PEP Quick Guide for Occupational Exposures

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These CCC post-exposure prophylaxis (PEP) recommendations will help you with urgent decision-making for occupational exposures to HIV and hepatitis B and C. Consultation can be obtained from Occupational Health or Employee Health Services, local experts, or the CCC's PEPline. The PEPline (888-448-4911) is available daily from 9 am – 2 am EST (6 am – 11 pm PST).

Commonly Asked Questions

Initial Evaluation: Assessing Exposures and Testing

What is considered to be a potential exposure to HIV, HBV or HCV?
For transmission of blood borne pathogens (HIV, HBV and HCV) to occur, an exposure must include both of the following:

- **Infectious body fluid**
  - Blood, semen, vaginal fluids, amniotic fluids, breast milk, cerebrospinal fluid, pericardial fluid, peritoneal fluid, pleural fluid and synovial flood can transmit HIV, HBV and HCV.
- **Note that** saliva, vomitus, urine, feces, sweat, tears and respiratory secretions do not transmit HIV (unless visibly bloody). The risk of HBV and HCV transmission from non-bloody saliva is negligible.
- **A portal of entry**
  (percutaneous, mucous membrane, cutaneous with non-intact skin).

If both of these factors are not present, there is no risk of transmission and further evaluation is not required.

What baseline testing should be performed after an exposure?
(If no exposure occurred or Source Person tests negative, no testing is clinically indicated. Testing may be considered for other purposes including medicolegal concerns or as per institutional protocols.)
Source Person (SP):
• HIV Ab (rapid HIV Ab testing preferred if accessible)*
• HCV Ab
• HBV surface Ag
If SP's rapid HIV Ab test is positive, assume this is a true positive and send confirmatory testing, usually with a Western Blot test. See below.
Exposed Person (EP):
• HIV Ab
• HCV Ab
• HBV testing: Depends on immunization status.
Note that most healthcare and public safety personnel have been vaccinated against hepatitis B. If previously vaccinated and they know they **responded** to the vaccination series (a positive titer is >10mIU/mL, but most do not know their titer), they are considered to have lifelong immunity and require **no further testing or treatment.** Similarly, if employee health records indicate they responded to the vaccination series, they are considered to be immune. **For all others, see the "Exposures to HBV and HCV" section of this guide.**

***Is the rapid HIV test accurate enough to decide on whether to give PEP?**
Yes, the rapid HIV test is extremely sensitive and specific and can be used to determine whether to offer PEP. A positive rapid HIV test should be considered a true positive for the purposes of PEP decision-making. A negative rapid test should be considered a true negative. Investigation of whether a source might be in the "window period" is unnecessary for determining whether HIV PEP is indicated unless acute retroviral syndrome is clinically suspected.
(See What if the source might be in the "window period" for HIV? below).

Deciding Whether to Give HIV PEP

What is the time frame for using PEP?
Efficacy is time sensitive: first dose should be given as soon as possible. Optimal time to start PEP is within hours of exposure, rather than days. Do not wait for SP test results (unless results of rapid test will be available within an hour or two) to proceed with a PEP decision and treatment, when indicated. The PEPline considers 72 hours post-exposure as the outer limit of opportunity to initiate PEP; however, a delay of that scale is believed to compromise PEP efficacy. The 72-hour outside limit recommendation is based on animal studies; no human data are available.
Note: PEP should be initiated as soon as possible; if additional information indicates PEP might not be needed, PEP can always be discontinued.

What is the risk of HIV transmission?

Route of exposure	Risk of exposure when source person is HIV positive	Factors increasing risk
Percutaneous	~ 1/300 episodes (0.3%)	hollow bore needles, visibly bloody devices, and deep injury, device used in an artery/vein
Mucous membrane	~ 1/1000 episodes (0.09%)	large volume
Cutaneous	< 1/1000 episodes (0.09%)	must involve non-intact skin integrity

Note: These estimates are from exposures to blood; risk for transmission from infectious fluids other than HIV-infected blood is probably considerably lower than for blood exposures.

Is PEP always recommended if the source person is HIV infected?
PEP is recommended when an exposure to an HIV positive patient has occurred.
(See What is considered to be a potential exposure to HIV, HBV or HCV?)
• Additional source person information (e.g., the SP's current or most recent viral load, HIV medications, history of resistance to HIV medications) can be helpful in PEP regimen selection, but initiation of PEP should not be delayed if this information or consultation is not available.

