South African Health Products
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ELECTRONIC SUBMISSION OF CLINICAL TRIAL DOCUMENTS (AMENDMENTS, BIOEQUIVALENCE STUDIES, RESPONSES, NOTIFICATIONS, AND SERIOUS ADVERSE EVENTS)

The purpose of this document is to notify applicants of the electronic submission process for major activities performed in the Clinical Trials Unit (CTU), South African Health Products Regulatory Authority (SAHPRA), in order to improve the turnaround times of applications. A number of e-mail addresses have been registered to support this initiative. Applicants are requested to use each specific e-mail address exclusively for a specific type of communication in order to minimize unintended delays in finalization of requests.

Document History

Final Version	Reason for Amendment	Effective Date
1	First issue and published for implementation	April 2015
2	Administrative Changes	April 2019
3	- Content structured on the new SAHPRA Guideline Template - Old guideline number 9.59 changed to SAHPGL-CEM-CT-01 - Form *CTF1* changed to GLF-CEM-CT-01A and GLF-CEM-CT-01B; Form *CTF2* changed to GLF-CEM-CT-01C and Form *CTF3* also changed to GLF-CEM-CT-01D	05 September 2022

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Contents

Glossary

Abbreviation/ Term	Meaning
CTF1	Clinical trial application form 1-New applications
CTF2	Clinical trial application form 2 -Protocol amendments
CTF3	Clinical trial application form 3- Additional sites and investigators
CTU	Clinical trials Unit
IB	Investigator Brochure
PIL/ICON	Patient information leaflet/informed consent
PHE	Public Health Emergency

1. INTRODUCTION

Electronic Communication regarding the conduct of clinical trials is the primary interface between SAHPRA and applicants conducting clinical trials. SAHPRA therefore recognises the importance and value of timeous evaluation of all communication linked to the conduct of a clinical trial and therefore strives to maintain an effortless and easy submission process for any document to be reviewed.

1.1 Purpose

This guideline is intended to outline the process of electronic document submission for the various activities linked to the Clinical trials unit.

1.2 Scope

This guideline applies to all applicants applying for the review of Clinical trials and any other related activity requiring documents to be provided to the clinical trials unit for review and notification. A number of e-mail addresses have been registered to support this initiative. Applicants are requested to use each specific e-mail address exclusively for a specific type of communication.

2. LEGAL PROVISION

This guideline is established in terms of Regulation 30 of the medicines and related substances act, 101 of 1965, conduct of clinical trials.

3. APPLICATIONS FOR NEW CLINICAL TRIAL APPLICATIONS

This applies to ONLY new Clinical Trial Applications and is NOT applicable to Bioequivalence (BE) studies. In case of BE studies, refer to section 6.)

The applicant is to refer to the SAHPRA website on https://www.sahpra.org.za/guidelines/ for submission due dates in order to submit a new clinical trial. Applicants are requested to alert the CTU via e-mail of the submission using the following e-mail address: ctcresponses@sahpra.org.za and to include the following information:

i. In the Subject title of the e-mail: Type of application, protocol number, SAHPRA predetermined cycle, email number in case of multiple emails.
e.g. New clinical trial application alert_NER000_May 2022 cycle_ email 1 of 5

ii. The following is important to note for all new clinical trial applications:
   - The submission email must include organised zipped folders for various sections of the (**GLF-CEM-CT-01A** and **GLF-CEM-CT-01B**, replaced the *old Form CTF1*) as per the CTF1 checklist. The (**GLF-CEM-CT-01A** and **GLF-CEM-CT-01B**, replaced the *old Form CTF1*) are found at: https://www.sahpra.org.za/clinical-trials-application-and-report-forms/
   - Individual site documents for each staff member must be uploaded into 1 document and labelled with the staff name and arranged in folders according to the site which they belong.
   - Incomplete documentation or sub-standard submissions will be rejected.
   - Applications submitted without Clinical Trial Insurance and Proof of payment will be rejected.

