HIV PROPHYLAXIS FOLLOWING OCCUPATIONAL EXPOSURE

What’s New – October 2014 Update

- The Medical Care Criteria Committee now recommends tenofovir disoproxil fumarate + emtricitabine* plus either raltegravir or dolutegravir as the preferred initial PEP regimen because of its excellent tolerability, proven potency in established HIV infection, and ease of administration. **Zidovudine is no longer recommended** in the preferred PEP regimen because it is believed to have no clear advantage in efficacy over tenofovir disoproxil fumarate while having significantly higher rates of treatment-limiting side effects.

- **Plasma HIV RNA testing of the source patient** is recommended in addition to HIV serologic screening in the following settings; PEP should be continued in these situations until results of the plasma HIV RNA assay are available:
  - If the source patient’s HIV screening result is negative but there has been a risk for HIV exposure in the previous 6 weeks
  - If the source patient’s HIV screening result is positive but the confirmatory antibody-differentiation assay is nonreactive or indeterminate

- The Committee continues to recommend the following from the from the October 2012 Update:
  - Occupational exposures require urgent medical evaluation. The Committee further emphasizes recommendations regarding the importance of initiating occupational PEP as soon as possible, ideally within 2 hours of exposure. A first dose of PEP should be offered while evaluation is underway. PEP should not be delayed while awaiting information about the source patient or results of the exposed worker’s baseline HIV test.
  - This guideline incorporates amendments to New York State regulations (10 NYCRR part 63) regarding testing of source patients and access to HIV-related information after occupational exposures (see Appendix C).
  - Baseline HIV testing of the exposed worker should always be obtained after an occupational exposure, even if the exposed worker declines PEP.
  - Regardless of whether the exposed worker accepts or declines PEP treatment, if the post-exposure evaluation determines that PEP is indicated, repeat HIV testing at 4 weeks and 12 weeks should be obtained. A negative HIV test result at 12 weeks post-exposure reasonably excludes HIV infection related to the occupational exposure; **routine testing at 6 months post-exposure is no longer recommended.**
  - Appendix B includes an updated comparison of occupational PEP recommendations from the New York State Department of Health AIDS Institute and the Centers for Disease Control and Prevention.

*Lamivudine may be substituted for emtricitabine.
I. INTRODUCTION

The purpose of these guidelines is to provide recommendations for prescribing HIV post-exposure prophylaxis (PEP) following occupational exposure. To develop these guidelines, the New York State Department of Health AIDS Institute’s (NYSDOH AI) Medical Care Criteria Committee has reviewed available literature addressing the biologic efficacy, effectiveness, and implementation of PEP, as well as current standards for the use of antiretroviral therapy (ART) in established HIV infection. Because randomized, placebo-controlled clinical trials of PEP in humans have not been conducted and are not feasible to design, the NYSDOH AI guidelines are based on existing published studies, best-practice evidence, and the considered opinion of the expert clinicians in the field of adult HIV medicine who comprise the Medical Care Criteria Committee. Expert opinion was frequently used to arrive at recommendations as the PEP literature leaves many questions unanswered or poorly studied.

New York State recommendations differ from those published by the Centers for Disease Control and Prevention (CDC) (see Appendix B). The guidelines of this committee stress simplicity and tolerability in the approach to PEP, recommending a potent but very well tolerated first-line triple therapy for all significant exposures. Recommended second choice regimens are potent and include the best tolerated boosted protease inhibitors.

These 2014 guidelines update any previously issued guidelines. Revisions are summarized in the What’s New box.

II. RATIONALE FOR PEP

Several clinical studies have demonstrated that HIV transmission can be significantly reduced by the post-exposure administration of antiretroviral agents. A dramatic decline in vertical transmission was observed in the AIDS Clinical Trial Group (ACTG) 076 study, in which pregnant women and their newborns received monotherapy with zidovudine (ZDV), and in the HIVNET 012 study, in which single-dose nevirapine was compared with ZDV. A CDC retrospective case-control study of ZDV use after occupational HIV exposure in healthcare workers (HCWs) showed an 81% reduction in risk of HIV infection in persons who received ZDV. This study also identified characteristics of both the exposure and the source patient that placed the HCWs at highest risk for HIV acquisition (see Section III: Risk Factors Associated With HIV Transmission).

Because the ultimate goals of PEP are to maximally suppress any limited viral replication that may occur and to shift the biologic advantage to the host cellular immune system to prevent or abort early infection, the Committee recommends the use of a three-drug PEP regimen for all significant risk exposures.

Experimental models of HIV infection demonstrate the following sequence of events: After percutaneous or mucosal exposure to HIV, local replication of virus occurs in tissue macrophages or dendritic cells; host cytotoxic T cells will kill productively infected target cells. However, if infection cannot be contained at this stage, it is followed within 2 to 3 days by replication of HIV in regional lymph nodes; viremia then follows within 3 to 5 days of virus inoculation. This sequence of events carries significant implications. Given the rapid appearance
of productively infected cells following the introduction of virus, regimens with the most rapid onset of activity, multiple sites of antiviral action, and greatest strength are likely most effective.

*In vitro* evidence from a small study of HCWs who were exposed percutaneously to HIV but who did not seroconvert suggests that limited viral replication may occur without establishment of infection.\(^4\) HIV-specific T-cell proliferative responses were observed in the majority of these individuals. Because the T-cell proliferative response is major histocompatibility complex (MHC) class I specific, limited viral replication within the tissue macrophages is inferred. This sequence of events also carries important implications. If limited HIV replication following exposure is a frequent event, then the argument to use a highly active PEP regimen (i.e., three drugs) to maximize potency becomes even stronger.

### III. RISK FACTORS ASSOCIATED WITH HIV TRANSMISSION

Considered collectively, the cases of seroconversion in exposed workers that have been reported to the CDC and the data from the CDC retrospective case-control study provide insight into the risk factors associated with occupational HIV infection. Blood or visibly bloody fluids or other potentially infectious material (e.g., semen; vaginal secretions; breast milk; and cerebrospinal, synovial, pleural, pericardial, and amniotic fluids) are the only source fluids that carry meaningful risk. Exposure to saliva, tears, sweat, or non-bloody urine or feces does not require PEP.

Table 1 shows the estimated per-act probability of acquiring HIV from a known HIV-infected source by exposure. The CDC is reviewing the most recent data and constructing mathematical models to update transmission risk. Also see Appendix D for a logistic-regression analysis from 1997 of risk factors for HIV transmission after percutaneous exposure to HIV-infected blood.

<table>
<thead>
<tr>
<th>Type of Exposure</th>
<th>Risk per 10,000 Exposures</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parenteral</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Blood Transfusion</td>
<td>9,000</td>
<td>5</td>
</tr>
<tr>
<td>Percutaneous (needlestick)</td>
<td>30</td>
<td>6</td>
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<tr>
<td>Other(^b)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biting</td>
<td>Negligible</td>
<td>7</td>
</tr>
<tr>
<td>Spitting</td>
<td>Negligible</td>
<td></td>
</tr>
<tr>
<td>Throwing body fluids (including semen or saliva)</td>
<td>Negligible</td>
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\(^a\)Factors that increase the risk of HIV transmission include early and late-stage HIV infection and a high level of HIV in the blood. Factors that reduce the risk of HIV transmission include low level of HIV in the blood and the use of ART.

\(^b\)HIV transmission through these exposure routes is technically possible but extremely unlikely and cases are not well documented.
Fifty-eight cases of documented seroconversion following occupational HIV exposure were reported to the CDC through 2013. The most recent confirmed case of occupationally acquired HIV that was reported occurred in 2008; however, no other cases have been reported to the CDC since 1999. The mean risk following an occupational percutaneous exposure is roughly 1 in 300 (0.3%). However, the mean risk may be significantly higher in cases in which more than one risk factor is present (e.g., in persons who incur a deep injury with a hollow-bore needle from an HIV-infected patient with a high viral load). Although the effect of viral load level has not been studied in the setting of occupational exposures, studies have shown that the probability of sexually transmitting HIV is correlated with HIV viral load. The risk of transmission can be expected to be increased in the setting of high HIV viral load levels in the source patient.

After a mucous membrane exposure, the average risk of seroconversion is approximately 9 in 10,000 (0.09%). In this analysis, the use of ZDV PEP by HCWs in the CDC study was shown to reduce the risk of HIV acquisition by 81%.

IV. RESPONSIBILITIES OF EMPLOYERS

RECOMMENDATIONS:
As part of a comprehensive plan to prevent the transmission of bloodborne pathogens, employers should implement the use of safety devices and educate workers about how to prevent needlestick injuries. (AIII)

Antiretroviral medications for PEP should be readily available to exposed workers who sustain a potential occupational exposure to HIV. (AIII) When establishing plans for providing PEP, employers should determine the following:

- who will perform the post-exposure evaluation
- who will provide counseling to the exposed worker regarding the exposure and indications for PEP (for off-hour exposures as well)
- how PEP will be made available within 2 hours of an exposure
- how a 3- to 5-day supply of PEP will be made available for urgent use
- who will be given authority for releasing drugs for this purpose
- how the exposed worker will obtain a continuous supply of PEP drugs to complete the 28-day regimen

Employers should determine who will pay for PEP and establish policies for submitting claims to their Workers’ Compensation plan. Exposed workers should not be expected to pay out-of-pocket for PEP, even if it is reimbursed at a later date.

