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| A Comparative Multicentric Non-Infireority Clinical Trial of WHOMBMDT with a New Monthly Chemotherapy Regime containing Rifampicin, Moxifloxacin and Clarithromycin (RMC) on Multibacillary patients from IndiaStandard Operating Procedure 12Withdrawal | | | |
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**1.PURPOSE**

This document outlines the process of patient withdrawal following study enrolment for the RMC trial

### 2. Background

Current WHOMDT does not kill 100% bacteria even after a full course of treatment in a subset of patients harboring a large bacterial load thus continuing transmission of the disease responsible for endemicity in some countries. The duration of MDT is long and promotes noncompliance. MDT continues to be controversial with limited evidence support resulting in multiple reformulations since the last 40 years. This calls for a search for newer, more efficacious drugs with shorter duration of action evidenced with well-designed clinical trials. Relapse, advocated as the key outcome measure of efficacy of MDT, has its drawbacks. Relapse studies require long years of follow up. The gold standard test for viability was Mouse foot pad studies which is costly and time consuming. Hence, we propose Molecular Viability Assays as outcome measure of efficacy which are newer and better techniques to test viability faster.

In this study, we propose to conduct a Randomized Controlled study comparing WHO MBMDT with a monthly regime consisting of currently most bactericidal and safe drugs of Rifampicin, Moxifloxacin and Clarithromycin in MB leprosy patients.

**3. Scope**

This SOP applies to participants withdrawal.

**4. Responsibilities**

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| **Role** | **Responsibility** |
| RMC trial Principal  Investigator | * Ultimately responsible for ensuring RMC trial study procedures obtain ethics approval and that ICH GCP guidelines and this SOP are adhered to by all staff. |
| Local Study researcher/ Clinician | Responsible for:   * Identifying potential reasons for withdrawal. * Counselling participant regarding withdrawal criteria. * Assuring participant who decides to withdraw will be cared for * Providing referral to all participants who withdraw from the study * Documenting withdrawal reason. |
| TLMTI centres RMC trial local investigators | Responsible for:   * Ensuring appropriate staff members are trained on the procedures of this SOP. * Following up that all participants who withdraw the study * Following up on the efficiency of data collection flow. |

### 6. PROCEDURE

Participants will be withdrawn from the study immediately if any of the following occur:

* + - * Clinically significant abnormal laboratory results that preclude continuation of study medication, as determined by the Investigator and/or including any of the following:
* AST or ALT > 3 × ULN
* Hemoglobin < 7 g/dL
* WBC count < 3 x109 cells/l
* AEs that preclude continuation of study medication, as determined by the Investigator.
* The Investigator believes it is in the best interest of the participant.
* The participant or participant's legally acceptable representative requests withdrawal from the study.
* Selection criteria violation was noted after the participant started study drug, and the Investigator determines that the participant should be discontinued.
* Participant is not compliant with study procedures/visits and study drug administration determined by the Investigator.

For the above scenarios, patients will be withdrawn from the study and treatment of such patients will be in conjunction with routine care, but the study team will provide support according local guidelines.

Study patients are free to withdraw from the study at any point without providing reason. Patients who withdraw from the study will receive the routine medical care provided by the local centre. Patients who withdraw from the study intervention should be asked if we can use collected data for the study. The reasons why should be explained and the patient’s right to refuse this will be respected.

If, during the course of the study, the participant must be prematurely discontinued, the procedures outlined for the Early Termination Visit must be completed at that visit or within 2 weeks of the last dose of study drug, and prior to the initiation of another therapy. However, these procedures should not interfere with the initiation of any new treatments or therapeutic modalities that in the Investigator's opinion are necessary to treat the participant's condition. Following discontinuation of the study drug, the participant will be treated in accordance with the Investigator's best clinical judgment. All attempts must be made to determine the date of last dose and the primary reason for Early Termination. This information will be entered into the appropriate CRF.

### 7. TRAINING

Each staff member has direct access to applicable SOP.

Each staff member reviews the applicable SOP once a year.

All SOP training is documented and tracked in the training log located in the Investigator Site File (ISF).

New staff are trained on applicable SOP within 30 days of employment and all SOPs within 90 days of employment.

Staff members whose duties fall within this SOP scope are retrained within 14 days of the approval of each SOP revision.

### 8. REFERENCES

1. Declaration of Helsinki, 2013: https://www.wma.net/policies-post/wma-declaration-ofhelsinki-ethical-principles-for-medical-research-involving-human-subjects/ accessed 10th March 2019

2. International Conference on Harmonisation (ICH) Guideline For Good Clinical Practice E6(R1), 1996

3. RMC trial Protocol