

Microbicide Trials Network

CLARIFICATION MEMO #01 TO:

MTN-017

A Phase 2 Randomized Sequence Open Label Expanded Safety and Acceptability Study  
of Oral Emtricitabine/Tenofovir Disoproxil Fumarate Tablet and Rectally-Applied  
Tenofovir Reduced-Glycerin 1% Gel

DAIDS Protocol #11857

IND #73,382

Date of Clarification Memorandum: 3 August 2012

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*Section 1: Summary of Clarifications and Rationale*

The procedures clarified in this Clarification Memorandum (CM) have been approved by the NIAID Medical Officer and are to be implemented immediately upon issuance. IRB approval of this CM is not required by the sponsor; however, investigators may submit the CM to the IRB overseeing the study at their site for information. This CM is official MTN-017 documentation and is effective immediately. A copy of this CM must be retained in each study site's Essential Documents file for MTN-017. No change in informed consent is necessitated by or included in this CM.

This CM updates the List of Abbreviations and Acronyms and in an effort to maintain consistency with the Sample Informed Consent, the protocol has been updated to include hepatitis B surface antibody (HBsAb) testing at the Screening Visit.

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*Section 2: Implementation*

Text to be deleted is noted below with a ~~strikethrough~~ and text to be added is in **bold**.

1. The following has been added to the *List of Abbreviations and Acronyms*:

**HBsAb**                      **Hepatitis B surface antibody**

2. Changes have been made to allow for the detection of HBV exposure or a successful vaccination against HBV to Sections, 7.1, *Screening Visit*, 7.12, *Laboratory Evaluations*, 9.7, *Hepatitis B Infection*, and Appendix I: *Schedule of Study Visits and Evaluations*, and to the new Appendix IV: *Algorithm For Management of Hepatitis B Serologic Assays Assessed at Screening*:

Section 7.1, *Screening Visit*, Table 4: *Screening, Laboratory* row, *Blood* column, *HBsAG* item:

Laboratory	Blood	• HBsAg and hepatitis B surface antibody (HBsAb)
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Section 7.12, *Laboratory Evaluations, Local Laboratory* section, *Blood Specimens* sub-section, *Hepatitis B surface antigen* item:

- Blood specimens
  - Hepatitis B surface antigen **and hepatitis B surface antibody**

Section 9.7, *Hepatitis B Infection*, first and second paragraphs are updated:

MTN-017 will be carried out in countries with high endemic rates of HBV infection. While TDF has potent activity against HBV, severe acute exacerbations of hepatitis B have been reported in patients who are **infected with HBV or** coinfecting with HBV and HIV, and have discontinued TDF. Although transaminitis associated with ongoing TDF use is uncommon, it has been reported. For these reasons, several mechanisms for protecting participants against AEs associated with TDF use, particularly in the setting of pre-existing or newly acquired HBV infection, are planned for the MTN-017 study.