Federal law requires covered employers to ensure that all medical evaluations and procedures, vaccines, and post-exposure prophylaxis are made available to the employee within a reasonable time and at a reasonable location and are made available at no cost to the employee (OSHA, 29 CFR, Part 1910.1030, CPL 2-02.069, 11/27/01, Enforcement Procedures for the Occupational Exposure to Bloodborne Pathogens).
As part of the employer’s plan to prevent transmission of bloodborne pathogens, the following measures can be taken to avoid injuries:

- elimination of unnecessary use of needles or other sharps
- use of devices with safety features
- verification of compliance with safety features
- avoidance of recapping of needles
- planning before beginning any procedure using needles or other sharps for safe handling and prompt disposal in sharps disposal containers
- promotion of education and safe work practices for handling needles and other sharps

For more information about prevention of needlestick injuries, refer to the NIOSH Alert: Preventing Needlestick Injuries in Health Care Settings.12

Even when effective prevention measures are implemented, exposures to blood and bodily fluid still occur. Employers of personnel covered by the Bloodborne Pathogen Standard are obligated to provide post-exposure care, including prophylaxis, at no cost to the employee. The employer may subsequently attempt to obtain reimbursement from Workers’ Compensation. Appendix C provides further information regarding employer responsibilities.

V. POST-EXPOSURE MANAGEMENT AND EVALUATION

RECOMMENDATION:
Occupational PEP should be initiated as soon as possible, ideally within 2 hours of the exposure. A first dose of PEP should be offered to the exposed worker while the evaluation is underway. (AII)

There are many factors to consider when deciding whether to implement occupational PEP. The uncertainties that are occasionally associated with a given exposure may complicate the decision-making process, especially for an inexperienced clinician, and may possibly delay prompt initiation of PEP. Figure 1 is meant to serve as a general guide. The sections that follow the figure provide more detail regarding the specific factors that are weighed in decision-making. Optimal management of the exposed worker following an occupational exposure to a bloodborne pathogen balances the benefits of preventing infection with the risks of medication-induced side effects and toxicity.
Offer exposed worker first dose of PEP while evaluation of exposure is underway.

Source patient KNOWN TO BE HIV-INFECTED by medical record

Source patient HIV STATUS UNKNOWN

Obtain consent for rapid HIV testing of source patient

See Appendix C

Source patient does not have capacity to consent

Source patient refuses HIV testing

Perform baseline confidential HIV testing of the exposed worker and refer to experienced clinician within 3 days of initiating PEP.

See Tables 4 and 5 for alternative regimens.

COMPLETE 28-DAY REGIMEN:

Recommended PEP Regimen\textsuperscript{b,c}

Tenofovir 300 mg PO qd

Emtricitabine\textsuperscript{d} 200 mg PO qd

PLUS

Raltegravir\textsuperscript{e} 400 mg PO bid or Dolutegravir\textsuperscript{e} 50 mg PO qd

- Perform baseline confidential HIV testing of the exposed worker and refer to experienced clinician within 3 days of initiating PEP.
- See Tables 4 and 5 for alternative regimens.

\textsuperscript{a} Depending on the test used, the window period may be shorter than 6 weeks. Clinicians should contact appropriate laboratory authorities to determine the window period for the test that is being used.

\textsuperscript{b} If the source is known to be HIV-infected, information about his/her viral load, ART medication history, and history of antiretroviral drug resistance should be obtained when possible to assist in selection of a PEP regimen.\textsuperscript{13} Initiation of the first dose of PEP should not be delayed while awaiting this information and/or results of resistance testing. When this information becomes available, the PEP regimen may be changed if needed in consultation with an experienced provider.

\textsuperscript{c} See Appendix A for dosing recommendations in patients with renal impairment.

\textsuperscript{d} Lamivudine 300 mg PO qd may be substituted for emtricitabine. A fixed-dose combination is available when tenofovir is used with emtricitabine (Truvada 1 PO qd).

\textsuperscript{e} See Appendix A for drug-drug interactions, dosing adjustments, and contraindications associated with raltegravir and dolutegravir.
A. Management of the Exposed Site

**RECOMMENDATION:**

Body sites exposed to potentially infectious fluid should be cleansed immediately. Wound and skin exposure sites should be washed with soap and water. Exposed mucous membranes should be flushed with water. The exposed worker should not attempt to “milk” the wound. (AII)

Exposed sites should be cleansed of contaminated fluid as soon as possible after exposure. Wounds and skin sites are best cleansed with soap and water, avoiding irritation of the skin. Exposed mucous membranes should be flushed with water. Alcohol, hydrogen peroxide, Betadine or other chemical cleansers are best avoided. HCWs should be trained to avoid “milking” or squeezing out needlestick injuries or wounds. Squeezing the wound may promote hyperemia and inflammation at the wound site, potentially increasing systemic exposure to HIV if present in the contaminating fluid.

B. Evaluating the Exposure

**RECOMMENDATIONS:**

Prompt initiation of PEP is recommended for exposure to blood, visibly bloody fluids, or other potentially infectious material (semen; vaginal secretions; breast milk; and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids) from HIV-infected or HIV-unknown sources in any of the significant exposure situations outlined in Table 2. (AII)

Initiation of PEP should be followed by telephone or in-person consultation with a clinician experienced in HIV PEP. Clinicians who do not have access to experienced HIV clinicians should call the Clinical Education Initiative CEI PEP Line at 1-866-637-2342. When using the PEP Line, providers from New York State should identify themselves as such.

Whenever a worker has been exposed to potentially HIV-infected blood, visibly bloody fluids, or other potentially infectious material through the percutaneous or mucocutaneous routes or through non-intact skin (see Table 2), PEP is indicated. For these exposures, prompt initiation of PEP followed by telephone or in-person consultation with a clinician experienced in HIV PEP is recommended (see Section XII: *Resources for Consultation*).
### TABLE 2
**EXPOSURES FOR WHICH PEP IS INDICATED**

- Break in the skin by a sharp object (including hollow-bore, solid-bore, and cutting needles or broken glassware) that is contaminated with blood, visibly bloody fluid, or other potentially infectious material, or that has been in the source patient’s blood vessel.
- Bite from a patient with visible bleeding in the mouth that causes bleeding in the exposed worker.
- Splash of blood, visibly bloody fluid, or other potentially infectious material to a mucosal surface (mouth, nose, or eyes).
- A non-intact skin (e.g., dermatitis, chapped skin, abrasion, or open wound) exposure to blood, visibly bloody fluid, or other potentially infectious material.

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C. HIV Testing of the Source Patient

**RECOMMENDATIONS:**

If the HIV serostatus of the source patient is unknown, consent for voluntary HIV testing of the source patient should be sought as soon as possible after the exposure. (AII) Rapid HIV testing with an FDA-approved fourth-generation antigen/antibody combination assay is strongly recommended for the source patient (see the CDC Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens). Organizations subject to OSHA regulations are required to perform rapid HIV testing rather than standard HIV testing. (AIII)

In New York State, when the source patient has the capacity to consent to HIV testing, informed consent is required; if consent is not obtained, HIV testing cannot be performed. When the source person does not have the capacity to consent, consent may be obtained from a surrogate, or anonymous testing may be done if a surrogate is not immediately available. See Appendix C for information regarding HIV testing when the source patient does not have the capacity to consent. **Clinicians should follow individual institutional policies for obtaining consent.**

If the source patient consents to HIV testing and the HIV screening test is positive, this preliminary result should be utilized in decision-making regarding PEP for the exposed worker. The preliminary positive result should be provided to the source patient and followed by confirmatory testing as soon as possible.* (AIII)

*When anonymous testing is performed, the results of the test cannot be disclosed to the source person or placed in the source person’s medical record (see Appendix C).
Plasma HIV RNA testing of the source patient is recommended in addition to HIV serologic screening in the following settings; PEP should be continued in these situations until results of the plasma HIV RNA assay are available:

- If the source patient’s HIV screening result is negative but there has been a risk for HIV exposure in the previous 6 weeks (BIII)
- If the source patient’s screening result is positive but the confirmatory antibody-differentiation assay is nonreactive or indeterminate (AI)

If the result from testing the source patient is not immediately available or a complete evaluation of the exposure is unable to be made within 2 hours of the exposure, PEP should be initiated while source testing and further evaluation are underway. (AII)

The source patient’s HIV serostatus, HIV exposure history, and other HIV-related information are critical factors to evaluate when considering PEP initiation after occupational exposure.

If the source patient is known to be HIV-infected, information about his/her viral load, ART history, and history of antiretroviral drug resistance should be obtained when possible to assist in the selection of a PEP regimen13; however, administration of the first dose of PEP should not be delayed while awaiting this information. See Section VIII: Recommended PEP Regimen.

