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REPRIEVE

Randomized Trial to Prevent Vascular Events in HIV

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Tips/Reminders from the Data Management Team

1. Date of last clinic evaluation.

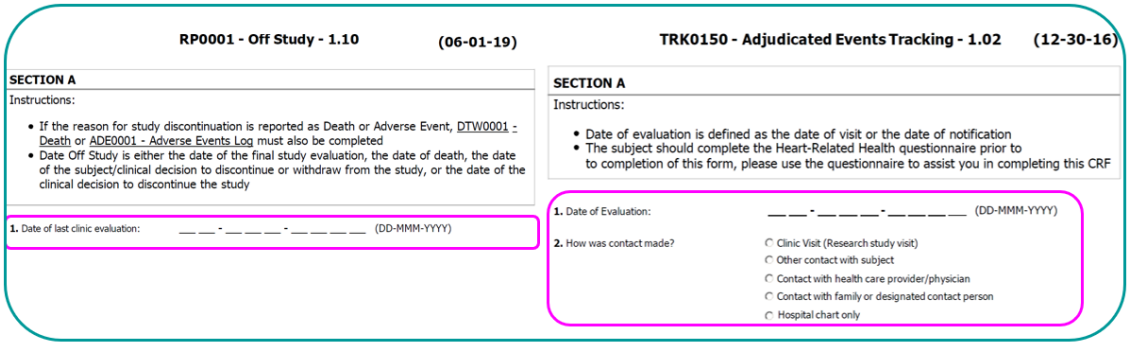
- REPRIEVE has evolved to allow remote contact but the **RP0001--Off Study CRF** Q1: *Date of last clinic evaluation* remained unchanged and has caused some confusion.

To clarify:

- On the RP0001, respond to Q1 *Date of last clinic evaluation* with *date of last contact with the participant*.
- This corresponds to the first two contact choices on the TRK0150 Q2: *How was contact made: Clinic visit* (Research study visit) or *Other contact with subject.*

See snip below to know which CRFs and Questions that are referred to above.

This should be done as of this notification going forward. Sites do not need to go back and update RP0001 CRFs already keyed.



RP0001 - Off Study - 1.10 (06-01-19)

SECTION A

Instructions:

- If the reason for study discontinuation is reported as Death or Adverse Event, DTW0001 - Death or ADE0001 - Adverse Events Log must also be completed
- Date Off Study is either the date of the final study evaluation, the date of death, the date of the subject/clinical decision to discontinue or withdraw from the study, or the date of the clinical decision to discontinue the study

1. Date of last clinic evaluation: __ __ - __ __ __ - __ __ __ __ (DD-MMM-YYYY)

TRK0150 - Adjudicated Events Tracking - 1.02 (12-30-16)

SECTION A

Instructions:

- Date of evaluation is defined as the date of visit or the date of notification
- The subject should complete the Heart-Related Health questionnaire prior to to completion of this form, please use the questionnaire to assist you in completing this CRF

1. Date of Evaluation: __ __ - __ __ __ - __ __ __ __ (DD-MMM-YYYY)

2. How was contact made?

- Clinic Visit (Research study visit)
- Other contact with subject
- Contact with health care provider/physician
- Contact with family or designated contact person
- Hospital chart only

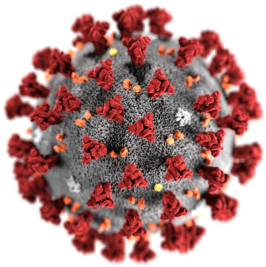
2. Complete vital status and endpoint evaluations for participants off study

- The Vital Status and Endpoint Assessment CRF (VSW0025) should be completed for participants who are off-study for reasons other than withdrawal of consent or death.
    - Completion of the form should be yearly, beginning one year from the Off-Study date for the participant based on the RP0001 CRF.
    - Note that keying the VSW0025 is based on the attempt of contacting a participant who is off study to obtain vital status or endpoint information. ***Even if contact is not obtained, the attempt and date of attempt should be recorded in Section A of the VSW0025.***
    - Section 12.6 of the A5332 MOPS has additional details about Vital Status and Endpoint Assessment

3. Review the AE Log and Medications Log!

- Remember to **review the AE Log and Medications Log at every visit and update the "Review Date"**, regardless of whether there were updates to make or the data were current.

Marissa Diggs (introduced below!) will be alerting sites of instances where the AE Log and/or Medications Log *Review Date* is earlier than the latest contact reported in the study database. This implies that the data on the log are not up to date. If you receive an email from Marissa, we ask that you please review the logs for PIDs you are notified about and update the data as needed. *Thank you for your attention to this!*



Do you have questions about COVID data collection and data entry?

Click here to download a reference tool redacted from the REPRIEVE MOPS to assist you with COVID data collection and data entry in REPRIEVE!

COVID Reporting Tip! ALL positive COVID tests (SARS-CoV-2 PCR and rapid antigen tests i.e., home tests) or COVID diagnoses are to be entered on the AE Log. This way we will know COVID incidence in the REPRIEVE population.