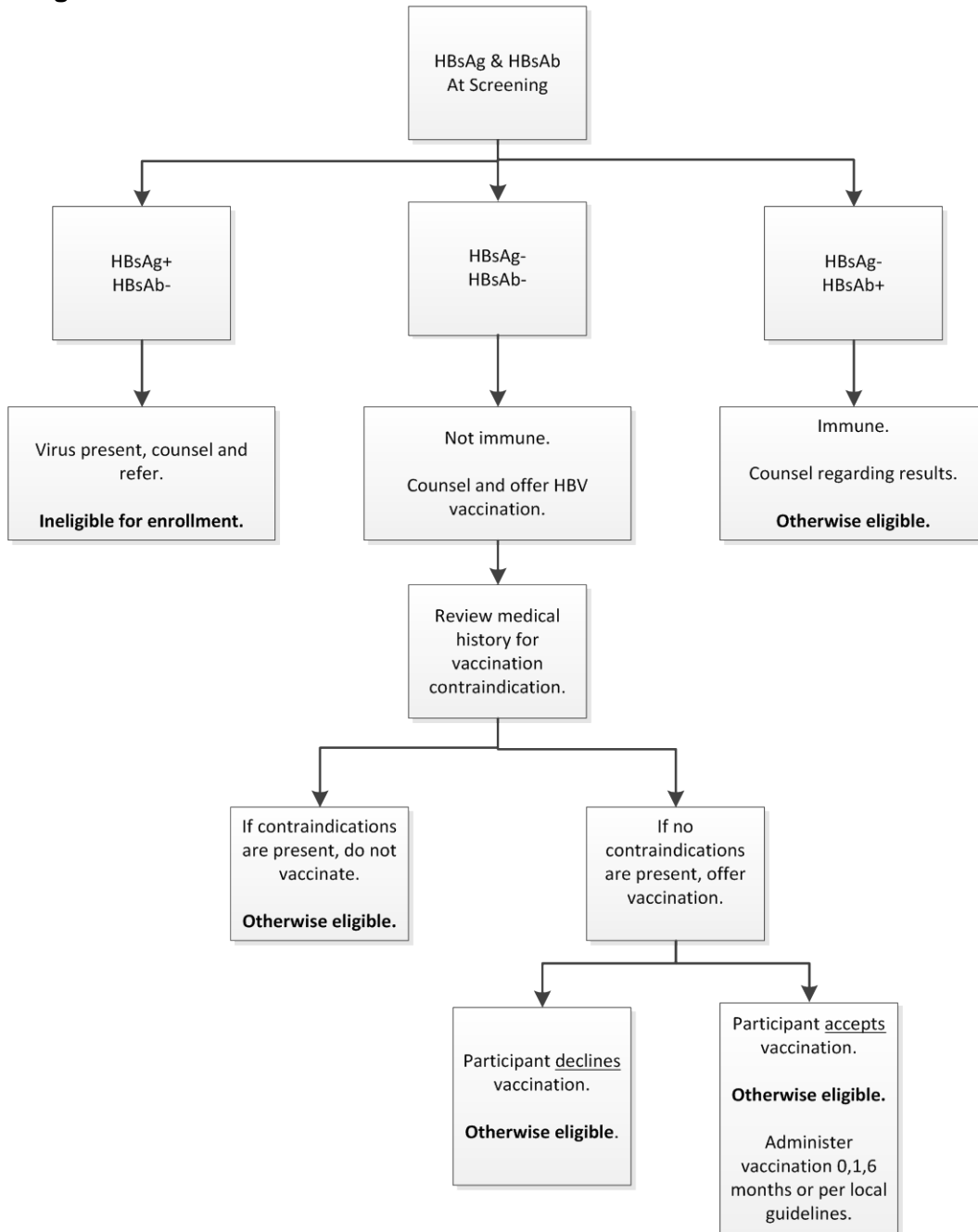
First, all participants undergo screening for ~~active~~ HBV **status** with assessment of ~~hepatitis B surface antigen (HBsAg)~~ **and HBsAb** at the screening visit. Those with active HBV infection receive standardized counseling relevant to natural history and transmission risks of HBV, and are excluded from enrollment. Those who test negative for HBsAg are considered eligible for enrollment. Those who test negative for both HBsAg and **HBsAb** are offered immunization against HBV ~~and are considered eligible for enrollment~~, **provided that they do not have any contraindications to the Hepatitis B vaccination**. Participants who decline HBV immunization are also eligible for enrollment. **See Appendix IV.**

Appendix I: *Schedule of Study Visits and Evaluations, Laboratory* section, *Blood* sub-section, the *HBsAg* item has been updated to include HBsAb:

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6	Visit 7	Visit 8	Visit 9	Visit 10
	SCR	ENR Initiate Period 1	Mid Period 1	End Period 1 Visit	Initiate Period 2 Visit	Mid Period 2 Visit	Period 2 End Visit	Initiate Period 3 Visit	Mid Period 3 Visit	End Period 3 Visit/ Final Clinic/ Early Term
<b>BLOOD</b>										
HBsAg <b>and HBsAb</b>	X									

Appendix IV, *Algorithm For Management of Hepatitis B Serologic Assays Assessed at Screening*, has been added to provide information on the management of Hepatitis B Serologic Assays Assessed at Screening.

**Appendix IV: Algorithm For Management of Hepatitis B Serologic Assays Assessed at Screening.**



The above information will be incorporated into the next version of the protocol at a later time if it is amended.