For source patients of unknown HIV serostatus, rapid HIV testing with an FDA-approved fourth-generation antigen/antibody combination assay is strongly recommended as soon as possible in order to aid in decision-making regarding PEP. Organizations subject to OSHA regulations are required to perform rapid HIV testing rather than standard HIV testing. Results from rapid testing are usually available within 60 minutes. If the test results are not immediately available, the initiation of PEP should not be delayed pending the test result.

Source patients who are in the “window period” prior to seroconversion may not be identified. When the source patient’s screening test result is negative and the clinician has ascertained that the source patient could have been exposed to HIV in the previous 6 weeks or when the source patient’s screening result is positive but the confirmatory assay is nonreactive or indeterminate, then a plasma HIV RNA assay should be obtained to determine the source patient’s HIV status. In these situations, PEP should be initiated and continued until results of the plasma HIV RNA assay are available.

For information regarding interpretation of HIV tests, see the CDC Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens.
D. Recording Information Following Occupational Exposure

RECOMMENDATIONS:
When an occupational exposure occurs, the following information should be recorded in the exposed worker’s confidential medical record (AIII):

- date and time of the exposure
- details of the procedure being performed and the use of protective equipment at the time of the exposure
- the type, severity, and amount of fluid to which the worker was exposed
- details about the source patient
- whether consent was obtained for HIV testing of the source patient
- medical documentation that provides details about post-exposure management

If the exposed worker declines PEP, this decision should be documented in the worker’s medical record.

Specific OSHA requirements regarding documentation may be found at Safety and Health Topics: Bloodborne Pathogens and Needlestick Prevention.

VI. BASELINE TESTING FOR THE EXPOSED WORKER

RECOMMENDATIONS:
Confidential baseline HIV testing* of the exposed worker should be obtained at the time the occupational exposure is reported or within 3 days of the exposure. (AIII) Testing must be performed in full compliance with New York State Public Health Law.

* A fourth-generation antigen/antibody combination assay is recommended (see the CDC Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens).

PEP should be started without waiting for the results of the HIV test. (AII)

Exposed workers should be counseled that it is in their best interest to receive a baseline HIV test to document their HIV status at the time of the exposure. In the rare event of seroconversion following an occupational exposure, a negative baseline test is the only way to show that the worker was infected as a result of the exposure.

Key Point:
A negative HIV test only demonstrates that the exposed worker was not previously infected with HIV before the exposure occurred; the baseline HIV test cannot determine whether the exposed worker was infected as a result of the exposure.

Baseline HIV testing of the exposed worker is also used to identify individuals who were already infected with HIV at the time of the exposure. This allows decisions to be made regarding the continuation of ART (see Antiretroviral Therapy, Section III: When to Initiate ART). However, the PEP regimen should not be discontinued until the positive result is repeated with a confirmatory assay.

PEP should be initiated without waiting for the results of the HIV test.
VII. TIMING OF INITIATION OF PEP

RECOMMENDATIONS:
When a potential occupational exposure to HIV occurs, every effort should be made to initiate PEP as soon as possible, ideally within 2 hours. (AII) A first dose of PEP should be offered to the exposed worker while the evaluation is underway.

Decisions regarding initiation of PEP beyond 36 hours post exposure should be made on a case-by-case basis with the understanding of diminished efficacy when timing of initiation is prolonged. (AIII)

Data from animal models of PEP have shown that effective antiretroviral treatment is most likely to prevent infection when initiated within 24 to 36 hours of exposure.14-19 HIV virions can traverse epithelial barriers in just hours, and many antiretroviral drugs require an intracellular activation step that delays the onset of antiviral activity. Therefore, every effort should be made to initiate PEP as soon as possible and ideally within 2 hours. An absolute elapsed time after which PEP should not be administered cannot be stated with certainty.

Prompt initiation of PEP followed by telephone or in-person consultation with an experienced HIV provider or occupational health clinician experienced in providing PEP is recommended. Expert advice may be obtained from the Clinical Education Initiative CEI PEP Line at 1-866-637-2342. When using the PEP Line, providers from New York State should identify themselves as such.

VIII. RECOMMENDED PEP REGIMEN

RECOMMENDATIONS:
The preferred PEP regimen is tenofovir disoproxil fumarate + emtricitabine* plus either raltegravir or dolutegravir (see Table 3 for dosing and Appendix A for description of each drug). Zidovudine is no longer recommended in the preferred PEP regimen. The first dose should be given as soon as possible after exposure, ideally within 2 hours. The recommended duration of PEP is 28 days.

*Lamivudine may be substituted for emtricitabine.

If the source patient is known to be HIV-infected and information is immediately available regarding past and present ART experience, current level of viral suppression, or resistance profile, the treating clinician, in consultation with a clinician experienced in managing PEP, should individualize the PEP regimen to maximize potential effectiveness against the exposed HIV strain. (AII) Initiation of the first dose and continuation of PEP should never be delayed while awaiting this information. (AII) If indicated, the regimen can be changed when more information becomes available.

Table 4 and Table 5 list recommended alternative PEP regimens that should be used in the setting of potential HIV resistance, toxicity risks, clinician preference, or constraints on the availability of particular agents. (AII)
Clinicians should switch exposed workers to an alternative regimen if the initial or subsequent PEP regimen is not well tolerated (see Appendix A for potential adverse events).

Treating clinicians should consult with a clinician experienced in managing PEP when alternative agents are prescribed or if there is doubt as to whether PEP should be continued after the first dose.

The prescribing clinician should ensure that the exposed worker has access to the full 28-day recommended course of antiretroviral medications (AIII) and is appropriately monitored for toxicities during the treatment (see Section IV: Responsibilities of Employers and Section IX: Follow-Up and Monitoring of the Exposed Worker Following Occupational Exposure).

Treating clinicians who do not have access to experienced HIV clinicians should call the Clinical Education Initiative CEI PEP Line at 1-866-637-2342. When using the PEP Line, providers from New York State should identify themselves as such.

<table>
<thead>
<tr>
<th>TABLE 3</th>
<th>RECOMMENDED REGIMEN FOR HIV PEP FOLLOWING OCCUPATIONAL EXPOSURE</th>
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</thead>
</table>
| Tenofovir disoproxil fumarate<sup>b</sup> 300 mg PO daily + Emtricitabine<sup>b,c</sup> 200 mg PO daily  
Plus  
Raltegravir<sup>d</sup> 400 mg PO twice daily or Dolutegravir<sup>d</sup> 50 mg PO daily |

<sup>a</sup>When the source is known to be HIV-infected, past and current ART experience, viral load data, and genotypic or phenotypic resistance data (if available) may indicate the use of an alternative PEP regimen. Consult with a clinician experienced in managing PEP. See Tables 4 and 5.

<sup>b</sup>The dosing of tenofovir disoproxil fumarate and emtricitabine/lamivudine should be adjusted in patients with baseline creatinine clearance <50 mL/min (see Appendix A for dosing recommendations). Tenofovir disoproxil fumarate should be used with caution in exposed workers with renal insufficiency or who are taking concomitant nephrotoxic medications. Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure.

<sup>c</sup>Lamivudine 300 mg PO daily may be substituted for emtricitabine. However, a fixed-dose combination is available when tenofovir disoproxil fumarate is used with emtricitabine (Truvada 1 PO daily).

<sup>d</sup>See Appendix A for drug-drug interactions, dosing adjustments, and contraindications associated with raltegravir and dolutegravir.

A. Duration of PEP Regimen

**RECOMMENDATIONS:**
When the source patient is confirmed to be HIV-negative, clinicians should discontinue the PEP regimen before completion (see Section V. C: HIV Testing of the Source Patient).

If the exposed worker’s baseline test shows evidence of HIV infection acquired before the exposure and initiation of PEP, decisions regarding continuation of ART should be based on current treatment guidelines (see Antiretroviral Therapy). However, the PEP regimen should not be discontinued until the positive result is repeated with a confirmatory assay.
If the exposed worker’s week 4 post-exposure HIV test results are indeterminate or the exposed worker has symptoms suggestive of acute HIV infection, clinicians should continue ART beyond 28 days until a definitive diagnosis is established.

The recommended 28-day treatment duration is based on limited animal data and expert opinion. When the source patient is confirmed to be HIV-negative, the PEP regimen should be discontinued before completion (see Section V. C: HIV Testing of the Source Patient).

If at any time acute HIV infection is suspected, consultation with a clinician experienced in managing acute HIV infection should occur immediately (also see Diagnosis and Management of Acute HIV Infection). Clinicians who do not have access to experienced HIV clinicians should call the Clinical Education Initiative CEI PEP Line at 1-866-637-2342. When using the PEP Line, providers from New York State should identify themselves as such.

B. Rationale for Recommended PEP Regimen

This Committee now recommends tenofovir disoproxil fumarate plus emtricitabine* and either raltegravir or dolutegravir as the preferred initial PEP regimen because of its excellent tolerability, proven potency in established HIV infection, and ease of administration.

*Lamivudine may be substituted for emtricitabine.

