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| **TGHN-256x151px**  **Standard Operating Procedure** | | | **SOP No:**  **Version: 1**  **Effective Date:** | |
| **Title: Non-compliance to protocol SOP** | | | | |
|  | NAME | **SIGNATURE** | | **DATE** |
| **PREPARED BY** |  |  | |  |
| **REVIEWED BY** |  |  | |  |
| **QA UNIT**  **AUTHORITY** |  |  | |  |
| **APPROVAL**  **AUTHORITY** |  |  | |  |

1. **Purpose/scope**

To describe the procedure for identifying, documenting and reporting non-compliance to the protocol, Good Clinical Practice and/or regulatory requirement during a clinical trial conducted by the [group/institution].

1. **Templates/forms**

QA02.1 Non-compliance report

QA02.2 Non-compliance log

1. **Glossary/definitions**

**Compliance**

Adherence to all the trial-related requirements, good clinical practice (GCP) requirements, and the applicable regulatory requirements (See ICH GCP E6, 1996).

**Exceptions**

The UCT Faculty of Health Sciences HREC defines exceptions as one-time intentional actions or processes that depart from the HREC-approved protocol, stipulating that these temporary or limited changes must receive HREC approval prior to implementation in order to prevent being non-compliant. However, for clinical trials of unregistered medicinal products the current international standard is that these exceptions (sometimes termed 'waivers') are not acceptable. Therefore no such exceptions will be allowed.

**Essential Documents**

Documents which individually and collectively permit evaluation of the conduct of a clinical trial and the quality of the data produced (See South African Good Clinical Practice Guideline, Second Edition. 2006. Appendix C).

**Investigator Site File (ISF)**

Files of Essential Documents held by the Investigator.

**Non-compliance**: An action by assigned staff which is not in accordance with documents applicable to the trial (e.g. trial protocol, relevant SOPs, GCP and applicable regulations). Non-compliance can be reported by staff, identified during a site monitoring visit, an internal or external audit or during an inspection. Non-compliance may include, but is not limited to one or more of the following:

* An action specifically prohibited by the protocol or relevant document
* An additional action not specified in the protocol or relevant document
* An omission of an action specifically stipulated in the protocol or relevant document.

**Major non-compliance**: Serious and/or persistent contravention of GCP and/or trial-related procedures that have an impact on participant safety, may substantially alter risks to participants, may have an effect on the integrity of the trial data, and/or the ethics of the trial (e.g. failure to perform a required safety assessment, written informed consent not appropriately obtained before initiation of trial-related procedures).

**Minor non-compliance**: A contravention of GCP or the protocol that does not impact participant safety, compromise the integrity of the trial data, and/or ethics of the trial (e.g. trial visit conducted outside of required timeframe, failure of participant to return trial medication). Several minor observations may collectively be considered as equal to a major non-compliance.

**Root cause analysis**: The investigation and identification of underlying causes of problems or events, in order to develop and implement corrective and preventive actions, to prevent recurrence of the events.

1. **Responsibilities and procedure**
   1. The investigator should not implement any deviation from, or changes of, the protocol without agreement from the Sponsor, and documented approval/favourable opinion of the human research ethics committee (HREC), and South African Medicines Control Council (MCC) if relevant. An exception is when it is necessary to eliminate an immediate hazard to trial participants. In the event of the latter, as soon as possible, the implemented deviation or change, the reasons for it, and, if appropriate, the proposed protocol amendment(s) should be submitted to the Sponsor for agreement, the HREC for review and approval, and, if required, to the regulatory authority as a notification. NB Logistical or administrative changes, which may not require prior HREC/MCC approval, should be discussed with the Sponsor before implementation.
   2. Unplanned non-compliance noted within the trial team should be brought to the attention of the PI and Sponsor as soon as possible. Form QA02.1 (or trial-specific equivalent document) will be completed, including the category, root cause analysis and corrective/preventive action taken:
      1. Major non-compliance will be reported to the institutional HREC on form FHS011 within seven calendar days of knowing about the incident. The MCC will also be informed.
      2. Minor non-compliance will be reported to the institutional HREC and MCC in the next progress report.
   3. The following allowable windows apply to the timing of pharmacokinetic samples, and their associated visit procedures (unless otherwise specified in a trial protocol), and will not be considered non-compliance:

|  |  |
| --- | --- |
| **Protocol scheduled time (post-dose)** | **Allowable window** |
| 0 minutes to ≤ 4 hours | ± 5 minutes |
| > 4 hours to ≤ 24 hours | ± 10 minutes |
| > 24 hours to ≤ 48 hours | ± 1 hour |
| > 48 hours to ≤ 72 hours | ± 4 hours |
| > 72 hours to ≤ 168 hours | ± 1 day |
| > 168 hours | ± 2 days |
| > 4 weeks | ± 3 days |
| > 6 weeks | ± 7 days |

* 1. Any documentation relating to non-compliance will be filed in the ISF.

1. **Document history:**

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| --- | --- | --- | --- |
| **Version No.** | **Date** | **Reviewer** | **Details of changes** |
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