Is PEP recommended if the source person has an unknown HIV status?
PEP is generally not warranted in cases of unknown status. However, consider PEP for exposures from a source with HIV risk factors. If questions exist, seek expert consultation from Occupational Health, Employee Health, local experts, or the PEPline.

Is PEP recommended if the source person is unknown (e.g. sharps box injury)?
PEP is generally not warranted in cases of an unknown source person. However, consider PEP in settings where exposure to HIV-infected persons is likely.

Should PEP be given if it is uncertain whether the exposure constitutes a significant risk?
Yes, if consultation is not available within a few hours, begin PEP and obtain consultation at a later time.

What if the source person might be in the "window period" for HIV?
If the source patient's HIV test is negative at the time of the exposure, they are generally considered uninfected and HIV PEP is not recommended.

• The “window period” for HIV Ab seroconversion (after the period between initial HIV infection and the development of detectable HIV antibodies) can cause patient and provider anxiety. The Guidelines state, “To date, no transmission to health care workers from an exposure source during the window period has been detected in the United States.”
• Therefore, investigation of whether a source patient might be in the “window period” is unnecessary for determining whether HIV PEP is indicated unless acute retroviral syndrome is clinically suspected, or recent high-risk exposure has occurred.
• Clinical suspicion can be implied when a source patient with risk factors has a history of recent (within 1-2 months) exposure (e.g. sexual, injection drug use, etc) and/or a recent illness consistent with possible acute HIV infection. If acute HIV is highly suspected, PEP should be started while confirmation with the source’s HIV RNA PCR viral load is sent.

Is PEP recommended for a patient who was stuck with a sharp device (e.g. needle, razor) from an unknown source outside of a healthcare setting?
This common occurrence falls into the classification of exposure to blood from an unknown SP. A “found needle” is the classic occurrence. No documented cases of HIV transmission from a “found needle” outside of a healthcare setting in the US have occurred. Therefore, the **PEPline generally discourages PEP in these cases.** Even within health care settings, “found needles” have only been implicated in two cases of transmission over the past two decades.

How should a human bite be managed?
• Human bite exposures can result in exposure to both the biter and the bitten person. The bitten sustains a cutaneous exposure to HIV if blood was present in the mouth of the biter before the bite. The biter sustains a mucous membrane exposure to HIV if blood from the bitten person enters the oral cavity of the biter.
• If the saliva is non-bloody, there is no risk to the exposed for HIV. The risk of HBV and HCV transmission from non-bloody saliva is negligible.

HIV PEP: What to Give

How to choose a PEP regimen?

Three-drug PEP regimens are now the recommended regimens for all exposures. The new guidelines no longer require assessing the degree of risk for the purpose of choosing a “basic” two-drug regimen vs. an “expanded” three-drug regimen, which was confusing for many treating clinicians. There are some special circumstances, however, in which a two-drug regimen can be used, especially when recommended antiretroviral medications are unavailable or there is concern about potential adherence problems or toxicity. In addition, the Guidelines state, “PEP is not justified for exposures that pose a negligible risk for transmission.” Consultation with an expert can help determine if the exposure poses a “negligible risk” to explore whether alternative approaches, including a modified regimen, are appropriate.

PREFERRED HIV 3-DRUG PEP REGIMEN:
Truvada™ 1 PO Once Daily
[Tenofovir DF (Viread®; TDF) 300mg + emtricitabine (Emtriva™; FTC) 200mg]
PLUS
Raltegravir (Isentress®; RAL) 400mg PO Twice Daily
ALTERNATIVE REGIMENS*
May combine one drug or drug pair from the left column with one pair of nucleoside/nucleotide reverse transcriptase inhibitors from the right column.

