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

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This report updates US Public Health Service recommendations for the management of healthcare personnel (HCP) who experience occupational exposure to blood and/or other body fluids that might contain human immunodeficiency virus (HIV). Although the principles of exposure management remain unchanged, recommended HIV postexposure prophylaxis (PEP) regimens and the duration of HIV follow-up testing for exposed personnel have been updated. This report emphasizes the importance of primary prevention strategies, the prompt reporting and management of occupational exposures, adherence to recommended HIV PEP regimens when indicated for an exposure, expert consultation in management of exposures, follow-up of exposed HCP to improve adherence to PEP, and careful monitoring for adverse events related to treatment, as well as for virologic, immunologic, and serologic signs of infection. To ensure timely postexposure management and administration of HIV PEP, clinicians should consider occupational exposures as urgent medical concerns, and institutions should take steps to ensure that staff are aware of both the importance of and the institutional mechanisms available for reporting and seeking care for such exposures. The following is a summary of recommendations: (1) PEP is recommended when occupational exposures to HIV occur; (2) the HIV status of the exposure source patient should be determined, if possible, to guide need for HIV PEP; (3) PEP medication regimens should be started as soon as possible after occupational exposure to HIV, and they should be continued for a 4-week duration; (4) new recommendation—PEP medication regimens should contain 3 (or more) antiretroviral drugs (listed in Appendix A) for all occupational exposures to HIV; (5) expert consultation is recommended for any occupational exposures to HIV and at a minimum for situations described in Box 1; (6) close follow-up for exposed personnel (Box 2) should be provided that includes counseling, baseline and follow-up HIV testing, and monitoring for drug toxicity; follow-up appointments should begin within 72 hours of an HIV exposure; and (7) new recommendation—if a newer fourth-generation combination HIV p24 antigen–HIV antibody test is utilized for follow-up HIV testing of exposed HCP, HIV testing may be concluded 4 months after exposure (Box 2); if a newer testing platform is not available, follow-up HIV testing is typically concluded 6 months after an HIV exposure.

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Preventing exposures to blood and body fluids (ie, primary prevention) is the most important strategy for preventing occupationally acquired human immunodeficiency virus (HIV) infection. Both individual healthcare providers and the institutions that employ them should work to ensure adherence to the principles of Standard Precautions, including ensuring access to and consistent use of appropriate work practices, work practice controls, and personal protective equipment. For instances in which an occupational exposure has occurred, appropriate postexposure management is an important element of workplace safety. This document provides updated recommendations concerning the management of occupational exposures to HIV.

The use of antiretrovirals as postexposure prophylaxis (PEP) for occupational exposures to HIV was first considered in guidelines issued by the Centers for Disease Control and Prevention (CDC) in 1990. In 1996, the first US Public Health Service (PHS) recommendations advocating the use of PEP after occupational exposure to HIV were published; these recommendations have been updated 3 times. Since

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publication of the most recent guidelines in 2005, several new
antiretroviral agents have been approved by the Food and
Drug Administration (FDA), and additional information has
become available regarding both the use and the safety of
agents previously recommended for administration for HIV
PEP.

As a direct result of 7 years' experience with the 2005
guidelines, several challenges in the interpretation and im-
plementation of those guidelines have been identified. These
challenges include difficulties in determining levels of risk of
HIV transmission for individual exposure incidents, problems
determining the appropriate use of 2 versus 3 (or more) drugs
in PEP regimens, the high frequency of side effects and tox-
icities associated with administration of previously recom-
manded drugs, and the initial management of healthcare per-
sonnel (HCP) with exposures to a source patient whose HIV
infection status was unknown. The PHS working group has
attempted to address both the new information that has been
developed and the challenges associated with the practical
implementation of the 2005 guidelines in this update.

This report encourages using HIV PEP regimens that are
optimally tolerated, eliminates the recommendation to assess
the level of risk associated with individual exposures to de-
termine the number of drugs recommended for PEP, modifies
and expands the list of antiretroviral medications that can be
considered for use as PEP, and offers an option for concluding
HIV follow-up testing of exposed personnel earlier than 6
months after exposure. This report also continues to em-
phasize the following: (1) primary prevention of occupational
exposures; (2) prompt management of occupational expo-
sures and, if indicated, initiation of PEP as soon as possible
after exposure; (3) selection of PEP regimens that have the
fewest side effects and that are best tolerated by prophylaxis
recipients; (4) anticipating and preemptively treating side ef-
cfects commonly associated with taking antiretroviral drugs;
(5) attention to potential interactions involving both drugs
that could be included in HIV PEP regimens and other med-
ications that PEP recipients might be taking; (6) consultation
with experts on postexposure management strategies (espe-
cially determining whether an exposure has actually occurred
and selecting HIV PEP regimens, particularly when the source
patient is antiretroviral treatment experienced); (7) HIV test-
ings of source patients (without delaying PEP initiation in the
exposed provider) using methods that produce rapid results;
and (8) counseling and follow-up of exposed HCP.

