**ACTG NETWORK COORDINATING CENTER**
**Social & Scientific Systems, Inc., a DLH Holdings Company**
**8757 Georgia Avenue, 12th Floor**
**Silver Spring, MD 20910-3714**
**Phone: 301-628-3000**

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# CLARIFICATION MEMO

DATE: December 12, 2022

TO: ACTG CTU Principal Investigators, CRS Leaders, and CTU/CRS Coordinators

FROM: A5362 Protocol Team

SUBJECT: Clarification Memo #1 for Protocol A5362, Version 2.0

**This clarification memo (CM) does not result in a change in the protocol informed consent document. The Division of AIDS does not require you to forward it to your institutional review board (IRB); however, you must follow your IRB's policies and procedures. If IRB review of clarification memos is required at your site, please submit this document for review.**

**Each site should file a copy of this CM with the protocol for reference.**

**Clarifications are being made to Protocol A5362, Version 2.0, 08Jul2022, titled, "A Phase IIc Trial of Clofazimine- and Rifapentine-Containing Treatment Shortening Regimens in Drug-Susceptible Tuberculosis: The CLO-FAST Study." The clarifications are described below and should be implemented immediately. These clarifications will be included in the next version of the A5362 protocol if it is amended at a future date.**

This CM is being issued to:

- Clarify inclusion criterion 4.1.1, for the identification of pulmonary TB within 5 days prior to entry by sputum sample.
- Move section 5.3 (Pharmacy: Product Supply, Distribution, and Accountability) to the correct location in the protocol.
- Clarify site enrollment capacity for the qualitative interview subgroup in section 6.3.17.
- Remove duplicate secondary outcome 10.2.2.1.B.

1. Inclusion criterion 4.1.1 reads:

   *Pulmonary TB (among participants with or without history of prior TB treatment) identified within 5 days prior to entry by: At least one sputum specimen positive for* M. tuberculosis *by molecular TB assay (Xpert) or line probe assay [LPA]) OR At least one sputum specimen positive (1+ or greater) for acid-fast bacilli (AFB) on smear microscopy.*

   *Note: TB diagnosis for purposes of meeting inclusion criterion can be from a study testing laboratory or from an outside laboratory, as long as it is from a sputum sample collected within 5 days prior to entry.*

The team would like to clarify that the sputum sample does not have to be collected within 5 days of the initial diagnosis, but can be any positive sputum sample collected within 5 days prior to study entry.

2. Section 5.3 (Pharmacy: Product Supply, Distribution, and Accountability) was inadvertently placed in section 6.0 (Clinical and Laboratory Evaluations); therefore, section 5.3 is being moved to its correct location (noted in bold or strikethrough) between section 5.2 (Formulations and Preparation) and section 5.4 (Concomitant Medications).

- Section 5.3 (Pharmacy: Product Supply, Distribution, and Accountability)

**5.3 Pharmacy: Product Supply, Distribution, and Accountability**

**5.3.1 Study Product Acquisition/Distribution**

**Clofazimine (Lamprene®) will be manufactured by Novartis.**

**Rifapentine (Priftin®) will be manufactured by Sanofi.**

**Isoniazid, pyrazinamide, ethambutol, and rifampicin will be manufactured by Macleods Pharmaceuticals.**

**Study products will be purchased through ACTG Leadership and Operations and made available through the NIAID Clinical Research Products Management Center (CRPMC). The site pharmacist should obtain the study product(s) for this protocol by following the instructions in the Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks.**

**Antiretroviral medications are NOT provided through the study and must be obtained locally by the site. Selection and dosing of ART in combination with RIF or RPT should adhere to local guidelines at each site.**

**Pyridoxine (vitamin B6) will NOT be provided through the study and must be obtained locally by the site.**

**5.3.2 Study Product Accountability**

**The site pharmacist is required to maintain complete records of all study products received from the NIAID CRPMC and subsequently dispensed. The site pharmacist at non-US CRSs must follow the instructions in the Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks for the destruction of unused study products.**

- Section 6.0 (Clinical and Laboratory Evaluations)

6.0 CLINICAL AND LABORATORY EVALUATIONS

~~5.3 Pharmacy: Product Supply, Distribution, and Accountability~~

~~5.3.1 Study Product Acquisition/Distribution~~

~~Clofazimine (Lamprene®) will be manufactured by Novartis.~~

~~Rifapentine (Priftin®) will be manufactured by Sanofi.~~

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~~Antiretroviral medications are NOT provided through the study and must be obtained locally by the site. Selection and dosing of ART in combination with RIF or RPT should adhere to local guidelines at each site.~~

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~~The site pharmacist is required to maintain complete records of all study products received from the NIAID CRPMC and subsequently dispensed. The site pharmacist at non-US CRSs must follow the instructions in the Pharmacy Guidelines and Instructions for DAIDS Clinical Trials Networks for the destruction of unused study products.~~

3. The team added the site enrollment capacity for the qualitative interview subgroup to section 6.3.17 (Open-Ended Qualitative Interview: Arm 1 and Arm 2 Only). To note, once sites reach enrollment capacity of six participants (three per Arm 1 and three per Arm 2), sites are responsible for updating their site-specific informed consent, following their local standard operating procedures and institutional review board guidelines.

    6.3.1**7** Open-Ended Qualitative Interview: Arm 1 and Arm 2 Only

    An open-ended interview will be conducted in 20 consenting participants in each arm balanced by site to obtain ethnographic data on the impact of perceived skin color changes on their quality of life. **Each site has an enrollment capacity of six participants (three per Arm 1 and three per Arm 2) to the qualitative interview subgroup. The protocol data managers will inform sites when they reach their enrollment capacity.**

4. The definitions for secondary outcomes 10.2.2.1.B and 10.2.2.1.C are the same; therefore, secondary outcome 10.2.2.1.B is being removed and secondary outcome 10.2.2.1.C will remain since 10.2.2.1.C includes reference to the corresponding objective.

    10.2.2 Secondary Outcomes

10.2.2.1 A. Efficacy: proportion with favorable clinical/bacteriologic outcome (definition 10.2.4.A) at 65 weeks post-randomization. [Objective 1.3.8]

~~B. Efficacy: proportion with favorable composite outcome including treatment completion (definition 10.2.4.B) at 65 weeks post-randomization.~~

**B**. Efficacy: proportion with favorable composite outcome including treatment completion (definition 10.2.4.B) at 65 weeks post-randomization. [Objective 1.3.1]