Raltegravir (Isentress® ; RAL)	Tenofovir DF (Viread® ; TDF) + emtricitabine (Emtriva™ ; FTC); available as Truvada™
Darunavir (Prezista® ; DRV) + ritonavir (Norvir® ; RTV)	Tenofovir DF (Viread® ; TDF) + lamivudine (Epivir® ; 3TC)
Etravirine (Intelence® ; ETR)_	Zidovudine (Retrovir™ ; ZDV; AZT) + lamivudine (Epivir® ; 3TC); available as Combivir®
Rilpivirine (Edurant™ ; RPV)	Zidovudine (Retrovir™ ; ZDV ; AZT) + emtrictabine (Emtriva™ ; FTC)
Atazanavir (Reyataz® ; ATV) + ritonavir (Norvir® ; RTV)	
Lopinavir/ritonavir (Kaletra® ; LPV/RTV)	

**The alternative regimens are listed in order of preference, however, other alternatives may be reasonable based upon patient and clinician preference.*

ANTIRETROVIRAL AGENTS FOR USE AS PEP ONLY WITH EXPERT CONSULTATION:
Abacavir (Ziagen® ; ABC), Efavirenz (Sustiva® ; EFV), Enfuvirtide (Fuzeon® ; T20), Fosamprenavir (Lexiva® ; FOSAPV), Maraviroc (Selzentry® ; MVC), Saquinavir (Invirase® ; SQV), Stavudine (Zerit® ; d4T)
ANTIRETROVIRAL AGENTS GENERALLY NOT RECOMMENDED FOR USE AS PEP:
Didanosine (Videx EC® ; ddI), Nelfinavir (Viracept® ; NFV), Tipranavir (Aptivus® ; TPV)
ANTIRETROVIRAL AGENTS CONTRAINDICATED AS PEP:
Nevirapine (Viramune® ; NVP)
ARV drug dosing and toxicity monitoring

HIV meds	Adult Dosing	Combination Form	Toxicity monitoring
Tenofovir@	300 mg po daily	Truvada™	BUN, Creatinine, LFTs
Emtricitabine@	200 mg po daily		Rash
Raltegravir	400 mg po BID		Nausea, headache
Zidovudine#	300 mg po BID	Combivir®	CBC, LFTs
Lamivudine#	150 mg po BID		Rash
Lopinavir/ritonavir& (200/50 mg)	2 tabs po BID	Kaletra ®	GI toxicity, especially diarrhea. LFTs *Note: Lopinavir/ritonavir has many drug-drug interactions with common medications; use with caution. (see below)

Zidovudine + Lamivudine: generic co-formulation available.

How long is PEP given?
PEP is given for 28 days. If source person testing is negative for HIV, PEP can be stopped before 28 days.

How to monitor and manage side effects of PEP?
Side effects can be a limiting factor in PEP adherence. Side effects are generally self-limited but sometimes can last the duration of the 28-day PEP course. Gastrointestinal side effects (nausea, vomiting, diarrhea) are most common. Headache, fatigue, insomnia and gastrointestinal upset are other side effects. Antiemetic and antidiarrheal medications can be prescribed to help with PEP adherence. If side effects are severe, consider changing to a different regimen. Toxicities are rare with the current preferred PEP regimens, are generally not life-threatening and are reversible.

The most important side effect of the preferred regiment, tenofovir + emtricitabine (Truvada™) plus raltegravir, is renal toxicity from tenofovir. This regimen should be used with caution in patients with impaired renal function.
Lab monitoring for drug toxicity: Test CBC, renal and hepatic function tests at baseline and two weeks after starting PEP.

What are common drug-drug interactions between PEP and the exposed person's medications?
• The following drugs should NOT be co-administered with lopinavir/ritonavir (Kaletra); lovastatin, pitavastatin, simvastatin, rifampin, rifapentine, cisapride, pimozide, midazolam, triazolam, dihydroergotamine, ergonovine, ergotamine, methylergonovine, St. John's wort, alfuzosin, salmeterol and sildenafil.
• Other Common medications may have interactions with PEP regimens and require dosing adjustments.
See Table 14 of the CDC Adult ARV Guidelines.
Contact a local expert or the PEPline the next day for further consultation regarding evaluation or management of drug-drug interactions.

Pregnancy and Breastfeeding

How should HIV exposures in pregnant women be managed?
• Starting PEP in pregnant exposed persons should be based on considerations similar to those of non-pregnant exposed persons.
• When deciding to start PEP, a pregnant exposed person should discuss with the treating clinician the potential risks of exposing her fetus to antiretroviral (ARV) medications.
• All pregnant women starting ARVs should be entered in the Antiretroviral Pregnancy Registry, a database designed to collect information on the outcomes of ARV-exposed pregnancies regardless of HIV status: http://www.apregistry.com.