The recommended regimen has a favorable side effect profile, fewer potential drug-drug interactions, and an expected efficacy similar to PEP regimens containing zidovudine or protease inhibitors. Studies have shown increased rates of adherence and regimen completion when tenofovir disoproxil fumarate + either emtricitabine or lamivudine have been used as components of the PEP regimen. Limited data show similar improved tolerability with tenofovir disoproxil fumarate + emtricitabine plus raltegravir. Additionally, tenofovir disoproxil fumarate + emtricitabine has been highly successful in recent studies of pre-exposure prophylaxis.

This Committee no longer recommends that zidovudine must be included in PEP regimens because it is believed to have no clear advantage in expected efficacy over tenofovir disoproxil fumarate while having significantly higher rates of treatment-limiting side effects. As experience with PEP continues to accumulate, it has become increasingly clear that tolerability is one of the most important factors in selecting a PEP regimen, especially when the source patient is not available for testing and the patient will need to complete the full 28-day course.

Unlike protease inhibitors, which block HIV replication in steps after integration with cellular DNA, all drugs in the recommended regimen (tenofovir, emtricitabine, and either raltegravir or dolutegravir) act before viral integration with cellular DNA, providing a theoretical advantage in preventing establishment of HIV infection.
C. Use of a Three-Drug PEP Regimen
Once a decision has been made that a significant risk exposure (see Section V. B: Evaluating the Exposure) has occurred and that PEP is warranted, this Committee recommends a three-drug regimen as the preferred option.

D. Preferred Alternative PEP Regimens

RECOMMENDATIONS:
The preferred alternative PEP regimen is tenofovir disoproxil fumarate + emtricitabine* plus ritonavir-boosted darunavir, atazanavir, or fosamprenavir (see Table 4).

*Lamivudine may be substituted for emtricitabine.

Clinicians should carefully assess for potential drug interactions between these agents and other medications (including prescription medications and over-the-counter drugs, such as proton pump inhibitors and H2-blockers) that the patient may be taking. See Appendix A for information regarding dosing, adverse effects, and drug interactions.

Clinicians should consult a clinician experienced in managing PEP or an occupational health clinician experienced in providing PEP when using alternative PEP regimens (AII). If consultation cannot be immediately obtained, the first dose of the regimen should be given rather than delaying initiation, with consultation occurring as soon as possible thereafter (AII). Clinicians who do not have access to experienced HIV clinicians should call the Clinical Education Initiative CEI PEP Line at 1-866-637-2342. When using the PEP Line, providers from New York State should identify themselves as such.

The alternative regimens in Table 4 are expected to be less well tolerated than the preferred regimen of tenofovir disoproxil fumarate + emtricitabine plus either raltegravir or dolutegravir, but significantly better tolerated than regimens containing zidovudine or lopinavir/ritonavir. Efficacy of the preferred alternative regimens is expected to be equivalent to other alternative regimens (Section E: Other Alternative PEP Regimens), unless the source patient’s HIV strain is resistant to one or more of the agents.

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<th>TABLE 4</th>
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<tr>
<td><strong>PREFERRED ALTERNATIVE PEP REGIMENS FOLLOWING OCCUPATIONAL EXPOSURE</strong></td>
</tr>
<tr>
<td>Tenofovir disoproxil fumarate(^a) 300 mg PO daily + Emtricitabine(^a,b) 200 mg PO daily</td>
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<td><strong>Plus</strong></td>
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<tr>
<td>Darunavir 800 mg PO daily,(^c) or Atazanavir 300 mg PO daily,(^c) or Fosamprenavir 1400 mg PO daily(^c)</td>
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<td><strong>and</strong></td>
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<tr>
<td>Ritonavir 100 mg PO daily(^c)</td>
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</tbody>
</table>

\(^a\)The dosing of lamivudine/emtricitabine, and tenofovir disoproxil fumarate should be adjusted in patients with baseline creatinine clearance <50 mL/min (see Appendix A for dosing recommendations). Tenofovir disoproxil fumarate should be used with caution in exposed workers with renal insufficiency or who are taking concomitant nephrotoxic medications. Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure.

\(^b\)Lamivudine 300 mg PO daily may be substituted for emtricitabine. However, a fixed-dose combination is available when tenofovir disoproxil fumarate is used with emtricitabine (Truvada 1 PO daily).

\(^c\)See Appendix A for dosing recommendations for protease inhibitors in exposed workers with hepatic impairment.
Potential for drug interactions in patients receiving protease inhibitors is increased due to the extensive cytochrome P450 interactions. For example, proton pump inhibitors may adversely affect the absorption of atazanavir. Clinicians should assess for potential interactions before prescribing a PEP regimen.

The following online resources provide information about antiretroviral drug interactions:

- Johns Hopkins POC-IT Center, available at: [www.hopkinsmedicine.org/poc-it](http://www.hopkinsmedicine.org/poc-it)
- University of Liverpool drug interactions site, available at: [www.hiv-druginteractions.org](http://www.hiv-druginteractions.org)
- PDR Network, available at: [www.pdr.net](http://www.pdr.net)
- Epocrates medical software, available at: [www.epocrates.com](http://www.epocrates.com)

### E. Other Alternative PEP Regimens

Other alternative PEP regimens are listed in Table 5 and may be acceptable in certain situations.

Some clinicians continue to favor use of zidovudine in PEP regimens based on the results of a retrospective study supporting the efficacy of the agent and from long-term experience in occupational PEP. Clinicians continuing to prescribe zidovudine in this setting should recognize and inform patients that the drug has significant side effects and that better-tolerated agents are available (see Appendix A for side effects associated with alternative PEP agents).

Some clinicians may favor use of lopinavir/ritonavir due to long-term experience in occupational PEP. It should be recognized that this agent has greater potential for drug interactions and side effects than raltegravir, dolutegravir, or the preferred protease inhibitors (darunavir, atazanavir, or fosamprenavir; with each protease inhibitor taken with ritonavir 100 mg daily), with little added efficacy benefit expected. Recent studies have demonstrated decreasing protease inhibitor resistance among HIV strains, suggesting that there may be diminishing benefit to choosing lopinavir/ritonavir for its activity against resistant HIV strains. The other recommended ritonavir-boosted protease inhibitor regimens listed in Table 4 also have excellent activity against protease inhibitor-resistant strains and are better tolerated than lopinavir/ritonavir.
TABLE 5
ALTERNATIVE PEP REGIMENS FOLLOWING OCCUPATIONAL EXPOSURE

- Tenofovir disoproxil fumarate + Emtricitabine<b> + Zidovudine
- Tenofovir disoproxil fumarate + Emtricitabine<b> + Lopinavir/ritonavir
- Zidovudine + Lamivudine<c> + one of the following ritonavir-boosted protease inhibitors: Darunavir, Atazanavir, Fosamprenavir, or Lopinavir

*a*See Appendix A for full dosing information for alternative ARV agents that may be used in the PEP regimen. Also see *HIV Drug-Drug Interactions* for important drug interactions. Dosing interval of zidovudine should be adjusted in patients with baseline creatinine clearance <15 mL/min. The dosing interval of lamivudine, emtricitabine, and tenofovir disoproxil fumarate should be adjusted in patients with baseline creatinine clearance <50 mL/min (see Appendix A for dosing recommendations in patients with renal impairment). Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure.

*b* Lamivudine 300 mg PO daily may be substituted for emtricitabine. However, a fixed-dose combination is available when tenofovir disoproxil fumarate is used with emtricitabine (Truvada 1 PO daily).

*c* Emtricitabine 200 mg PO daily may be substituted for lamivudine. However, a fixed-dose combination is available when zidovudine is used with lamivudine (Combivir 1 PO twice daily).

Although this Committee recommends a three-drug regimen, the PEP regimen could be reduced to a two-drug regimen if tolerability was a concern. Use of a two-drug regimen would be preferred to discontinuing the regimen completely. An early case control study of occupational exposure demonstrated an 81% reduction in seroconversion with the use of zidovudine monotherapy alone, suggesting that treatment with any active antiretroviral agent is beneficial in reducing risk.

F. Antiretroviral Drugs to Avoid as PEP Components

Consultation with a clinician experienced in managing PEP is recommended before using any of the following non-preferred antiretroviral drugs in a PEP regimen (see Section X: *PEP for Exposed Workers Who Are Pregnant or Breastfeeding* for drugs to avoid in exposed workers who are pregnant or breastfeeding):

- **Efavirenz**: Although efavirenz is considered a preferred agent for treatment of chronic HIV infection, it is not recommended as part of an initial PEP regimen for several reasons: 1) central nervous system (CNS) side effects are common, complicating the need to provide a first dose at any time of the day; 2) CNS side effects may impair work after the initial and subsequent doses; 3) efavirenz should be avoided in pregnant women, women intending to become pregnant, or women of childbearing potential who are not using effective contraception; and 4) substantial efavirenz resistance continues to be found in community HIV isolates. If efavirenz is used in women of childbearing potential, a pregnancy test should be obtained before initiation and the woman should be counseled about the use of effective contraception while taking efavirenz.
- **Nevirapine** is contraindicated for use in PEP due to the potential for severe hepatotoxicity.
- **Abacavir** should not be used due to the potential for hypersensitivity reactions.
- **Stavudine** and **Didanosine** should not be used due to the possibility of toxicities.
• *Nelfinavir* and *Indinavir* are generally poorly tolerated
• *CCR5 co-receptor antagonists* should not be used due to lack of activity against potential CXCR4 tropic virus
• *Rilpivirine* and *Etravirine* have not been commonly used in PEP

**IX. FOLLOW-UP AND MONITORING OF THE EXPOSED WORKER FOLLOWING OCCUPATIONAL EXPOSURE**

**RECOMMENDATIONS:**
All exposed workers receiving PEP should be re-evaluated within 3 days of the exposure. (AIII) This allows for further clarification of the nature of the exposure, review of available source patient data, and evaluation of adherence to and toxicities associated with the PEP regimen.