Timeline for September 2022 DSMB Review!

Please mark these important dates in your calendar and note that **Friday, August 5th** is the data entry deadline. To ensure that the DSMB is reviewing complete data, ***please make sure that all data related to potential adjudicated events have been entered*** in the study electronic data capture (OpenClinica) ***and that packets for potential adjudicated events with workup complete have been submitted for adjudication*** by Friday, August 5th. We would appreciate if sites could continue to pay careful attention to this data collection for an additional month until the final data download (Friday, September 9th) for the meeting.

Responsibility	Task	Due Date* (2022)	Weeks to DSMB
Sites	Last date for evaluation for which complete data will be included	Jul 22 (Fri)	10
Sites	**All data for visits through July 22 entered into OpenClinica**	**Aug 5 (Fri)**	**8**
Sites	All adjudication packets for potential MACE by July 22 with work-up complete submitted to MGH DCC**	Aug 5 (Fri)	8
Sites	All queries resolved	Sep 2 (Fri)	4
	Labor Day Holiday (observed in the US)	*Sep 5 (Mon)*	
Sites/TIMI	Resolution of last minute critical queries	Sep 9 (Fri)	3
	DSMB MEETING	**Sep 29 (Thu)**	**0**

*Deadlines are close-of-business on the given date.

**Please ensure that you have responded to all queries and clarifications from the DCC regarding source documents submitted for adjudicated events. This will ensure that the DCC is able to submit complete packets to TIMI for adjudication prior to the DSMB.

Now Available! Talking points related to trial extension

We have developed **talking points*** to facilitate conversations about why the trial has been extended and the importance of this additional follow-up. Please find these talking points attached and be sure to submit to your local IRB/EC if required.

**These talking points have been approved by the IRB for the Clinical Coordinating Center; they revise previous talking points that addressed the first trial extension.*

Reporting Non-Adjudicated Events

Three things to know about non-adjudicated events in REPRIEVE:

1. They are considered as secondary and/or safety events and as such, ***should be entered on the AE Log.***
2. They should be assessed for at every visit.
3. They do not go through an adjudication process.

There are two groups of non-adjudicated events to remember:

1. Non-cardiovascular Disease Events

- AIDS-defining events (including AIDS-defining cancers)
    - Refer to Appendix I of the MOPS for the list of events that qualify as AIDS-defining and enter the event descriptor as given in Appendix I on the AE Log.
- Non AIDS-defining cancers (*except squamous/basal cell of the skin*)
- End-stage kidney disease (requiring initiation of dialysis or renal transplantation)
- End-stage liver disease (cirrhosis or hepatic decompensation requiring hospitalization)
- Incident diabetes mellitus requiring the use of hypoglycemic agents

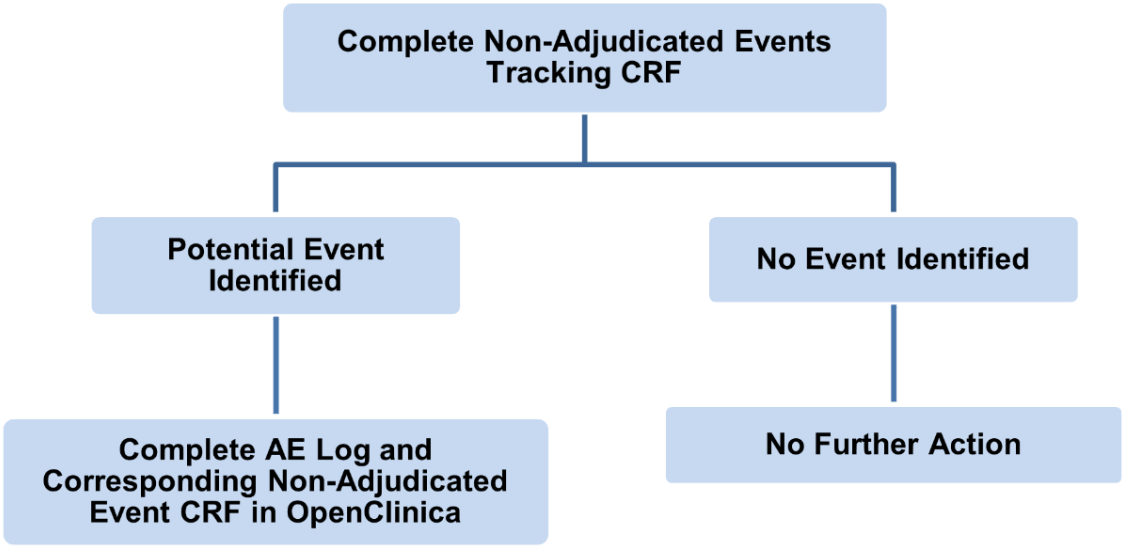
2. Other Events Requiring Reporting

- Incident hypertension
- Incident active hepatitis B (HBV) infection
- Incident active hepatitis C (HCV) infection
- Incident venous thromboembolism (VTE)
- Incident pulmonary thromboembolism (PTE)

The event-specific CRFs for non-adjudicated events require the signature of the local PI or designee confirming that they have reviewed the documentation and agree with the diagnosis and the level of evidence.