Special considerations
• The pregnant exposed person and her fetus are at risk for HIV acquisition.
• Acute HIV in pregnancy incurs a high risk of vertical transmission.
• The use of most PEP medications can be justified when the benefits outweigh the risk of infant exposure to ARVs.
• Based on limited data, use of ARVs in pregnancy, including in the first trimester, does not appear to increase the risk of birth defects compared to the general population.
• Toxicities from currently recommended PEP drugs are not thought to be increased in pregnancy.

PEP options in pregnancy

If PEP is to be started in a pregnant exposed person, reasonable options include:

Tenofovir/emtricitabine (Truvada, TDF/FTC) 1 tab daily + raltegravir (Isentress, RAL) 400 mg BID	
Pros • Well-tolerated • TDF/FTC is a preferred agent in treating HIV+ pregnant women per DHHS guidelines • RAL is a preferred agent in treating HIV+ pregnant women per DHHS guidelines • Very low potential for drug-drug interactions	Cons • More limited experience using RAL in pregnancy vs protease inhibitors (PIs)

or

Zidovudine/lamivudine (Combivir, also avail as generic, AZT/3TC) 1 tab BID + *lopinavir/ritonavir (Kaletra, LPVr) 2-3# tablets BID**atazanavir (Reyataz) 300-400 mg# QD + ritonavir 100 mg QD may be used in place of lopinavir/ritonavir#PK data in pregnant women suggest increasing to 3 tabs BID of lopinavir/ritonavir and to 400 mg QD of atazanavir in the 2nd and 3rd trimesters*	
Pros • Extensive experience with use of AZT/3TC in pregnancy • Lopinavir/ritonavir as well as atazanavir/ritonavir are preferred agents in treating HIV+ pregnant women per DHHS guidelines	Cons • More side effects: nausea, vomiting, diarrhea, headache, fatigue • AZT associated with hematologic toxicity • High drug-drug interaction potential with lopinavir/ritonavir or other PIs

Other PEP options may be considered in the event of intolerance, source patient with resistant virus, ARV access, or EP preference. In these instances, providers should seek expert consultation.

How should HIV exposures in lactating exposed persons be managed?

• Breastfeeding is not a contraindication for PEP.

• When deciding to start PEP, lactating exposed persons should discuss with the treating clinician the potential risks and benefits of infant exposure to antiretroviral (ARV) medications through breastmilk. The decision to take PEP and/or continue breastfeeding is complex, and expert consultation is recommended.

Special considerations:

The lactating exposed person and her infant are at risk for HIV acquisition

Acute HIV in a breastfeeding mother greatly increases the risk of HIV transmission to her infant.

• There is limited data on PEP medications in breastmilk:

o Tenofovir (TDF, component of Truvada) and protease inhibitors can be detected in breastmilk only in very limited amounts

o Lamivudine (3TC, Epivir) can penetrate the breast milk in significant amounts
o Emtricitabine (FTC, component of Truvada)—unknown extent of breast milk penetration
o Raltegravir (RAL, Isentress)—unknown unknown extent of breast milk penetration
• For women who choose to take PEP, pumping and dumping is an option to allow continuation of lactation while preventing infant ARV and HIV exposure
• For women who choose not to take PEP, pumping and storing breastmilk while waiting for the source person's HIV testing results is an option. This allows continuation of lactation while not exposing infants to PEP medications or potentially to HIV

Exposures to HBV and HCV

How are exposures to HBV managed?
• **We strongly encourage Source Patient testing for Hepatitis B surface antigen.**
• If Source Patient is known to be hepatitis B uninfected, no hepatitis B testing or treatment of the Exposed Person is needed.
• If Exposed Person is known to be immune (e.g., they were told they had a positive response to the vaccine series, as measured by a follow-up HBsAb titer ≥10 mIU/mL), they are considered to have life-long immunity and need no hepatitis B testing or treatment.