The exposed worker should be evaluated weekly while receiving PEP to assess treatment adherence, side effects of treatment, interval physical complaints, and emotional status. (AIII) Longitudinal care of the exposed worker during PEP treatment and the follow-up period should be provided by an occupational health provider familiar with PEP or directly by or in consultation with a clinician experienced in managing PEP. Providers who do not have access to a clinician experienced in PEP should use the Clinical Education Initiative CEI PEP Line at 1-866-637-2342 for phone consultation. When using the PEP Line, providers from New York State should identify themselves as such.

Clinicians should provide risk-reduction counseling to HIV-exposed workers to prevent secondary transmission during the 12-week follow-up period. HIV-exposed workers should be advised to:
• use condoms to prevent potential sexual transmission
• avoid pregnancy and breastfeeding
• avoid needle-sharing
• refrain from donating blood, plasma, organs, tissue, or semen

During the PEP treatment period, other blood tests may be indicated to monitor for side effects of treatment. The timing and specific testing indicated varies based on the PEP regimen used (see Table 6).
TABLE 6
MONITORING RECOMMENDATIONS AFTER INITIATION OF PEP REGIMENS FOLLOWING OCCUPATIONAL EXPOSURE

<table>
<thead>
<tr>
<th>Clinic Visit</th>
<th>Baseline</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
<th>Week 4</th>
<th>Week 12</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td>√</td>
</tr>
<tr>
<td>Or by telephone</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pregnancy Test</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum liver enzymes, BUN, creatinine, CBC</td>
<td>√</td>
<td>√</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>HIV test</td>
<td>√</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>√</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>√</td>
</tr>
</tbody>
</table>

*For post-exposure management for hepatitis B and C, see Section XI: Occupational Exposures to Hepatitis B and C.

*CBC should be obtained for all exposed workers at baseline. Follow-up CBC is indicated only for those receiving a zidovudine-containing regimen.

*Recommended even if PEP is declined.

Post-exposure care involves simultaneous attention to multiple issues: the emotional state of the exposed worker, adherence to the PEP regimen, monitoring for potential adverse effects, and sequential HIV testing to exclude acquisition of infection. Clinicians should be aware of the resources within the community that offer medical and counseling services needed following occupational exposure.

A. Adherence to the PEP Regimen

Follow-up care is necessary for patients receiving PEP to monitor for adverse effects of the PEP regimen and to maximize adherence to the prescribed regimen. Adherence to a 28-day PEP regimen has historically been modest (40-60%), although newer studies using tenofovir disoproxil fumarate + either lamivudine or emtricitabine as components for PEP regimens show increased rates of adherence. Limited data show similar improved tolerability with tenofovir disoproxil fumarate + emtricitabine plus raltegravir.

If the recommended regimen is not well tolerated, an early switch to an alternative regimen is encouraged to improve adherence. Consultation with a clinician experienced in managing PEP should occur when switching to an alternative regimen due to tolerability or resistance.
B. Sequential HIV Testing

**RECOMMENDATIONS:**
Sequential confidential HIV testing should be obtained at baseline, week 4, and week 12 post-exposure:

- HIV testing at 6 months post-exposure is no longer recommended
- HIV testing of the exposed worker at 4 weeks and 12 weeks should be performed with laboratory-based fourth-generation antigen/antibody combination HIV tests rather than point-of-care HIV tests
- If the post-exposure evaluation determined that PEP was indicated, but the exposed worker declines PEP, serial testing should still be obtained (see Table 6)

If at any time the HIV test result is positive, a confirmatory assay must be performed to confirm the diagnosis of HIV infection.

If the exposed worker presents with signs or symptoms of acute HIV seroconversion, an HIV serologic screening test should be used in conjunction with a plasma HIV RNA assay (All) to diagnose acute HIV infection. A fourth-generation HIV antigen/antibody combination test is the recommended serologic screening test (see the CDC Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens). Immediate consultation with a clinician experienced in managing ART should be sought for optimal treatment options.

When workers are potentially exposed to HIV, longitudinal medical follow-up is necessary regardless of whether PEP is initiated or completed, in order to test sequentially for HIV infection.

HIV seroconversion will generally occur within 2 to 4 weeks if chronic HIV infection develops after an exposure. HIV testing at baseline, 4 weeks, and 12 weeks is recommended after significant exposures, regardless of whether the worker accepts or declines PEP treatment. Point-of-care HIV tests are slightly less sensitive than laboratory-based HIV tests; therefore, exposed workers should be tested with laboratory-based HIV tests whenever possible.

HIV testing at 6 months after exposure is no longer recommended. Late seroconversion (i.e., after 3 months) has been rarely reported and has not been described since 1990.\(^{32,33}\) It is unclear if these rare events were related to the original or subsequent exposures. Taking into consideration the infrequency of this occurrence, the increased sensitivity of standard HIV tests to detect early infection and seroconversion, and the added anxiety and significant consequences of an additional 3 months of precautions and testing for exposed workers, this Committee believes that the benefit of routinely testing all workers for HIV at 6 months is outweighed by the negative consequences of routinely extending post-exposure HIV follow-up testing to 6 months.

Patients acutely infected with HIV will often experience at least some symptoms of the acute retroviral syndrome. Fever and flu- or mono-like symptoms are common in acute HIV infection but are nonspecific. Rash, mucocutaneous ulcers, oropharyngeal candidiasis, and meningismus are more specific. Symptoms may also include fatigue or malaise, joint pain, headache, loss of
appetite, night sweats, myalgias, lymphadenopathy, oral and/or genital ulcers, nausea or diarrhea, or pharyngitis. Acute HIV infection is often not recognized in the primary care setting because of the similarity of the symptom complex with that of the flu or other common illnesses. When infection occurs and a third-generation ELISA antibody test is used, it will generally be positive within 3 weeks of the onset of symptoms and is virtually always positive within 3 months following exposure. However, the CDC now recommends fourth-generation antibody/antigen combination immunoassays for initial HIV screening. These tests can simultaneously detect both HIV-1/HIV-2 antibodies and HIV-1 p24 antigens and will generally be positive within 14-15 days of infection. Western blot, which may yield an indeterminate result during the early stages of seroconversion, is no longer recommended as the confirmatory test. Instead, HIV screening should be confirmed with an FDA-approved HIV-1/HIV-2 antibody-differentiation assay. When acute HIV infection is suspected based on the clinical scenario or when there is a discrepancy between screening and confirmatory serologic testing, plasma HIV RNA assay should be obtained to diagnose HIV infection. (AII) For information regarding interpretation of HIV tests, see the CDC Recommended Laboratory HIV Testing Algorithm for Serum or Plasma Specimens.

X. PEP FOR EXPOSED WORKERS WHO ARE PREGNANT OR BREASTFEEDING

A. Exposed Workers Who Are Pregnant

RECOMMENDATIONS:
Based on increasing clinical experience with ART, PEP is indicated at any time during pregnancy when a significant exposure has occurred, despite possible risk to the woman and the fetus. (AII) Expert consultation should be sought. When occupational exposure to HIV occurs, every effort should be made to initiate PEP within 2 hours. (AII) The recommended PEP regimen is the same for pregnant women as for non-pregnant adults (see Section VIII: Recommended PEP Regimen). (AII)

Before administering PEP to a pregnant woman, the clinician should discuss the potential benefits and risks to her and to the fetus.

The agents listed in Table 7 are all non-preferred agents for use in PEP regimens and are not likely to be used; however, clinicians should be aware that these agents should not be prescribed in exposed workers who are pregnant. Initiation of PEP at any time during pregnancy requires a careful discussion of the risks and benefits.
TABLE 7

PEP DRUGS TO AVOID DURING PREGNANCY

<table>
<thead>
<tr>
<th>Drug(s) to Avoid</th>
<th>Toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efavirenz</td>
<td>Teratogenicity</td>
</tr>
<tr>
<td>Combination of stavudine and didanosine</td>
<td>Mitochondrial toxicity</td>
</tr>
<tr>
<td>Nevirapine</td>
<td>Hepatotoxicity</td>
</tr>
<tr>
<td>Unboosted indinavir in the 2rd or 3rd trimester</td>
<td>Substantially lower antepartum indinavir plasma concentrations; risk for nephrolithiasis</td>
</tr>
</tbody>
</table>

**Key Point:**
In addition to the risk of seroconversion for the exposed worker, the high viral load levels associated with the acute retroviral syndrome markedly increase the risk of transmission to the fetus or breastfeeding infant.34

Although birth defects and adverse effects on human fetuses have generally not been associated with the antiretroviral agents that are currently available, exposure of a fetus to antiretroviral agents during pregnancy carries a theoretical risk of teratogenicity.