Recommendations concerning the management of occu-
pational exposures to hepatitis B virus and/or hepatitis C virus
(HCV) have been published previously5'7 and are not included
in this report. Recommendations for nonoccupational (eg,
sexual, pediatric, and perinatal) HIV exposures also have been
published previously.8-10

METHODS

In 2011, the CDC reconvened the interagency PHS working
group to plan and prepare an update to the 2005 Updated

U.S. Public Health Service Guidelines for the Management of
Occupational Exposures to HIV and Recommendations for Post-
exposure Prophylaxis.8 The PHS working group was comprised
of members from the CDC, the FDA, the Health Resources
and Services Administration, and the National Institutes of
Health. Names, credentials, and affiliations of the PHS work-
ing group members are listed as the byline of this guideline.
The working group met twice a month to monthly to create
a plan for the update as well as draft the guideline.

A systematic review of new literature that may have become
available since 2005 was not conducted; however, an initial
informal literature search did not reveal human randomized
trials demonstrating superiority of 2-drug antiretroviral med-
ication regimens versus those with 3 (or more) drugs as PEP
or an optimal PEP regimen for occupational exposures to
HIV. Because of the low risk of transmission associated with
occupational exposures (ie, approximately 0.3% per exposure
when all parenteral exposures are considered together),11 nei-
ther the conduct of a randomized trial assessing efficacy nor
the conduct of trials assessing the comparative efficacy of 2-
versus 3-drug regimens for PEP is practical. In light of the
absence of such randomized trials, the CDC convened a meet-
ing of the interagency PHS working group and an expert
panel of consultants in July 2011 to discuss the use of HIV
PEP and develop the recommendations for this update. The
expert panel consisted of professionals in academic medicine
considered to be experts in the treatment of HIV-infected
individuals, the use of antiretroviral medications, and PEP.
Names, credentials, and affiliations of the expert panel of
consultants are listed in "Expert Panel Consultants" at the
end of this guideline.

Prior to the July 2011 meeting, the meeting participants
were provided an electronic copy of the 2005 guidelines and
asked to review them and consider the following topics for
discussion at the upcoming meeting: (1) the challenges asso-
ciated with the implementation of the 2005 guidelines, (2)
the role of ongoing risk stratification in determining the use
of 2-drug PEP regimens versus those with 3 or more drugs,
(3) updated drug choices for PEP, (4) the safety and toler-
ability of antiretroviral agents for the general population and
for pregnant or lactating HCP, and (5) any other topics in
the 2005 guideline that needed to be updated.

At the July 2011 meeting, a CDC representative presented
a review of the 2005 guideline recommendations, surveillance
data on occupational exposures from the National Sewell-
lance System for Healthcare Workers,12 and data from the
National Clinicians' Post-Exposure Prophylaxis Hotline (PEPline)
on the number of occupational exposures to HIV
managed annually, PEP regimens recommended, and chal-
genches experienced with implementation of the 2005 guide-
lines. An FDA representative presented a review of the new
medications that have become available since 2005 for the
treatment of HIV-infected individuals, information about
medication tolerability and toxicity, and the use of these med-
ications during pregnancy. These presentations were followed
by a discussion of the topics listed above.

REFERENCES
Among the challenges discussed regarding implementation of the 2005 guidelines were the difficulties in determining level of risk of HIV transmission for individual exposure incidents, which in turn determined the number of drugs recommended for HIV PEP. The consensus of the meeting participants was to no longer recommend exposure risk stratification (discussed in detail in "Recommendations for the Selection of Drugs for HIV PEP" below). To update the drug choices for PEP, all drugs available for the treatment of HIV-infected individuals were discussed with regard to tolerability, side effects, toxicity, safety in pregnancy and lactation, pill burden, and frequency of dosing. A hierarchy of recommended drugs/regimens was developed at the meeting and utilized in creating the PEP regimen recommendations (Appendixes A and B) in these guidelines. Among other topics identified as needing an update were the acceptable HIV testing platforms available for source patient and follow-up testing of exposed HCP; the timing of such testing, depending on the platform used; and the potential utility of source patient drug-resistance information/testing in PEP regimens.