If Source Patient is known to have had hepatitis B or the Source Patient's hepatitis B status is unknown, manage blood exposures as follows:

Recommendations for Post Exposure Prophylaxis After Exposure to HBV

EXPOSED PERSON VACCINATION STATUS	TEST RECOMMENDED	TREATMENT
Previously Vaccinated (see below *)		
Responder (HBsAb ≥10 mIU/mL)	None	No action needed
Response unknown	HBsAb	If ≥10 mIU/mL: No action needed
	HBsAb	If <10 mIU/mL: HBIG** and revaccinate

Non-responder (HBsAB ≤10 mIU/mL after one series of 3 doses)	HBcAb (total)	HBIG** and revaccinate
Non-responder (HBsAb ≤10 mIU/mL after two series of 3 doses)		HBIG** x 2 (one month apart)
Unvaccinated or Incompletely Vaccinated		
Unknown	HBcAb (total) Follow-up at 6 months: HBcAb (total) and HBsAg	HBIG** and vaccinate/revaccinate

* HBV (vaccine): The series is usually given at baseline, 1 month, and 6 months, followed by HBsAb to confirm immunity (HBsAb ≥10 mIU/mL). For persons previously immunized with the series of 3 immunizations but have negative HBsAb titer when tested at the time of exposure and source patient is negative for HBsAg, the first injection in the series can be followed with a HBsAb at 4-6 weeks; if positive (≥10 mIU/mL) the person is considered immune and no further treatment is needed.** HBIG: 0.06mL/kg ASAP. All persons receiving HBIG should have HBsAg and HBsAb drawn before HBIG administration. HBIG is considered effective up until a week in the occupational setting. **Note:** Testing the exposed HCP for prior HBV infection is not required before vaccinating unless the exposed is at independent risk of HBV infection (e.g., from HBV endemic area). *Adapted from: CDC guidance for evaluating health-care personnel for hepatitis B virus protection and for administering postexposure management. MMWR: December 20, 2013*

How soon do hepatitis B vaccine and HBIG need to be given?
In general, if hepatitis B vaccine and/or HBIG are required, the sooner they are administered the better. The effectiveness of HBIG when given after 7 days for occupational exposures is unknown.

How are exposures to HCV managed?
• The risk of transmission of HCV attributed to needlestick exposure is about 1 in 56 (1.8%) exposures when the source patient is HCV-infected. There is no post-exposure prophylaxis for HCV.
• Direct viral testing with HCV RNA PCR viral load at 6 weeks, before HCV Ab seroconversion has occurred, allows for early identification of transmission and subsequent referral for early evaluation and potential HCV treatment. The rate of spontaneous clearance of HCV infection is about 25% in healthy persons. However, early diagnosis and treatment may increase HCV clearance to 90% or greater.
• HCV antibody testing should be performed at 4-6 months to rule out HCV infection.

Follow-Up Testing

What follow-up testing should be performed?

Source Person:

The SP does not need follow-up testing.

Exposed Person:

Standard follow-up for an EP should include the following:

HIV

• If SP is HIV positive, check HIV Ab at 6 weeks, and a 4th generation Ag/Ab test or HIV RNA test at 3-4 months. If these tests are not available, standard antibody testing should be performed at 3 and 6 months. Extended testing to 12 months is only indicated for HCP who actually became infected with HCV after exposure to an HCV-HIV co-infected source. Symptoms of acute HIV should prompt immediate evaluation.
• If SP cannot be tested for HIV or SP is unknown, testing should be as above.
• If SP tests negative for HIV, no follow-up HIV testing is recommended for the EP.

HBV

• Serologic follow-up testing for HBV exposures is only required for persons who do not have baseline positive HBV surface Ab. Testing at 6 months consists of HBsAg and HBcAb (total).
(See also Exposures to HBV and HCV)

HCV

• If SP is HCV positive or has risk factors for HCV but unknown HCV status, obtain HCV RNA PCR viral load at 6 weeks and HCVAb at 4-6 mo. We generally recommend at 6 months to match with HIV testing.
• Symptoms of acute hepatitis should prompt immediate evaluation.
• If SP is HCV negative, no follow-up testing is recommended for EP.

Guidance for Exposed Persons

What do I do if I am the exposed individual?

Exposure to HIV, HBV, and HCV requires immediate evaluation by a medical professional (e.g., emergency room, urgent care, Occupational/Employee Health service, personal physician). Report your exposure to your supervisor immediately.

For a comprehensive description of HIV post-exposure management, see the 2013 CDC occupational post-exposure prophylaxis guidelines:

- **Updated US Public Health Service Guidelines for the Management of Occupational Exposures to Human Immunodeficiency Virus and Recommendations for Postexposure Prophylaxis, 2013**