For additional information, refer to NYSDOH guidelines on *Use of ART in HIV-Infected Pregnant Women.*

**B. Exposed Workers Who Are Breastfeeding**

**RECOMMENDATION:**
Clinicians should advise women who may have been exposed to HIV through occupational exposure to avoid breastfeeding for 3 months after the exposure. (AII) If HIV infection is definitively excluded in the source patient at any time prior to 3 months post-exposure, the woman may resume breastfeeding.

Initiation of PEP in exposed workers who are breastfeeding requires careful discussion. Both HIV and antiretroviral drugs may be found in breast milk; therefore, breastfeeding should be avoided for 3 months after the exposure to prevent HIV transmission and potential drug toxicities.34 Clinicians should discuss the risks and benefits with the exposed worker. The infant’s pediatrician should be informed of any potential exposure to HIV or antiretroviral medications.

**XI. OCCUPATIONAL EXPOSURES TO HEPATITIS B AND C**

**RECOMMENDATION:**
When an occupational exposure occurs, the source patient should be evaluated for both hepatitis B and hepatitis C. (AII)
The risk of transmission of hepatitis B virus (HBV) and hepatitis C virus (HCV) from an occupational exposure is significantly greater than the risk of HIV transmission. The risk of HCV infection following a needlestick is 1.8%, whereas the risk of HBV infection ranges from 1% to 30% depending on the presence of hepatitis e antigen (see Table 8). The risk of transmission of HCV from a single mucous membrane exposure is negligible.

### Table 8
**Average Risk for Transmission of Hepatitis B and C Viruses After Needlestick (compared with HIV)**

<table>
<thead>
<tr>
<th>Source</th>
<th>Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBV</td>
<td></td>
</tr>
<tr>
<td>HBeAg+</td>
<td>22.0% – 30.0%</td>
</tr>
<tr>
<td>HBeAg-</td>
<td>1.0% – 6.0%</td>
</tr>
<tr>
<td>HCV+</td>
<td>1.8%</td>
</tr>
<tr>
<td>HIV+</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

A. Hepatitis B Virus Post-Exposure Management

For the most current information regarding HBV post-exposure management, please refer to the December 20, 2013 [CDC’s Guidance for Evaluating Health-Care Personnel for Hepatitis B Virus Protection and for Administering Postexposure Management](https://www.cdc.gov/hepatitis/pedped.htm).

B. Hepatitis C Virus Post-Exposure Management

**Recommendations:**
Clinicians should consider concurrent exposure to HCV when exposed workers present with an HIV exposure. (AII)

Neither immunoglobulin nor antiviral agents are recommended for HCV PEP.

When HCV infection is identified, the exposed worker should be referred for medical management to a clinician with experience in treating HCV. (AII)

Currently, no effective prophylaxis for HCV has been identified. Immunoglobulin and antiviral agents are not recommended for HCV PEP. However, if an individual becomes acutely infected with HCV and is diagnosed at that time, immediate referral to a specialist experienced in the treatment of HCV is strongly recommended. Data suggest that early treatment of acute HCV with interferon for 24 weeks is highly effective, perhaps as high as 98%. However, the best regimen or duration of therapy is unknown, and no data currently exist for treating acute infection with newer direct-acting HCV antiviral therapy.
Whether standard interferon, pegylated-interferon with or without ribavirin, or treatment with direct-acting antiviral agents is used will depend on the individual scenario, as there have been no randomized, controlled trials to guide this decision.

1. Baseline Management

**RECOMMENDATIONS:**

*Following an exposure to blood or body fluid, the clinician should assess the risk for exposure to HCV.* (AII) *Wounds should be washed with soap and water, and should not be squeezed.* (AII) *Mucous membranes should be flushed with water.*

Once the clinician has determined that exposure to blood or body fluid has occurred, the following baseline tests should be obtained (see Table 9 for follow-up according to baseline results):

**Source Patient:**
- HCV antibody test (e.g., EIA/ELISA) and, if positive, HCV RNA test

**Exposed Worker:**
- Liver panel including liver enzymes
- HCV antibody and, if positive, HCV RNA test

If the source patient is tested with an EIA/ELISA and found to be positive, then follow-up testing is necessary to confirm the source patient’s status. HCV RNA may be used as the confirmatory test. When the source patient tests positive with the HCV RNA test, the exposed worker should be managed as though the source has chronic HCV.

<table>
<thead>
<tr>
<th>Clinical Scenario</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Source patient is HCV-antibody negative</td>
<td>No further testing or follow-up is necessary for source patient or the exposed worker&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Source patient is unavailable or refuses testing</td>
<td>Exposed worker: Follow-up HCV antibody at 3 and 6 months&lt;sup&gt;b&lt;/sup&gt;</td>
</tr>
<tr>
<td>Source patient is HCV-antibody positive and HCV RNA negative</td>
<td>Manage the exposed worker as if the source patient has chronic hepatitis C (see Section XI. B. 2: <em>Post-Exposure Follow-Up for HCV</em>)&lt;sup&gt;c&lt;/sup&gt;</td>
</tr>
<tr>
<td>Source patient is positive for both HCV antibody and HCV RNA and Exposed worker is HCV-antibody negative</td>
<td>Source patient: Counsel and manage as chronic hepatitis C regardless of status of exposed worker</td>
</tr>
<tr>
<td>Exposed worker tests positive for both HCV antibody and HCV RNA</td>
<td>Counsel and manage as chronic hepatitis C</td>
</tr>
</tbody>
</table>

<sup>a</sup> Refer to Appendix E for information about HCV tests and how to interpret results.

<sup>b</sup> If at any time the serum ALT level is elevated in the exposed worker, the clinician should test for HCV RNA to assess for acute HCV infection.

<sup>c</sup> A single negative HCV RNA result does not exclude active infection.
Clinicians should educate exposed workers about the natural history of HCV infection and should counsel exposed workers about the following:

- **Avoidance of alcohol and, if possible, medications that may be toxic to the liver**
- **Risk of transmission related to:**
  - Blood-to-blood contact, including sharing personal care items that may have come in contact with another person’s blood, such as razors or toothbrushes; occupational needlestick injuries; and sharing needles, syringes, or other equipment to inject drugs
  - Sexual activity
  - Donating blood, plasma, organs, tissue, or semen
  - Perinatal transmission
- **HCV is not spread via food or water and is not transmitted by:**
  - Sharing eating utensils
  - Hugging, kissing, or holding hands
  - Coughing or sneezing
  - Breastfeeding: HCV is not transmitted by breastfeeding; however, clinicians should advise women who may have been exposed to HIV to avoid breastfeeding\textsuperscript{34} for 3 months after the exposure

Factors that may increase the risk of sexual transmission include sex with multiple partners, history of STIs, including HIV, or any other practice that might disrupt mucous membranes. The potential need for mental health counseling should be anticipated and offered as needed.

### 2. Post-Exposure Follow-Up for HCV

**RECOMMENDATIONS:**

If the source patient is known to be positive for HCV antibody and/or HCV RNA, the follow-up schedule for the exposed worker should be as follows (AII):

- **Week 4:** HCV RNA and liver panel
- **Week 12:** HCV RNA and liver panel
- **Week 24:** Liver panel and HCV antibody

If at any time the serum ALT level is elevated, the clinician should repeat HCV RNA testing to confirm acute HCV infection. (AIII)

At any time that exposed workers test positive for HCV RNA, the clinician should refer for medical management and possible treatment by a clinician with experience in treating HCV. (AIII)

For individuals exposed to HCV-infected source patients, regular follow-up with HCV RNA testing is recommended in addition to HCV antibody testing, because HCV RNA testing can identify acute infection within 2 weeks of exposure, whereas accuracy of the antibody test can be delayed up to several months after acute infection (i.e., “window period”).
Seroconversion with the ELISA antibody test occurs in 50% of patients within 9 weeks of exposure, in 80% of patients within 15 weeks of exposure, and in at least 97% of patients within 6 months of exposure. The ELISA test is highly sensitive but relatively nonspecific, resulting in a low positive predictive value in low-prevalence populations. Positive HCV ELISA antibody test results require confirmation by a quantitative viral load assay, such as HCV PCR.

XII. RESOURCES FOR CONSULTATION

Persons who have responsibility for providing PEP may need expert advice and consultation, as well as assistance in helping their clients obtain medication. The following resources are available:

- The Clinical Education Initiative CEI PEP Line at 1-866-637-2342. When using the PEP Line, providers from New York State should identify themselves as such.
- For further education of health providers or for consultation regarding setting up PEP services, contact: the HIV/HCV Center of Excellence.