After the expert consultation, the expert panelists received draft copies of these guidelines as they were updated and provided insights, information, suggestions, and edits and participated in subsequent teleconferences with the PHS working group, to assist in developing these recommendations. Proposed recommendation updates were presented to the Healthcare Infection Control Practices Advisory Committee in November 2011 and June 2012 during public meetings. The PHS working group considered all available information, expert opinion, and feedback in finalizing the recommendations in this update.

DEFINITION OF HCP AND EXPOSURE

The definitions of HCP and occupational exposures are unchanged from those used in 2001 and 2005. The term HCP refers to all paid and unpaid persons working in healthcare settings who have the potential for exposure to infectious materials, including body substances (eg, blood, tissue, and specific body fluids), contaminated medical supplies and equipment, and contaminated environmental surfaces. HCP might include but are not limited to emergency medical service personnel, dental personnel, laboratory personnel, autopsy personnel, nurses, nursing assistants, physicians, technicians, therapists, pharmacists, students and trainees, contractual staff not employed by the healthcare facility, and persons not directly involved in patient care but potentially exposed to blood and body fluids (eg, clerical, dietary, housekeeping, security, maintenance, and volunteer personnel). The same principles of exposure management could be applied to other workers with potential for occupational exposure to blood and body fluids in other settings.

An exposure that might place HCP at risk for HIV infection is defined as a percutaneous injury (eg, a needlestick or cut with a sharp object) or contact of mucous membrane or non-intact skin (eg, exposed skin that is chapped, abraded, or affected with dermatitis) with blood, tissue, or other body fluids that are potentially infectious. In addition to blood and visibly bloody body fluids, semen and vaginal secretions are also considered potentially infectious. Although semen and vaginal secretions have been implicated in the sexual transmission of HIV, they have not been implicated in occupational transmission from patients to HCP. The following fluids are also considered potentially infectious: cerebrospinal fluid, synovial fluid, pleural fluid, peritoneal fluid, pericardial fluid, and amniotic fluid. The risk for transmission of HIV infection from these fluids is unknown; the potential risk to HCP from occupational exposures has not been assessed by epidemiologic studies in healthcare settings. Feces, nasal secretions, saliva, sputum, sweat, tears, urine, and vomitus are not considered potentially infectious unless they are visibly bloody.

Any direct contact (ie, contact without barrier protection) to concentrated virus in a research laboratory or production facility requires clinical evaluation. For human bites, clinical evaluation must include the possibility that both the person bitten and the person who inflicted the bite were exposed to bloodborne pathogens. Transmission of HIV infection by this route has been reported rarely, but not after an occupational exposure.

RISK FOR OCCUPATIONAL TRANSMISSION OF HIV

Factors associated with risk for occupational transmission of HIV have been described; risks vary with the type and severity of exposure. In prospective studies of HCP, the average risk for HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.3% (95% confidence interval [CI], 0.2%–0.5%) and that after a mucous membrane exposure to be approximately 0.09% (95% CI, 0.006%–0.5%). Although episodes of HIV transmission after nonintact skin exposure have been documented, the average risk for transmission by this route has not been precisely quantified but is estimated to be less than the risk for mucous membrane exposures. The risk for transmission after exposure to fluids or tissues other than HIV-infected blood also has not been quantified but is probably considerably lower than that for blood exposures.

Epidemiologic and laboratory studies suggest that multiple factors might affect the risk of HIV transmission after an occupational exposure. In a retrospective case-control study of HCP who had percutaneous exposure to HIV, increased risk for HIV infection was associated with exposure to a larger quantity of blood from the source person as indicated by (1) a device (eg, a needle) visibly contaminated with the patient’s blood, (2) a procedure that involved a needle being placed directly in a vein or artery, or (3) a deep injury. The risk also was increased for exposure to blood from source persons with terminal illness, likely reflecting the higher titer of HIV in blood late in the course of acquired immunodeficiency syndrome (AIDS). Taken together, these factors suggest a direct inoculum effect (ie, the larger the viral inoculum, the higher
the risk for infection). One laboratory study that demonstrated that more blood is transferred by deeper injuries and hollow-bore needles lends further credence to the observed variation in risk related to inoculum size.23