3.1 Responses for new Clinical Trial Application

i. Responses to the screening checklist and the review of recommendations letter from the Clinical Trials Expert Committee of SAHPRA, must be sent to the following e-mail address: ctcresponses@sahpra.org.za and include labelled attachments to the required documents.
ii. Submit the responses to Clinical Trials Committee (CTC) recommendation in MSWord format and Pdf formats.
iii. Submit all other accompanying documents in Portable Document Format (PDF).
- Files should be PDF v1.4, 1.5, 1.6 or 1.7 and should be legible with the Acrobat Reader search plug in or any other freeware viewer.
- PDF files should be saved as "Optimised" to reduce the size and allow faster opening when viewed via an internet connection. The use of additional software to navigate and work with the files is not acceptable.
- If PDF files are not produced from an electronic source document but from scanned paper, readability and file size should be balanced; the following is recommended: resolution 300 dpi (photographs up to 600 dpi), avoid gray-scale or colour where possible, use only lossless compression techniques.
- The file must be searchable (OCR scanned).

iv. The maximum size of documents allowed per e-mail is 5 MB.
v. The subject title of the e-mail should include the following information:
Type of application, Protocol number, and SAHPRA database tracking number.
e.g. CTC Response_NER000_20220203
vi. As per arrangement with CTU, in case of a big file of documents and documents need to be couriered, the waybill should indicate the type of application, protocol number and SAHPRA database tracking number.
e.g. CTC Response, NER000, 20150320

Public Health Emergency (PHE) Applications are expedited with the response provided within 10 working days.

4. APPLICATIONS FOR PROTOCOL AMENDMENTS DURING CONDUCT OF CLINICAL TRIALS

In the event of a request for an amendment to the approved Protocol, the Protocol amendment and accompanying documents must be emailed to : ctcamendments@sahpra.org.za and the application form form for protocol amendments (**GLF-CEM-CT-01C**, replaced the *old Form CTF2*) is found on the SAHPRA website at : https://www.sahpra.org.za/clinical-trials-application-and-report-forms/

i. Submit the cover letter, application form for protocol amendment (**GLF-CEM-CT-01C**, replaced the *old Form CTF2*), amended protocol and/or investigators' brochure (IB) and/or patient information leaflet/informed consent (PIL/ICON) documents with track changes in MSWord format and other documents according to the screening checklist.
ii. Submit clean copies of the (**GLF-CEM-CT-01C**, replaced the *old Form CTF2*), investigators' brochure (IB) and/or patient information leaflet/informed consent (PIL/ICON) documents in Portable Document Format (PDF), as well as all other accompanying documents, as described in section 3.1, iii-iv.
iii. The subject title of the e-mail should include the following information:
Type of application, Protocol number, and SAHPRA database tracking number.
e.g. Protocol amendment_NER000_20220203
iv. As per arrangement with CTU, in case of a big file of documents and documents need to be

couriered, the waybill should indicate the type of application, protocol number and SAHPRA database tracking number.
e.g. CTC Amendment_ NER000_ 20150320

Note: **All queries related to protocol amendments, and related communications should also be sent to this email address: ctcamendments@sahpra.org.za**

Public Health Emergency (PHE) Applications are expedited with the response provided within 10 working days.

4.1 Responses to Protocol amendments recommendations

i. For response to non-approval of protocol amendments, submit the following information: cover letter (MS-word and PDF format) with outstanding documents and/or responses to recommendations as outlined (MS-word and PDF format)
ii. The subject title of the e-mail should include the following information:
Type of application, Protocol number, and SAHPRA database tracking number.
e.g. responses_Protocol amendment_NER000_20220203
iii. As per arrangement with CTU, In case of a big file of documents and documents need to be couriered, the waybill should indicate the type of application, protocol number and SAHPRA database tracking number.
e.g. Responses Protocol amendment_ NER000_ 20220203

Note: **All responses to protocol amendments, related queries, and amendment notifications should also be sent to this email address: ctcamendments@sahpra.org.za**

5. APPLICATIONS FOR ADDITIONAL INVESTIGATORS AND SITES DURING CONDUCT OF CLINICAL TRIALS

Additional Investigators and Sites applications and accompanying documents must be emailed to the following address: ctcinvestigators@sahpra.org.za. The Application Form (**GLF-CEM-CT-01D**, replaced the *old Form CTF3*) is to be found on the SAHPRA website at : https://www.sahpra.org.za/clinical-trials-application-and-report-forms/

i. Submit the Cover Letter, Application Form (**GLF-CEM-CT-01D**, replaced the *old Form CTF3*) for additional investigators and sites in MSWord format.
ii. Submit all other accompanying documents in Portable Document Format (PDF) as described in section section 3.1, iii-iv
iii. Subject title should include the following information: Type of application, protocol number, and SAHPRA database tracking number.
e.g. Additional site_NER000_20220203
e.g. Additional investigators_NER000_20220203
iv. As per arrangement with CTU, in case of a big file of documents and documents need to be couriered, the waybill should indicate the type of application, protocol number and SAHPRA database tracking number.
e.g. Additional site and Investigators, NER000, 20220203, OR
e.g. Additional Investigators, NER000, 20220203