Appendix C provides information regarding employer issues and responsibilities.
REFERENCES


36. Centers for Disease Control and Prevention. Recommendations for preventing transmission of infections among chronic hemodialysis patients. *MMWR Recomm Rep.* 2001;50(RR-5):1-43 Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/rr5005a1.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5005a1.htm)
APPENDIX A. ANTIRETROVIRAL DRUGS

The medications listed below include antiretroviral agents recommended for PEP (tenofovir disoproxil fumarate, emtricitabine, and either raltegravir or dolutegravir) as well as alternative antiretroviral drugs that may be used in the setting of potential HIV resistance, toxicity risks, or constraints on the availability of particular agents. For information on all antiretroviral medications, see Antiretroviral Therapy.

More information about these antiretroviral agents, including dosage and dose adjustment, potential adverse events and drug interactions, and FDA pregnancy categories, can be found in Antiretroviral Therapy, Appendix A: FDA-Approved HIV Medications and FDA Pregnancy Categories. Before using these drugs, package inserts should also be consulted.

Recommended PEP Medications:
- Tenofovir disoproxil fumarate (TDF)
- Emtricitabine (FTC)
- Raltegravir (RAL)
- Dolutegravir (DTG)
- Lamivudine (3TC) – equivalent substitute for emtricitabine

Alternative PEP Medications:
- Atazanavir (ATV)
- Lopinavir/ritonavir (LPV/r)
- Darunavir (DRV)
- Fosamprenavir (FPV)
- Zidovudine (ZDV)

FDA Pregnancy Categories

A Adequate and well-controlled studies of pregnant women fail to demonstrate a risk to the fetus during the first trimester of pregnancy (and there is no evidence of risk during later trimesters).

B Animal reproduction studies fail to demonstrate a risk to the fetus and adequate and well-controlled studies of pregnant women have not been conducted.

C Safety in human pregnancy has not been determined, animal studies are either positive for fetal risk or have not been conducted, and the drug should not be used unless the potential benefit outweighs the potential risk to the fetus.

D Positive evidence of human fetal risk based on adverse reaction data from investigational or marketing experiences, but the potential benefits from the use of the drug in pregnant women may be acceptable despite its potential risks.

X Studies in animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.
### APPENDIX B. OCCUPATIONAL EXPOSURE TO HIV: COMPARISON OF NYSDOH AND CDC RECOMMENDATIONS

<table>
<thead>
<tr>
<th>NYSDOH AI Recommendations (2014)</th>
<th>CDC Recommendations (2013)*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication for PEP</strong></td>
<td></td>
</tr>
<tr>
<td>Percutaneous or mucocutaneous exposure with blood or visibly bloody fluid or other potentially infectious material.</td>
<td>Percutaneous injury or contact of mucous membrane or nonintact skin with blood, tissue, or potentially infectious body fluids, such as semen, vaginal secretions, and visibly bloody fluids and reasonable suspicion that the source patient is HIV-infected.</td>
</tr>
<tr>
<td><strong>HIV Testing of the Source Patient</strong></td>
<td></td>
</tr>
</tbody>
</table>
| If HIV serostatus of the source is unknown, voluntary HIV testing of the source should be sought. Rapid testing is strongly recommended for the source patient, and for those organizations subject to OSHA regulations, rapid testing of the source patient is mandated for occupational exposures. When the source patient’s rapid test result is negative, and the clinician has ascertained that the source patient could have possibly been exposed to HIV in the previous 6 weeks, a plasma HIV RNA assay should be used in conjunction with the rapid HIV antibody test. In these situations, PEP should be initiated and continued until results of the plasma HIV RNA assay are available. In New York State, when the source patient has the capacity to consent to HIV testing, specific informed consent is required (see Appendix C). | HIV Testing of the Source Patient
Although concerns have been expressed regarding HIV-negative sources being in the window period for seroconversion, no case of transmission involving an exposure source during the window period has been reported in the United States. Rapid HIV testing of source patients can facilitate making timely decisions regarding use of HIV PEP after occupational exposures to sources of unknown HIV status. |
| **Recommendations for Number of Drugs in PEP Regimen** | Recommendations for Number of Drugs in PEP Regimen
A three-drug PEP regimen is the preferred option for all significant-risk occupational exposures. A regimen containing three (or more) antiretroviral drugs is recommended for all occupational exposures. Clinicians facing challenges associated with a three-drug regimen might consider a two-drug regimen in consultation with an expert. |

Table continues...
**Recommended PEP Regimen**

- Tenofovir disoproxil fumarate 300 mg PO daily + Emtricitabine 200 mg PO daily or Lamivudine 300 mg PO daily
  - plus
  - Either Raltegravir 400 mg PO twice daily or Dolutegravir 50 mg PO daily

**Duration of PEP:** 4 weeks

**HIV Antibody Testing of Healthcare Worker**
- Baseline
- 4 weeks post-exposure
- 12 weeks post-exposure

**Timing of Initiation of PEP**
When a potential occupational exposure to HIV occurs, every effort should be made to initiate PEP, as soon as possible, ideally within 2 hours. A first dose of PEP should be offered to the exposed worker while the evaluation is underway. In addition, PEP should not be delayed while awaiting information about the source or results of the exposed individual’s baseline HIV test. Decisions regarding initiation of PEP beyond 36 hours post exposure should be made on a case-by-case basis with the understanding of diminished efficacy when timing of initiation is prolonged.

**Recommended PEP Regimen**

- Tenofovir disoproxil fumarate 300 mg PO daily + Emtricitabine 200 mg PO daily
  - plus
  - Raltegravir 400 mg PO twice daily

**Duration of PEP:** 4 weeks

**HIV Antibody Testing of Healthcare Worker**
- Baseline
- 6 weeks post-exposure
- 12 weeks post-exposure
- 6 months post-exposure

Alternatively, if the clinician is certain that a fourth-generation antibody/antigen combination assay is being used, then HIV testing could be performed at baseline, 6 weeks, and concluded at 4 months post-exposure.

**Timing of Initiation of PEP**
PEP should be initiated as soon as possible, preferably within hours of exposure. Initiation of PEP should not be delayed while awaiting the results of a source patient’s HIV test, nor should it be delayed during consultation with experts to determine ideal PEP regimens.

APPENDIX C. POST-EXPOSURE MANAGEMENT: EMPLOYER ISSUES AND RESPONSIBILITIES

Organizations that employ health professionals or other persons who are at risk for occupational exposure to blood, body fluids, or other potentially infectious materials are generally required to establish policies and procedures that guide the management of such exposures. Employers must conform to the OSHA Bloodborne Pathogen Standard (OSHA Bloodborne Pathogen Standard 29 CFR § 1910.1030, and Compliance Directive CPL 02-02-069, 11/27/01, Enforcement Procedures for the Occupational Exposure to Bloodborne Pathogens), which are applicable to New York public employers under the New York Public Employee Safety and Health (PESH) Act (Labor Law § 27-a) and regulations (12 NYCRR Part 800). OSHA and PESH standards with regard to occupational exposure to bloodborne pathogens are identical. These regulations require that a management plan be in place.

The employer should ensure that any employee who sustains an occupational exposure has access to post-exposure services within 1 to 2 hours of a reported event. Services must be available 24 hours per day, 7 days per week. Organizations that do not have on-site occupational health services are encouraged to form agreements or contracts with another facility, Emergency Department, or private practitioner for such services.

I. DEFINITION OF PERSONS COVERED

New York State regulations apply to staff, employees, or volunteers in the performance of employment or professional duties in:

- A medical or dental office.
- A facility regulated, authorized, or supervised by the Department of Health, Office of Mental Health, Office of Mental Retardation and Developmental Disabilities, Office of Children and Family Services, Office of Alcoholism and Substance Abuse Services, or the Department of Correctional Services.
- Emergency response employee (paid or volunteer, including an emergency medical technician, a firefighter, a law enforcement officer or local correctional officer, or medical staff).

Post-exposure policies should define who is included as an “employee” for purposes of providing care. In addition to staff who are clearly employed by an organization (e.g., nurses, laboratory personnel, housekeepers), consideration must be given to whether other individuals (e.g., medical/nursing students, house staff, attending physicians, volunteers, and pre-hospital care personnel) will be covered by the institution’s policy. In addition, the scope of services that will be provided must be delineated (e.g., laboratory testing, occupational health services, prophylactic drugs or vaccines), including whether there are limitations within the categories of individuals covered particularly with regard to Workers’ Compensation benefits.
II. ACCESS TO OCCUPATIONAL HEALTH SERVICES

Exposed workers who sustain an occupational exposure should be ensured access to post-exposure services within 1 to 2 hours of a reported event. This may require 24-hour and weekend coverage. Procedures should identify how workers access services during regular work hours and, if different, how they access services during evening, night, or weekend shifts. Organizations that do not have on-site occupational health services should consider forming agreements or contracts with another facility or private practitioner for such services.