Exposure to a source patient with an undetectable serum viral load does not eliminate the possibility of HIV transmission or the need for PEP and follow-up testing. While the risk of transmission from an occupational exposure to a source patient with an undetectable serum viral load is thought to be very low, PEP should still be offered. Plasma viral load (eg, HIV RNA) reflects only the level of cell-free virus in the peripheral blood; persistence of HIV in latently infected cells, despite patient treatment with antiretroviral drugs, has been demonstrated,14,25 and such cells might transmit infection even in the absence of viremia. HIV transmission from exposure to a source person who had an undetectable viral load has been described in cases of sexual and mother-to-child transmissions.26,27

**ANTIRETROVIRAL AGENTS FOR PEP**

Antiretroviral agents from 6 classes of drugs are currently available to treat HIV infection.28 These include the nucleoside and nucleotide reverse-transcriptase inhibitors (NRTIs), nonnucleoside reverse-transcriptase inhibitors (NNRTIs), protease inhibitors (PIs), a fusion inhibitor (FI), an integrase strand transfer inhibitor (INSTI), and a chemokine (C-C motif) receptor 5 (CCR5) antagonist. Only antiretroviral agents approved by the FDA for treatment of HIV infection are included in these guidelines, although none of these agents has an FDA-approved indication for administration as PEP. The rationale for offering antiretroviral medications as HIV PEP is based on our current understanding of the pathogenesis of HIV infection and the plausibility of pharmacologic intervention in this process, studies of the efficacy of antiretroviral chemoprophylaxis in animal models,29,30 and epidemiologic data from HIV-exposed HCP.25 The recommendations in this report provide guidance for PEP regimens comprised of 3 (or, when appropriate, more) antiretrovirals, consonant with currently recommended treatment guidelines for HIV-infected individuals.28

**TOXICITY AND DRUG INTERACTIONS OF ANTIRETROVIRAL AGENTS**

Persons receiving PEP should complete a full 4-week regimen.3 However, previous results show that a substantial proportion of HCP taking an earlier generation of antiretroviral agents as PEP frequently reported side effects,12,32-40 and many were unable to complete a full 4-week course of HIV PEP due to these effects and toxicities.10-37 Because all antiretroviral agents have been associated with side effects (Appendix B),28 the toxicity profile of these agents, including the frequency, severity, duration, and reversibility of side effects, is a critical consideration in selection of an HIV PEP regimen. The majority of data concerning adverse events has been reported primarily for persons with established HIV infection receiving prolonged antiretroviral therapy and therefore might not reflect the experience of uninfected persons who take PEP. In fact, anecdotal evidence from clinicians knowledgeable about HIV treatment indicates that antiretroviral agents are tolerated more poorly by HCP taking HIV PEP than by HIV-infected patients on antiretroviral medications. As side effects have been cited as a major reason for not completing PEP regimens as prescribed, the selection of regimens should be heavily influenced toward those that are best tolerated by HCP receiving PEP. Potential side effects of antiretroviral agents should be discussed with the PEP recipient, and, when anticipated, preemptive prescribing of agents for ameliorating side effects (eg, antiemetics and antispasmodics) may improve PEP regimen adherence.

In addition, the majority of approved antiretroviral agents might have potentially serious drug interactions when used with certain other drugs, thereby requiring careful evaluation of concomitant medications, including over-the-counter medications and supplements (eg, herbs), used by an exposed person before prescribing PEP and close monitoring for toxicity of anyone receiving these drugs.28 PIs and NNRTIs have the greatest potential for interactions with other drugs. Information regarding potential drug interactions has been published, and up-to-date information can be found in the *Guidelines for the Use of Antiretroviral Agents in HIV-1-Infected Adults and Adolescents*.28 Additional information is included in manufacturers' package inserts. Consultation with a pharmacist or physician who is an expert in HIV PEP and antiretroviral medication drug interactions is strongly encouraged.

**SELECTION OF HIV PEP REGIMENS**

Guidelines for treating HIV infection, a condition typically involving a high total body burden of HIV, recommend the use of 3 or more drugs. Although the applicability of these recommendations to PEP is unknown, newer antiretroviral agents are better tolerated and have preferable toxicity profiles than agents previously used for PEP.28 As less toxic and better-tolerated medications for the treatment of HIV infection are now available, minimizing the risk of PEP noncompletion, and the optimal number of medications needed for HIV PEP remains unknown, the PHS working group recommends prescribing 3 (or more) tolerable drugs as PEP for all occupational exposures to HIV. Medications included in an HIV PEP regimen should be selected to optimize side effect and toxicity profiles and a convenient dosing schedule to encourage HCP completion of the PEP regimen.