For more information, refer to the A5332 MOPS, section 6.2.

Below is a workflow on how to report non-adjudicated events:



What has the data management team noticed about reporting non-adjudicated events?

Problem: Some events entered on the AE Log seem to be non-adjudicated events, but there is no Non-Adjudicated Events Tracking CRF (TRK0152) and/or applicable CRF in the database.

Why is this an issue? This results in underestimation of event incidence for these important clinical events in our study population.

Solution: After entering the event on the AE Log, record it on the TRK0152 and if applicable, the corresponding clinical event CRF(s).

•***Be sure to enter the correct AE identifier*** and make sure the event term and other information are consistent between the AE Log and TRK0152!

Respond to queries to resolve inconsistencies in the study database; consult with your site PI or designee and the REPRIEVE core team as needed.

Example query: The following event reported on the AE Log seems to be a REPRIEVE non-adjudicated event but there is no corresponding entry on TRK0152 and/or clinical event form. Please review the database and key the forms to report a non-adjudicated event or confirm that the event does not meet the reporting criteria specified in the MOP.

Congratulations to the first sites to register Protocol A5332 Version 6.0!

Abbott Northwestern Hospital CRS 31921
University of Colorado Hospital CRS 6101
Cincinnati Clinical Research Site 2401
UCSD Antiviral Research Center CRS 701
Case Clinical Research Site 2501
Washington University Therapeutics CRS 2101

We appreciate your ongoing efforts and dedication to ensuring the REPRIEVE Trial is a success!

If you haven't don't so already, don't forget to submit an amendment registration packet to the DAIDS PRO upon receiving final IRB/EC approval!

All sites that have received protocol registration approval for the previous protocol version (Version 5.0) must submit the Version 6.0 protocol amendment to their local institutional review boards or ethics committees (IRBs/ECs) as soon as a possible.

Upon receiving final IRB/EC and any other applicable regulatory entity approval(s) for this amendment, sites should implement the amendment immediately.

Sites are required to submit an amendment registration packet to the DAIDS PRO at the RSC. For additional information on the protocol registration process and specific documents required for initial and amendment registrations, refer to the current version of the DAIDS Protocol Registration Manual and section 4.0 of the protocol document.

For Sites Participating in the Mechanistic Substudy of REPRIEVE (A5333s)

Earlier this year REPRIEVE leadership asked sites participating in A5333s to not de-register the protocol with DAIDS. However, questions from sites about this are still being received, therefore leadership feels it is acceptable for sites to de-register the A5333s protocol with DAIDS, but please do not close the protocol with your local IRB/EC as the study needs to remain open for analysis.

If a study visit is added at a later date (through a protocol amendment) sites can (re)-register the protocol with DAIDS.

Meet Marissa Diggs, new CRC for the REPRIEVE CCC at MGH!

We are pleased to welcome Marissa Diggs as the new study coordinator for the REPRIEVE Clinical Coordinating Center (CCC)! Marissa recently graduated from Harvard College with a degree in Molecular and Cellular Biology. She is eager to be stepping into the world of clinical research, and we are thrilled to welcome her aboard REPRIEVE! Marissa can be reached by email at mdiggs@mgh.harvard.edu.

Next Team/Site Call!
July 19th

During this call we will be providing updates and reminders, training on the recent protocol amendment, and reporting non-adjudicated events. Please join us!

1:00 PM US (EDT)
1:00 PM HAITI (EDT)
1:00 PM PERU (PET)
2:00 PM PUERTO RICO (ADT)
3:00 PM BRAZIL (BRT)
8:00 PM BOTSWANA (CAT)***
8:00 PM SOUTH AFRICA (SAST)***
8:00 PM ZIMBABWE (CAT)***
9:00 PM UGANDA (EAT)***
11:30 PM INDIA (IST)***
1:00 AM 04/20/2021 THAILAND (ICT)***
****We do not expect site staff to join these calls during their off-work hours*. Instead we will update you on other scheduled calls, e.g., your calls with the ACTG NCC.

Remember that questions are always welcome at actg.corea5332@fstrf.org and if there are slides used for a call, they are available on the PSWP in the Protocol Training >> Site Calls folder.

REPRIEVE (A5332): Are You Up to Date?

For A5332 please use:

Protocol Version 6.0 *dated 05/16/2022*
MOPS Version 6.0 *dated 06/10/2022*
LPC for ACTG Sites Version 6.0 *dated 06/03/2022*
LPC for Non-ACTG Sites Version 6.0 *dated 06/10/2022*
These documents are on the A5332 PSWP

For future reference, all newsletters are available on the REPRIEVE Website

We welcome ideas and suggestions for future newsletters. Please submit any comments or suggestions to the REPRIEVE News team at reprieve.news@fstrf.org

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REPRIEVE Trial Clinical Coordinating Center
Massachusetts General Hospital
55 Fruit Street, 5LON 207
Boston, MA USA 02114