Post-exposure services for exposures to all bloodborne pathogens include but are not limited to:

- Post-exposure evaluation and follow-up post-exposure vaccinations
- Arrangements for a full course of post-exposure prophylaxis medications, at no cost to the employee
- Care provided under the supervision of a licensed physician or other licensed healthcare professional
- Availability of a rapid HIV test for source patient testing
- Supportive counseling

Federal law requires covered employers to ensure that all medical evaluations and procedures, vaccines, and post-exposure prophylaxis are made available to the employee within a reasonable time and at a reasonable location and are made available at no cost to the employee (OSHA, 29 CFR, Part 1910.2030, CPL 2-02.069, 11/27/01, Enforcement Procedures for the Occupational Exposure to Bloodborne Pathogens).

PESH and OSHA’s Bloodborne Pathogen Standards indicate that the covered employer is responsible for all costs associated with an exposure incident. An employer may not require any out-of-pocket expenditures on behalf of the employee, such as requiring the employee to utilize workers’ compensation if prepayment is required or compelling an employee to use health insurance to cover these expenses unless the employer pays all premiums and deductible costs associated with the employees’ health insurance. In addition to services listed above, NYS Guidelines, HIV Prophylaxis Following Occupational Exposure, state that the following should be considered by the employer when establishing plans for providing PEP for exposures to HIV:

- who will perform the post-exposure evaluation
- who will provide counseling to the exposed worker regarding the exposure and indications for PEP (for off-hour exposures as well)
- how PEP will be made available within 2 hours of an exposure
- how a 3- to 5-day supply of PEP will be made available for urgent use
- who will be given authority for releasing drugs for this purpose
- how the exposed worker will obtain PEP drugs to complete the 28-day regimen
III. DETERMINING HIV STATUS OF SOURCE PATIENT

Procedures to facilitate rapid evaluation and voluntary testing for HIV, HBV, HCV and other bloodborne pathogens and/or disclosure of related information of the source individual should be in place.

The employer is responsible for establishing and implementing policies to protect the confidentiality of both the exposed employee and the exposure source (New York Public Health Law §§ 2135, 2782; 10 NYCRR § 63.6).

A. Access to Source Patient HIV-Related Information

New York law and regulations (Public Health Law § 2781(6)(e); 10 NYCRR § 63.8(m)) authorize disclosure of existing HIV-related information to providers of persons who have been exposed in the workplace when significant risk exposure has occurred.

When the source patient is already known to be infected with HBV, HCV, or HIV, testing for the source individual’s known HBV, HCV, or HIV status does not need to be repeated. Testing for other bloodborne pathogens should still occur.

If the exposed worker is part of the healthcare team, he/she may have access to the medical record and know the HIV status of the source patient, as well as information about drug resistance. Information related to drug regimens, and, if available, resistance information, should be made available to the exposed employee’s provider to determine the best regimen for the employee. However, initiation of PEP should not be delayed while awaiting this information.

B. HIV Testing of the Source Patient

- Consistent with recommendations by the Centers for Disease Control and Prevention (CDC), the US Department of Labor, Occupational Safety and Health Administration (OSHA) mandates that medical facilities subject to OSHA authority use rapid HIV antibody tests when testing the source patient after potential exposure to a bloodborne pathogen. The CDC recommends testing with a fourth-generation antibody/antigen combination assay.
- The source patient should be tested as soon as possible to determine HIV infectivity.
- Results of the source individual’s HIV testing should be made available to the exposed worker’s provider. Patient authorization for release of this information is not required for necessary communication of information from provider to provider for timely treatment of the exposed worker.

Source Patient Has Capacity to Consent for HIV Testing:

- Informed consent from the source patient should be obtained.
- If consent is not obtained for HIV testing, the employer should document that consent cannot be obtained and testing cannot be performed.
**Source Patient Does Not Have Capacity to Consent for HIV Testing:**

If the source is comatose or is determined by his or her attending professional to lack mental capacity to consent, and the source person is not expected to recover in time for the exposed person to receive appropriate medical treatment, the Health Care Proxy Law and Family Health Care Decisions Act (FHCDA) give providers the ability to locate someone who has the legal authority to consent to HIV testing (the healthcare agent or FHCDA Surrogate).

New York regulations (§§ 63.3(d)(7), 63.8(n)) also authorize anonymous testing when no person authorized to consent on behalf of the source patient is immediately available.

**An anonymous test* may be performed if:**
- the healthcare agent or FHCDA Surrogate, who has legal authority to consent, is not available or reasonably likely to become available in time for the exposed person to receive appropriate medical treatment, **and**
- the exposed person will benefit medically by knowing the source person’s HIV test results
  
  **or**
  
  - The source patient is deceased

* The law requires that results of anonymous source patient testing are given only to the provider of the exposed person solely for assisting the exposed person in making appropriate decisions regarding post-exposure medical treatment. The results of the test cannot be disclosed to the source patient or placed in the source patient’s medical record. The source patient may be told that the exposure occurred and an HIV test was performed. The source patient should be offered confidential testing so that they may have access to information about his/her own HIV status.

**IV. WORKERS’ COMPENSATION PROGRAM**

The Workers’ Compensation Law (WCL) has specific implications for employees exposed to HIV, as well as those rare cases that result in seroconversion. Individuals who manage such exposures should be familiar with these implications, as they should be able to counsel employees and refer them for legal and medical assistance accordingly. The organization’s Workers’ Compensation provider should be contacted as situations arise.

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**NYS Workers’ Compensation Board:** [www.wcb.ny.gov](http://www.wcb.ny.gov)

Worker benefits and information regarding how to file a claim:
[www.wcb.ny.gov/content/main/Workers/Workers.jsp](http://www.wcb.ny.gov/content/main/Workers/Workers.jsp)

Advocate for Injured Workers, for questions related to injured workers:
-(518) 474-8182
-(800) 580-6665
FAX: (518) 486-7510
## APPENDIX D. LOGISTIC REGRESSION ANALYSIS OF RISK FACTORS FOR HIV INFECTION AFTER PERCUTANEOUS EXPOSURE TO HIV-INFECTED BLOOD

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Adjusted odds ratio (95% CI)³</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>US Casesᵃ</td>
</tr>
<tr>
<td></td>
<td>All Casesᵇ</td>
</tr>
<tr>
<td>Deep injury</td>
<td>16.1 (6.1-44.6)</td>
</tr>
<tr>
<td>Visible blood on device</td>
<td>5.2 (1.8-17.7)</td>
</tr>
<tr>
<td>Procedure involving needle in artery or vein</td>
<td>5.1 (1.9-14.8)</td>
</tr>
<tr>
<td>Terminal illness in source patientᵈ</td>
<td>6.4 (2.2-18.9)</td>
</tr>
<tr>
<td>Postexposure use of zidovudine</td>
<td>0.2 (0.1-0.6)</td>
</tr>
</tbody>
</table>


ᵃ All risk factors were significant (P < 0.02).
ᵇ All risk factors were significant (P < 0.01).
ᶜ Odds ratios are for the odds of seroconversion after exposure in workers with the risk factor as compared with those without it.
ᵈ Terminal illness was defined as disease leading to the death of the source patient from AIDS within two months after the health care worker’s exposure.
## APPENDIX E. INTERPRETATION OF RESULTS OF TESTS FOR HEPATITIS C VIRUS INFECTION AND FURTHER ACTION

<table>
<thead>
<tr>
<th>Test Outcome</th>
<th>Interpretation</th>
<th>Further Action</th>
</tr>
</thead>
</table>
| HCV antibody nonreactive | No HCV antibody detected | - Sample can be reported as nonreactive for HCV antibody. No further action required.  
- If recent HCV exposure in person tested is suspected, test for HCV RNA. |
| HCV antibody reactive | Presumptive HCV infection | A repeatedly reactive result is consistent with current HCV infection, or past HCV infection that has resolved, or biologic false positivity for HCV antibody. Test for HCV RNA to identify current infection. |
| HCV antibody reactive and HCV RNA detected | Current HCV infection | Provide person tested with appropriate counseling and link person tested to medical care and treatment. |
| HCV antibody reactive and HCV RNA not detected | No current HCV infection | - No further action required in most cases.  
- If distinction between true positivity and biologic false positivity for HCV antibody is desired, and if sample is repeatedly reactive in the initial test, test with another HCV antibody assay.  
- In certain situations, follow up with HCV RNA testing and appropriate counseling. |

Reproduced from Centers for Disease Control and Prevention (CDC). Testing for HCV infection: An update of guidance for clinicians and laboratorians. MMWR Morb Mortal Wkly Rep 2013;62:362-365. Available at: [www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a5.htm](http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6218a5.htm)

*a* If HCV RNA testing is not feasible and person tested is not immunocompromised, perform follow-up testing for HCV antibody to demonstrate seroconversion. If the person tested is immunocompromised, consider testing for HCV RNA.

*b* It is recommended before initiating antiviral therapy to retest for HCV RNA in a subsequent blood sample to confirm HCV RNA positivity.

*c* If the person tested is suspected of having HCV exposure within the past 6 months, or has clinical evidence of HCV disease, or if there is concern regarding the handling or storage of the test specimen.