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| SIX MONTHLY PROGRESS REPORT FORMFOR CLINICAL TRIALS |

# INSTRUCTIONS

1. This form is to be completed six-monthly from the date of approval of the clinical trial by the South African Health Products Regulatory Authority (SAHPRA).
2. The applicant/sponsor must complete Parts A and B.
3. Part A is specifically for the study participants in South Africa.
4. Part B is an overall safety line listing for the study in South Africa (and any other issues of special concern outside South Africa) and includes all Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARS) for all participants in this study.
5. *Note:* Protocol Deviations must be reported separately, six-monthly to SAHPRA. Protocol deviations are not part of the report but should be submitted as a separate communication at the same time as this report.
6. The End of Study progress Report should include the summary of investigational product authorized for importation (initial and amendment), quantity imported, used and remaining (destroyed) at end of the study.

*Note:* The End of Study report should be submitted 30 days after completion or termination of a Clinical Trial.

# CLINICAL TRIAL SIX-MONTHLY PROGRESS REPORT

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| PART A: STUDY OVERVIEW SOUTH AFRICA | |
| 1. SAHPRA Database tracking number | n/a |
| 1. Study Title | Innovative machine learning and multi-source data analysis towards the development of an urban heat-health Early Warning System for African cities |
| 1. Protocol number | HEAT002 |
| 1. *Details of Sponsor / Applicant:* |  |
| * 1. Name of Sponsor | Fogarty International Center and National Institute of Environmental Health Sciences (NIEHS) and OD/Office of Strategic Coordination (OSC) of the National Institutes of Health under Award Number U54 TW 012083 |
| * 1. Name of Applicant | Prof Matthew Chersich |
| * 1. Contact Person | Mr. Craig Parker |
| * + 1. Telephone number | 011 3855300 |
| * + 1. Fax number |  |
| * + 1. Cell-phone number | +27 792848593 |
| * + 1. E-mail address | cparker@wrhi.ac.za |
| 1. List of all active trial sites, address and Principal Investigators (PIs) | n/a |
| 1. *Trial Information:* |  |
| * 1. Date of approval of study | 06 June 2023 |
| * 1. Treatment hold (if applicable) with reasons (start date and stop date of hold should be included) | n/a |
| * 1. Expected date of completion | June 2026 |
| 1. *Number of participants in the trial (per site), (this section should be accumulative):* |  |
| * 1. Screened (signed consent) | n/a |
| * 1. Randomised | n/a |
| * 1. Withdrawn from treatment (continue in follow up), with reasons | n/a |
| * 1. Withdrawn from study (early termination), with reasons | n/a |
| * 1. Study completed | n/a |
| * 1. Lost to follow-up | n/a |
| * 1. Deaths | n/a |
| 1. Applicant/Sponsor comment on progress to date | We are pleased to report on the considerable strides made in the study screening process for our ongoing project, RP2.  **Study Screening:**  From the period spanning 2000 to 2022, we embarked on a comprehensive screening of 2267 studies conducted in Johannesburg. The aim was to identify studies that align with our project's eligibility criteria. We were able to identify 42 studies that met our requirements for inclusion. However, we encountered ambiguities with 18 studies, which are currently undergoing a more thorough review to clarify their eligibility. A significant number, precisely 2205 studies, did not meet our eligibility criteria and were consequently excluded.  **Eligible Studies by Research Units:**  Out of the 42 eligible studies, they are associated with the following prestigious research units:   1. PHRU - Perinatal HIV Research Unit: 14 studies 2. WRHI - Wits Reproductive Health & HIV Institute: 9 studies 3. VIDA - The Vaccine and Infectious Diseases Analytics Research Unit: 6 studies 4. CHRU - Clinical HIV Research Unit: 5 studies 5. Ezintsha: 4 studies 6. DPHRU - Developmental Pathways for Health Research Unit: 1 study 7. ECRU - Effective Care Research Unit: 1 study 8. WCR Bara Clinical Trial Centre: 1 study 9. Lynn Morris - Virology: 1 study   **Current Data Transfer Agreements (DTAs):**  We are currently collaborating with VIDA and DPHRU to facilitate data transfer agreements for the following studies:   1. **Surveillance among Healthcare Workers for SARS-Coronavirus–2 Infection (COVID‐HCW study):** This study focused on the surveillance of SARS-Coronavirus-2 infection among healthcare workers. 2. **ChadOx1 SARSCoV-2 Vaccine Trial:** This trial examined the effectiveness of the ChadOx1 SARSCoV-2 Vaccine.   **Acquired Datasets:**   |  | **Study title** | **Number of participants** | **Location** | | --- | --- | --- | --- | | 1 | Improved neuropsychological and neurological functioning across three antiretroviral regimens in diverse resource-limited settings. We will request data on the effects of different antiretroviral regimens on neuropsychological and neurological functioning in resource-limited settings. | 143 | Johannesburg | | 2 | Timing of antiretroviral therapy for HIV-1 infection and tuberculosis. We will request data on the optimal timing of antiretroviral therapy initiation in the context of HIV-1 and tuberculosis co-infection. | 806 | Johannesburg | | 3 | An Evaluation of Strategies to Accelerate Entry-into-care following HIV Diagnosis among Adults in Gauteng and Limpopo Provinces, South Africa | 1250 | Johannesburg | | 4 | Optimal Combination Therapy After Nevirapine Exposure | 106 | Johannesburg | | 5 | A randomized, Phase II, open-label study to compare twice daily and once daily potent antiretroviral therapy and to compare self-administered therapy and therapy administered under direct observation | - | Johannesburg | | 6 | Collection of Comparison Neurocognitive Data in Resource-Limited Settings | - | Johannesburg | | 7 | A Phase IV, prospective, randomized, open-label evaluation of the efficacy of once-daily protease inhibitor- and once-daily non-nucleoside reverse transcriptase inhibitor-containing therapy combinations for initial treatment of HIV-1 infected individuals from resource-limited settings (PEARLS) trial. | 1571 | Johannesburg | | 8 | Determinants of Type 2 Diabetes Mellitus Risk in Middle-aged Black South African Men and Women: A Longitudinal Study | 1400 | Johannesburg | | 9 | A 96-week Randomised, Phase 3 Non-inferiority Study of DTG + TAF + FTC Compared with DTG + TDF + FTC and EFV + TDF+FTC in Patients Infected with HIV-1 Starting First-line Antiretroviral Therapy | 1053 | Johannesburg | | 10 | Low-dose ritonavir-boosted darunavir once daily versus ritonavir-boosted lopinavir for participants with less than 50 HIV RNA copies per mL (WRHI 052): a randomised, open-label, phase 3, non-inferiority trial” | 300 | Johannesburg | | 11 | A randomised, double-blind, multi-centre, parallel- group phase 3B study to demontrate non-inferiority of stavudine (20mg twice daily) compared with Tenofovir Disproxil Fumarate (300mg once daily) when administered in combination with Lamivudine and Efavirenz in Antiretroviral-naive patients infected with HIV-1 | 600 | Johannesburg | | 12 | Breastfeeding Version of the PROMISE Study (Promoting Maternal and Infant Survival Everywhere): (1077 BF /PROMISE) | 268 | Johannesburg | | 13 | Novel TB Prevention Regimens for HIV-Infected Adults | 1148 | Johannesburg | | 14 | Feasibility of HIV Prevention Cohort Studies Among MSM in Sub-Saharan Africa | 101 | Johannesburg | | 15 | Uptake and adherence to daily oral PrEP as a primary prevention strategy for young African women: A Vanguard Study | 137 | Johannesburg | |
| 1. Summary Data Safety Monitoring Board or Safety Committee recommendations | n/a |