**RESISTANCE TO ANTIRETROVIRAL AGENTS**

Known or suspected resistance of the source virus to antiretroviral agents, particularly to 1 or more of those that might be included in a PEP regimen, raises concerns about reduced PEP efficacy.41 Drug resistance to all available antiretroviral agents has been reported, and cross-resistance within drug
classes occurs frequently.45 Occupational transmission of drug-resistant HIV strains, despite PEP with combination drug regimens, has been reported.44-45 If a source patient is known to harbor drug-resistant HIV, expert consultation is recommended for selection of an optimal PEP regimen. However, awaiting expert consultation should not delay the initiation of HIV PEP. In instances of an occupational exposure to drug-resistant HIV, administration of antiretroviral agents to which the source patient's virus is unlikely to be resistant is recommended for PEP.

Information on whether a source patient harbors drug-resistant HIV may be unclear or unavailable at the time of an occupational exposure. Resistance should be suspected in a source patient who experiences clinical progression of disease, a persistently increasing viral load, or a decline in CD4+ T cell count despite therapy and in instances in which a virologic response to therapy fails to occur. However, resistance testing of the source virus at the time of an exposure is impractical because the results will not be available in time to influence the choice of the initial PEP regimen. If source patient HIV drug resistance is suspected in the management of an occupational exposure to HIV, consultation with an expert in HIV management is recommended so that antiretroviral agents to which the source patient's virus is unlikely to be resistant may be identified and prescribed. However, awaiting expert consultation should, again, not delay initiation of HIV PEP. If drug resistance information becomes available later in a course of PEP, this information should be discussed with the expert consultant for possible modification of the PEP regimen.

**ANTIRETROVIRAL DRUGS DURING PREGNANCY AND LACTATION**

The decision to offer HIV PEP to a pregnant or breast-feeding healthcare provider should be based on the same considerations that apply to any provider who sustains an occupational exposure to HIV. The risk of HIV transmission poses a threat not only to the mother but also to the fetus and infant, as the risk of mother-to-child HIV transmission is markedly increased during acute HIV infection during pregnancy and breast-feeding.46 However, unique considerations are associated with the administration of antiretroviral agents to pregnant HCP, and the decision to use antiretroviral drugs during pregnancy should involve both counseling and discussion between the pregnant woman and her healthcare provider(s) regarding the potential risks and benefits of PEP for both the healthcare provider and her fetus.

The potential risks associated with antiretroviral drug exposure for pregnant women, fetuses, and infants depend on the duration of exposure as well as the number and type of drugs. Information about the use of newer antiretroviral agents, administered as PEP to HIV-uninfected pregnant women, is limited. For reasons including the complexities associated with appropriate counseling about the risks and benefits of PEP as well as the selection of antiretroviral drugs in pregnant women, expert consultation should be sought in all cases in which antiretroviral medications are prescribed to pregnant HCP for PEP.

In general, antiretroviral drug toxicity has not been shown to be increased during pregnancy. Conflicting data have been published concerning the risk of preterm delivery in pregnant women receiving antiretroviral drugs, particularly PIs;47 in studies that have reported a positive association, the increase in risk was primarily observed in women who were receiving antiretroviral drug regimens at the time of conception and continued during pregnancy. Fatal48 and nonfatal48 lactic acidosis has been reported in pregnant women treated throughout gestation with a combination of stavudine and didanosine. Prescribing this drug combination for PEP is not recommended. Physiologic changes that occur during pregnancy may alter antiretroviral drug metabolism and, therefore, optimal drug dosing. The clinical significance of these changes is not clear, particularly when used for PEP in HIV-uninfected women. For details on antiretroviral drug choice and dosing in pregnancy, see Recommendations for Use of Antiretroviral Drugs in Pregnant HIV-1-Infected Women for Maternal Health and Interventions to Reduce Perinatal HIV Transmission in the United States.10