5.1 Responses to application of additional investigators and sites during conduct of clinical trials

i. For response to non-approval of investigators and sites, submit the following information: cover letter (MS-word and PDF format), outstanding documents and/or responses which led to non-approval in PDF format. The PDF attachments must be well labeled in order to facilitate for a speedy review.
ii. The subject title of the e-mail should include the following information:
Type of application, Protocol number, and SAHPRA database tracking number.
e.g. responses_additional investigators and sites_NER000_20220203

Note: **All responses to additional investigators and sites and related queries should also be sent to this e-mail address: ctcinvestigators@sahpra.org.za**

6. APPLICATION FOR BIOEQUIVALENCE STUDIES

Submit all Bioequivalence (BE) protocol applications, Bioequivalence Additional investigators and Sites, Bioequivalence amendments, and accompanying documents to the following address: ctcbeprotocols@sahpra.org.za . The Application Form (**GLF-CEM-CT-01A**, replaced the *old Form CTF1*) is to be found on the SAHPRA website at : https://www.sahpra.org.za/clinical-trials-application-and-report-forms/

i. Submit the cover letter, Clinical Trial Forms (**GLF-CEM-CT-01A** and **GLF-CEM-CT-01B**, replaced the *old Form CTF1*), protocol, IB, PIL/ICON in MSWord format.
ii. Submit all other accompanying documents in Portable Document Format (PDF) as described in section 3.1, iii-iv
iii. As per arrangement with CTU, in case of a big file of documents and documents need to be couriered, the waybill should indicate the type of application, protocol number and SAHPRA database tracking number.
For new BE study: e.g. Bioequivalence study, NER000
For BE responses: e.g. BE responses, NER000, 20220203
For BE Amendments: e.g. BE Amendment, Amend3, V2, 31 April 2015, NER000, 20220203
For BE Investigators and sites: e.g BE Investigators/Sites, NER000, 20220203
iv. Subject title of the e-mail should include the following information:
For new BE study: Type of application, and protocol number
e.g. Bioequivalence study, NER000
For BE responses: Type of application, protocol number, and SAHPRA database tracking number
e.g. Bioequivalence response_NER000_20220203
For BE amendment: Type of application, amendment number, version number, amendment date, protocol number, and SAHPRA database tracking number,
e.g. BEAmendment_Amend3, V2, 31 April 2015_NER000_20220203
For BE Additional investigators and Sites: Type of application, protocol number, and SAHPRA database tracking number
e.g. Bioequivalence response_NER000_20220203

Note: **All responses to BE protocols, BE investigators and sites, BE notifications, BE amendments and related queries should also be sent to this e-mail address: ctcbeprotocols@sahpra.org.za**

Public Health Emergency (PHE) Applications are expedited with the response provided within 10 working days.

7. NOTIFICATIONS AND NOTIFICATION STUDIES

Submit all Notifications (excluding amendments- and BE-related notifications) to the following email address: ctcnotifications@sahpra.org.za. The Two-Weekly Progress Report form (**GLF-CEM-CT-01F**) and Six-Monthly Progress Report form (**GLF-CEM-CT-01G**) and Notification Studies for Phase IV form (**GLF-CEM-CT-01E**) are to be found on the SAHPRA website at: https://www.sahpra.org.za/clinical-trials-application-and-report-forms/

i. Submit the cover letter, notification in MS-Word format or PDF, where applicable.
ii. The email subject title should include the following information: Type of notification, protocol number, and SAHPRA database tracking number (if available).
e.g. Six-Monthly Progress Report, NER000, 20220203
iii. Notifications related to investigators and sites should also be sent to this email address.

Note: **All responses and/or communication, and related queries should also be sent to this e-mail address: ctcnotifications@sahpra.org.za.**

8. INDIVIDUAL SERIOUS ADVERSE EVENTS

Submit all Serious Adverse Events (SAEs) to the following email address ctcsaes@sahpra.org.za

i. Submit cover letter detailing the following information: Title of the study, SAHPRA reference number, protocol number, name of site, patient study ID, cause of SAE, causality and SAE reporting form or any information if applicable.
ii. The email subject title should include the following information: SAE, protocol number, and SAHPRA database tracking number.
e.g. SAE_NER000_20220203

Note: **This e-mail is applicable to individual SAEs only. Line listing must be submitted with six-monthly progress reports to the notification e-mail address.**

NOTE FOR ALL APPLICATIONS:

- Incomplete documents will not be accepted.
- Failure to comply may delay processing of the application.

