Toolkit and Example Documents for Use with DHQ v2.1

Implementation of the Updated Recommendations in Association Bulletin #22-03 on PrEP, PEP and ART including Injectable PrEP

09/08/22
Examples for Use with DHQ v2.1 and Related Materials
Implementation of the Updated Recommendations in Association Bulletin #22-03
Updated Recommendations on Donor Deferral for Use of Antiretroviral Medications for HIV Prevention and Treatment including Long-Acting Injectable PrEP and the Impact on Blood Safety

AABB created this Donor History Questionnaire (DHQ) Toolkit to provide example documents and a checklist for use when implementing the recommendations of the Updated Association Bulletin #22-03 (Bulletin). This Toolkit is for use with DHQ v2.1 and Related Materials. The information provided in this Toolkit is not intended to replace your review of the information and recommendations of the Bulletin. Refer to the Bulletin for an in-depth review of the background and basis for these recommendations.

It is important to emphasize that the need to assess the risk for false-negative test results in individuals taking medications for HIV prevention and treatment extends to all donors and is not limited to specific subgroups.

Background Summary:

- Based on new information regarding the impact of donor use of long-acting, injectable cabotegravir medication (trade name Apretude) as pre-exposure prophylaxis (PrEP) approved by FDA in late December 2021, the AABB’s Transfusion Transmitted Diseases Committee developed updated recommendations for donor deferral.
- These medication deferral recommendations are based upon available scientific evidence describing the long-acting pharmacokinetic properties of injectable PrEP medication, additional information and a list of references are provided below), collaboration with national researchers and subject matter experts, and communication with the Food and Drug Administration.
- The Donor History Task Force has developed example documents and an implementation checklist for use with the DHQ v2.1 system of documents. The changes outlined in the Bulletin have been incorporated into DHQ v3.0 in the appropriate time order and will be submitted to FDA for review and acceptance.

CHECKLIST

_____ STEP 1: Read the following:
- **Association Bulletin #22-03** for:
  - Background information on the decision to take action to update the recommendations
  - Complete details and basis for the recommended medication deferrals related to donor use of PrEP, PEP and ART including injectable PrEP.
- **DHQ v2.1 User Brochure** for:
  - Limitations and instructions for appropriate use, including adding questions, reformatting materials, etc.

_____ STEP 2: Review AABB’s Communication Tools and train blood donor center staff:
- AABB developed the following Question and Answer (Q&A) Communication Tools to assist with staff training and help answer questions from the general public about these medication deferrals:
  - **PrEP/PEP Q&A Resource for Blood Collectors**
STEP 3: Update the AABB DHQ v2.1

- Follow your policies and procedures for adding questions to the area for additional questions of the DHQ v2.1.
- Add three questions to the area designated for additional questions found at the end of the DHQ v2.1 to evaluate donor use of PrEP, PEP and ART medications.

- Donor eligibility will be evaluated using three additional questions placed at end of the DHQ. Refer to the Example DHQ v2.1 with PrEP, PEP, ART

<table>
<thead>
<tr>
<th>Use this area for additional questions</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>xx. In the past 3 months, have you taken any medication by mouth to prevent an HIV infection?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>xx. In the past 2 years, have you received an injection or shot to prevent an HIV infection?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>xx. Have you EVER taken any medication to treat an HIV infection?</td>
<td></td>
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</tr>
</tbody>
</table>

- “In the past 3 months, have you taken any medication by mouth to prevent an HIV infection?” As described in the flowchart, the individual is deferred for 3 months from the date of the last dose of antiretroviral medication taken by mouth by an HIV uninfected person to prevent an HIV infection.
- “In the past 2 years, have you received an injection or shot to prevent an HIV infection?” As described in the flowchart, the individual is deferred for 2 years from the date of the last injection received by an HIV uninfected person to prevent an HIV infection.
- “Have you EVER taken any medication to treat an HIV infection?” As described in the flowchart, an individual taking ART is indefinitely deferred because ART is prescribed for treatment of an established HIV infection (based on a positive test for HIV). A positive test for HIV is evidence of a relevant transfusion-transmitted infection and requires deferral under current FDA regulations and recommendations. [21 CFR 610.41(a) and (c) and August 2020 HIV Risk guidance]

