the eCRF application. This will be saved and reviewed by the PV Office following the processes detailed in sections 3.2 and 3.3.

3.2 Tracking and Storage

All SAE reports, completed SAE Processing Forms (Form 55.015A) and related SAE correspondence will be saved electronically in the relevant filestore folders. Hard copies will also be printed and filed in study SAE folders.

SAE reports will be saved as .pdf files and named according to the following format:
SAE_ParticipantNumber_OnsetDate_ReportNumber

An SAE processing form will be prepared and completed by the PV Office member handling the SAE. It will be saved to the study folder in the following format:
PF_ParticipantNumber_OnsetDate_ReportNumber

3.3 SAE Review

3.3.1 Initial SAE Reports:

PV Office personnel will perform the following checks on receipt of an initial SAE report:

a. Are the trial and subject identifiers included in a paper report?
b. Has the SAE been reported within 24 hours of the site becoming aware of the event? If not, PV Office personnel will notify the PV and Safety Manager.
c. Is there a diagnosis? If there is no text provided in the diagnosis field, or if the text indicates the event is unknown, this should be queried with site staff until resolution. Should any of the text be unclear, the PV and Safety Manager (or Sponsor delegate) should be notified – for example, by noting this on the SAE Processing Form.
d. Has a narrative been provided and are any dates consistent with date fields elsewhere on the report?
e. Has seriousness criteria been assigned?
f. Have causality and expectedness been assigned and reviewed by the PI/CI or an authorised clinician? It is essential that causality and expectedness are assigned to a SAE as these govern the requirement to report the event to the REC. While the site submitting the SAE to the Sponsor may have assigned causality and expectedness, if clinical review has not taken place, this will be queried by the PV Office. All related events must be notified to the PV and Safety Manager.
g. Does the SAE have an outcome?

Should any of the items above be missing or inconsistent, the PV Office should query the information with the site personnel responsible for submitting the SAE and/or notify the PV and Safety Manager as required.

The PV and Safety Manager will be responsible for:

a. Reviewing the SAE form for clinical consistency and data discrepancies, including whether the SAE contains multiple events which require splitting.
b. For events assigned as related, reviewing and confirming the expectedness assessment against the approved protocol or with the lead investigator(s) for the study. Any inconsistencies should be raised with the study leads. Should the PV and Safety Manager be unable to carry out the review of the expectedness assessment according to the required timelines (e.g. due to holiday or absence), the PV Office will contact

the lead investigator(s) to review and confirm the expectedness assessment of any related events.

c. For events assigned as related to the study procedures and unexpected (i.e. potential related and unexpected SAEs), consulting the study protocol or liaising with the lead investigator(s) to ensure that the assignment is correct. In all cases, once the event has been classified as a related and unexpected SAE, it should be reported to the REC.

The regulatory timeline for the reporting of a related and unexpected SAE to the REC is 15 days.

3.3.2 Follow-Up SAE Reports:

Upon receipt of a follow-up report for an SAE, the PV Office will check whether the causality and/or expectedness of the event have changed. If so, the follow-up report will require review by an authorised member of the study team and potentially by the lead investigator(s). The SAE should be processed according to section 3.

4. Downgrading of an SAE report

If a follow-up report identifies that a previously reported event is no longer considered by the investigator to be an SAE, the report will not be removed from the SAE file, but it will be identified as "Not an SAE" and will be excluded from any study reports.

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