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| PART B: OVERALL SAFETY LINE LISTING | | | |
| 1. Safety Line Listing of all Serious Adverse Events (SAEs) and Suspected Unexpected Serious Adverse Reactions (SUSARS) for all participants per site in this study in South Africa   *Note: Detailed Site Specific Line listing may be submitted as an attachment (should not be accumulative) as per Safety Reporting guideline* | | | |
| **SAEs and SUSARS** | **Relationship to study medicine (investigator’s opinion)** | | **Outcome(s)** |
| **Site 1: (name of site)** | | | |
| n/a | Possible (2)  Probable (1)  Definite (2)  Unrelated (2)  unknown (0) | | 7 patients recovered  2 still treated |
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| **Site 2: (name of site)** | | | |
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| **Site 3: (name of site)** | | | |
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| **Any safety issues of special concern outside South Africa** | | | |
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| 1. Line Listing of all critical and major protocol violations at the site:   Protocol *Violation* is any change, divergence, or departure from the study design or procedures defined in the protocol that might significantly affect participants’ safety, and well-being and/or the reliability of the study data.  Protocol *Deviation* is accidental or unintentional changes to, or non-compliance with the research protocol that does not increase risk or decrease benefit or does not have a significant effect on the participants, safety or well-being; and/or the reliability of the study data.  *Note: South African Site Specific Line Listing of all major protocol violations may be submitted as an attachment*  *Site specific Protocol Deviations must be reported separately to SAHPRA, six-monthly.* | | | |
| **Critical and Major Protocol Violations** | | **Resolution/Action taken** | |
| **Site 1: (name of site)** | | | |
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| **Site 2: (name of site)** | | | |
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| **Site 3: (name of site)** | | | |
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| 1. National Principal Investigator comment on other major safety concerns (this should include information impacting on the risk-benefit profile, including changes in nature, severity or frequency of risk factors, *etc.*) | | n/a | |
| 1. Provide proof of current registration on South African National Clinical Trials Registry (SANCTR) | | n/a | |
| * 1. DoH Number | | n/a | |
| * 1. Enclose transcript reflecting current information from SANCTR | | n/a | |
| 1. Provide the summary of investigational product:  * Authorized for importation * Imported * Used during the Clinical Trial * Destroyed (include the destruction certificate(s)) and * Quantity to be exported or exported | | n/a | |
| 14.1 Overall comment on Investigational Product Reconciliation | | n/a | |
| 1. Planned date for provision of trial results to SAHPRA and SANCTR (applicable to final progress report) | | n/a | |
| We, the undersigned, agree that we have reviewed the above-mentioned report and is accurate. The trial is conducted according to the approved protocol, South African legal, ethical and regulatory requirements. In case of deviation or Violation those are reported accordingly. | | | |
| **Signature of National Principal Investigator** | | **Date** | |
| **Signature of Applicant/Sponsor** | | **Date** | |
| **FOR SAHPRA USE ONLY:**  **Comments:**   |  | | --- | |  |   **Action: Continue Trial**   |  | | --- | |  |   **Further information required from Applicant / Sponsor**   |  | | --- | |  |   **Refer to Clinical Trials Committee and / or Inspectorate**  **Reviewed by:** **Date:**  **Signature:** | | | |

# UPDATE HISTORY

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| **Date** | **Reason for Update** | **Version & Publication** |
| November 2017 | First version published for implementation | Version 1, January 2018 |
| May 2018 | Changes to sections 1, 4, 5, 6, Part A, Part B, including change from MCC to SAHPRA | Version 2, June 2018 |
| April 2020 | Administrative | Version 3, April 2020 |
| June 2022 | Addition of sections 13, 14 and 15  Document number changed from 6.27 to GLF-CEM-CT-06A | Version 4, June 2022 |