STEP 4: Add the PrEP, PEP and ART Flowcharts

- Use of these Example flowcharts is optional if the blood center develops and follows an equivalent method for evaluating responses to the AABB DHQ, as described in the AABB DHQ v2.1 User Brochure. Flowcharts may be revised by blood centers to reflect local policy, provided deferrals are either consistent with or more restrictive than those required by AABB and FDA. The example Flowcharts are located at the end of the DHQ v2.1 Flowcharts.
- Add the PrEP and PEP flowchart consistent with DHQ v2.1 question numbering.
  - Refer to Example Flowchart v2.1 with PrEP and PEP taken by mouth (oral) page 47
  - Refer to Example Alternative Flowchart v2.1 with PrEP and PEP taken by mouth (oral) page 48.
  - The alternative flowchart tracks deferral for centers that wish to differentiate between use of PrEP and PEP medications.
- Add the Injectable PrEP flowchart consistent with DHQ v2.1 question numbering.
Refer to Example Flowchart v2.1 with Injectable PrEP page 49

✓ Add the ART flowchart consistent with DHQ question numbering.
  o Refer to Example Flowchart v2.1 with ART page 50
  This flowchart assesses donor eligibility and includes deferral criteria for use of ART. An individual answering “Yes” to this question acknowledges the use of ART for the treatment of HIV infection. For that reason, the individual would also be expected to be deferred by the Question “Have you ever had a positive test for the HIV/AIDS virus?” Policies and SOPs must address the process to resolve discrepant responses.

STEP 5: Update the MDL v2.1 to include PrEP, PEP, and ART medications.
  ✓ Refer to Example MDL v2.1 with PrEP, PEP, ART
  The Example MDL has been updated to identify if the donor has:
  o Taken an antiretroviral medication by mouth to prevent HIV (PrEP and PEP) in the past 3 months.
  o Received an injection or shot to prevent HIV (PrEP) in the past 2 years.
  o Ever taken an antiretroviral medication for therapy (ART), to treat an established HIV infection.

STEP 6: Update the Blood Donor Educational Materials v2.1 to include PrEP, PEP and ART medications.
  ✓ Refer to Example Blood Donor Educational Material v2.1 with PrEP, PEP, ART
  The Example Blood Donor Educational Material has been updated by inserting new information regarding medications to treat or prevent HIV:

  DO NOT DONATE if you:
  • Are taking any medication to prevent an HIV infection. These medications may be called: PrEP, PEP, TRUVADA, DESCOVY, APRETUDE or many other names.
  • Have taken any medication by mouth in the past 3 months to prevent an HIV infection.
  • Have received an injection or shot in the past 2 years to prevent an HIV infection.
  • Have EVER taken any medication to treat an HIV infection.

STEP 7: Reporting minor, more restrictive changes to the FDA:
  ✓ These are minor changes that must be reported to FDA in your annual report under 21 CFR 601.12(d), noting the date the process was implemented and describing the modifications to the AABB DHQ documents. Refer to current FDA guidance recognizing the DHQ v2.1 as acceptable for use.
  ✓ The FDA recognizes AABB DHQ as acceptable for use as part of a system. The addition of questions is permitted in the area designated at the end of the AABB DHQ only if the changes
  ✓ are NOT less restrictive. In this Bulletin, AABB is recommending changes that are more restrictive.
  ✓ The changes must be included in the Annual Report to FDA and do not require submission of a Prior Approval Supplement. [21 CFR 601.12]
Questions and Answers

- **Which version of the Donor History Questionnaire will be revised to implement the changes recommended in this Bulletin?**
  The current AABB DHQ v2.1 and Related Materials should be revised to include this information and is the only DHQ formally recognized by FDA at this time.

- **Will there be a new version of the AABB DHQ with the PrEP and PEP information?**
  Yes. The DHTF has already incorporated the information from this Bulletin, along with other updates, into the next version of the DHQ (version 3.0), which will be submitted to FDA for formal review and acceptance in the very near future. Until FDA formally recognizes the new version 3.0 DHQ, blood centers can use these recommendations with DHQ v2.1 to address the potential impact of PrEP/PEP and ART medications on donor testing for HIV.