Important email addresses to use for communication:

E-mail address for new applications and responses to new Clinical Trial applications and related queries: **ctcresponses@sahpra.org.za**

E-mail address for new Protocol amendments, responses to amendments and related queries: **ctcamendments@sahpra.org.za**

E-mail address for Additional Investigators & Sites, responses to additional and related queries: **ctcinvestigators@sahpra.org.za**

E-mail address for Bioequivalence studies, BE amendments, responses to BE studies and related queries: **ctcbeprotocols@sahpra.org.za**

E-mail address for Notifications and related queries: **ctcnotifications@sahpra.org.za**

E-mail address for Individual Patient Serious Adverse Events and related queries: **ctcsaes@sahpra.org.za**

9. VALIDITY

This guideline is valid for a period of 5 years from the effective date of revision and replaces the old guideline for Electronic Submission of Clinical Trials, document number 9.59. It will be reviewed on this timeframe or as and when required.

10. ADDENDA

10.1 ADDENDUM 1: ACCOMPANYING DOCUMENTS

A PROTOCOL AMENDMENTS

The accompanying documents for protocol amendments should include the following, but are not limited to:

- Cover letter
- Application for protocol amendment form (**GLF-CEM-CT-01C**, replaced the *old Form CTF2*), in MSWord
- Proof of payment
- Original protocol
- Protocol with changes/amendments (with track changes)
- Summary of changes
- Any other documents which may be required by SAHPRA.

B ADDITIONAL INVESTIGATORS AND SITES

The accompanying documents for additional investigators and sites should include the following, but are not limited to:

Investigators and Sites

- Cover letter
- Application for additional investigator(s) or change of investigator(s) and application for additional sites form (**GLF-CEM-CT-01D**, replaced the *old Form CTF3*)
- Proof of payment
- Valid Malpractice insurance certificate
- Declaration(s)
- Valid Good Clinical Practice (GCP) certificate
- Proof of registration with statutory bodies
- Valid Dispensing licences
- Workload
- *Curriculum vitae* in SAHPRA format
- Details of emergency trolley and services for the site
- Any other documents which may be required by SAHPRA.

Additional/Support staff

- *Curriculum vitae* in SAHPRA format
- Declaration(s)
- Valid Good Clinical Practice (GCP) certificate
- Proof of registration with statutory bodies
- Any other documents which may be requested by SAHPRA.

C BIOEQUIVALENCE STUDIES

The accompanying documents for bioequivalence studies will be the same as for application for new clinical trial, documented in clinical trial forms (**GLF-CEM-CT-01A** and **GLF-CEM-CT-01B**, replaced the *old Form CTF1*).

The accompanying documents for Bioequivalence amendments (**GLF-CEM-CT-01C**, replaced the *old Form CTF2*) and additional investigators and sites (**GLF-CEM-CT-01D**, replaced the *old Form CTF3*) will be the same as those in section A and B above.

D NOTIFICATIONS AND NOTIFICATION STUDIES

The accompanying documents for notifications should include the following, but are not limited to:

- **Phase IV study:**
  - Cover letter
  - Completed form
  - Protocol, in MS Word
  - Patient Information Leaflet/Informed Consent Document (PIL/ICON)
  - Copy of Ethics approval
  - Professional Information (Package Insert)
  - Proof of payment
  - Any other documents which may be requested by SAHPRA
- **Other Notifications:** This may include but not limited to:
  - Cover letter
  - Investigator's Brochure
  - Six-Monthly Progress Report
  - Study Deviations
  - Study Violations
  - Study Closure
  - Site closure
  - Line Listing
  - Additional or removal of site staff
  - Any other notification
  - Any other documents which may be requested by SAHPRA

E SERIOUS ADVERSE EVENTS (SAEs)

The accompanying documents for SAEs should include the following, but are not limited to:

- Cover letter.
  - This should include title of the study, SAHPRA reference number, protocol number, name of site, patient study ID, cause of SAE, causality
- SAE reporting form or any information if applicable.