- **Given that cabotegravir is a new drug just approved by FDA, how did the committees decide that a deferral period of 24 months was more appropriate than 18 months?**
  The TTD Committee and the DHTF carefully reviewed the available data for this new medication. Published data demonstrates the presence of cabotegravir out to 76 weeks (19 months) following the last injection. Experts do not know what level of residual cabotegravir may act to modify HIV acquisition or detection after the last injection. Modeling with log-linear regression curves show the potential for the drug to remain in the plasma far longer than 19 months (Slide 1, below). The 75th percentile of the time to below the limit of quantitation, meaning the time to undetectable cabotegravir for 75% of all participants, was nearly 24 months for women and 16 months for men. The upper end of the range for persons with quantifiable concentrations of cabotegravir was over 4 years for women and nearly 3 years for men with the longer durations observed in individuals with a higher body mass index (Slide 2, below).

The uncertainty surrounding the persistence of the drug and its potential impact on HIV testing led to the 2-year deferral recommendation.

**Slide 1 Hot Topic Discussion** (courtesy of Brian Custer, PhD, MPH, Vitalant Research Institute)

**Figure 1:** Individual participant log-linear regression curves of plasma cabotegravir concentrations using time between the maximum measured concentration and the last quantifiable concentration after the last injection by sex at birth.

The geometric mean of the $T_{1/2}$ (apparent terminal phase half-life) for detectable cabotegravir was 45.3 days (95% CI 37.6–54.5) for male participants and 60.4 days (52.9–69.0) for female participants. But the rate of decline to LLOQ was highly variable by sex and additional characteristics such as body mass index.

Landovitz et al. Lancet HIV 2020
https://doi.org/10.1016/S2352-3018(20)30106-5
• Are the PrEP and PEP medication deferrals related to HIV risk associated with sexual activity or groups at risk for HIV historically?

No, the medication deferrals are not related to risk posed by sexual activity, nor gender of sexual partners. The medication deferral is not related to MSM deferrals or other HIV risk deferrals.

The medication deferral addresses the impact of the drug itself on HIV testing and the resulting risk for false-negative HIV test results.

The risk exists precisely because PrEP works so well by suppressing HIV to a level that it is undetectable when tested. Even when a blood donor screening test is unable to detect these low levels of virus, an infected person taking PrEP can unknowingly transmit HIV to a patient through a blood transfusion.

• When should these changes be implemented?

The recommendations in this Bulletin should be implemented as defined in your facility’s SOPs. This approach provides blood centers with adequate flexibility for effective implementation.

  o The AABB DHQ v2.1 and Related Materials provided in the Toolkit contain a “with Inj PrEP added” date that represents the month and year AABB released the example materials.

  o This date, used for version control purposes, is not intended to serve as an effective date.

• Do these changes require a Prior Approval Supplement?

No, under 21 CFR 601.12, a Prior Approval Supplement is not required for these minor changes. The addition of questions is permitted in the area designated at the end of the AABB DHQ v2.1 if the changes are NOT less restrictive. This Bulletin contains recommended changes that are more restrictive.

• How should I report these changes to the FDA?

If implemented as recommended, the changes should be reported to FDA in your annual report as a minor change under 21 CFR 601.12(d).
• **Where can I find additional information about implementing changes to the AABB DHQ v2.1 and Related Materials?**
The [AABB DHQ v.1 User Brochure](#) describes change control and limitations on changes to the documents recognized by the FDA.

• **Who should I contact if I have additional questions?**
Please don’t hesitate to contact AABB Regulatory Affairs with questions at regulatory@aabb.org.

## References and Resources


Other Resources

FDA
Requirements for blood and blood components intended for transfusion or for further manufacturing use – Final Rule May 22, 2015
Revised recommendations for reducing the risk of human immunodeficiency virus transmission by blood and blood products – August 2020

Centers for Disease Control and Prevention
HIV Risk and Prevention

NIH CLINICAL INFO.HIV.gov Glossary
HIV/AIDS Glossary

AABB
2022 Hot Topic Discussion Impact of injectable PrEP on donor testing and screening (22EL-766)
– eCast On-Demand
2021 Annual Meeting AM21-24: Hot topic: Men who have sex with men (MSM): Movement toward individual risk assessment

2020 Annual Meeting AM20-87: Keeping up with the Donor History Task Force: Major changes in blood donor screening

Blood Donor History Questionnaires v2.1 and Related Materials

The Feasibility of MSM Individual Risk Assessment Using the AABB DHQ – a 2018 Report of the DHTF