Prospective data from the Antiretroviral Pregnancy Registry do not demonstrate an increase in overall birth defects associated with first-trimester antiretroviral drug use. In this population, the birth defect prevalence is 2.9 per 100 live births, similar to the prevalence in the general population in the CDC's birth defect surveillance system (ie, 2.7 per 100 live births).50 Central nervous system defects were observed in fetal primates that experienced in utero efavirenz (EFV) exposure and that had drug levels similar to those representing human therapeutic exposure; however, the relevance of in vitro laboratory and animal data to humans is unknown.49 While human data are reassuring,51 1 case of meningomyelocele has been reported among the Antiretroviral Pregnancy Registry prospective cases, and data are insufficient to conclude that there is no increase in a rare outcome, such as neural tube defect, with first-trimester EFV exposure.50 For these reasons, we recommend that pregnant women not use EFV during the first trimester.10 If EFV-based PEP is used in women, a pregnancy test should be done to rule out early pregnancy, and nonpregnant women who are receiving EFV-based PEP should be counseled to avoid pregnancy until after PEP is completed. HCP who care for women who receive antiretroviral drugs during pregnancy are strongly advised to report instances of prenatal exposure to the Antiretroviral Pregnancy Registry (http://www.APRegistry.com/). The currently available literature contains only limited data describing the long-term effects (eg, neoplasia and mitochondrial toxicity) of in utero antiretroviral drug exposure. For this reason, long-term follow-up is recommended for all children who experience in utero exposures.50,52-53

Antiretroviral drug levels in breast milk vary among drugs,
with administration of some drugs resulting in high levels (eg, lamivudine), while other drugs, such as PIs and tenofovir (TDF), are associated with only limited penetration into milk. Administration of antiretroviral triple-drug regimens to breast-feeding HIV-infected women has been shown to decrease the risk of transmission to their infants and infant toxicity has been minimal. Prolonged maternal antiretroviral drug use during breast-feeding may be associated with increased infant hematologic toxicity, but limited drug exposure during 4 weeks of PEP may also limit the risk of drug toxicity to the breast-feeding infant. Breast-feeding should not be a contraindication to use of PEP when needed, given the high risk of mother-to-infant transmission with acute HIV infection during breast-feeding. The lactating healthcare provider should be counseled regarding the high risk of HIV transmission through breast milk should acute HIV infection occur (in a study in Zimbabwe, the risk of breast milk HIV transmission during the 3 months after seroconversion was 77.6 infections per 100 child-years). To completely eliminate any risk of HIV transmission to her infant, the provider may want to consider stopping breast-feeding. Ultimately, lactating women with occupational exposures to HIV who will take antiretroviral medications as PEP must be counseled to weigh the risks and benefits of continued breast-feeding both while taking PEP and while being monitored for HIV seroconversion.

MANAGEMENT OF OCCUPATIONAL EXPOSURE BY EMERGENCY PHYSICIANS

Many HCP exposures to HIV occur outside of occupational health clinic hours of operation and at sites at which occupational health services are unavailable, and initial exposure management is often overseen by emergency physicians or other providers who are not experts in the treatment of HIV infection or the use of antiretroviral medications. These providers may not be familiar with either the PHS guidelines for the management of occupational exposures to HIV or the available antiretroviral agents and their relative risks and benefits. Previous focus groups conducted among emergency department physicians who had managed occupational exposures to blood and body fluids in 2002 identified 3 challenges in occupational exposure management: evaluation of an unknown source patient or a source patient who refused testing, inexperience in managing occupational HIV exposures, and counseling of exposed workers in busy emergency departments. For these reasons, the PHS working group recommends that institutions develop clear protocols for the management of occupational exposures to HIV, indicating a formal expert consultation mechanism (eg, the in-house infectious diseases consultant or PEPline), appropriate initial source patient and exposed provider laboratory testing, procedures for counseling the exposed provider, identifying and having an initial HIV PEP regimen available, and a mechanism for outpatient HCP follow-up. In addition, these protocols must be distributed appropriately and must be readily available (eg, posted on signs in the emergency department, posted on a website, or disseminated to staff on pocket-sized cards) to emergency physicians and any other providers who may be called on to manage these exposure incidents.

RECOMMENDATIONS FOR THE MANAGEMENT OF HCP POTENTIALLY EXPOSED TO HIV

Exposure prevention remains the primary strategy for reducing occupational bloodborne pathogen infections. However, when occupational exposures do occur, PEP remains an important element of exposure management.

HIV PEP

The recommendations provided in this report apply to situations in which a healthcare provider has been exposed to a source person who has HIV infection or for whom there is reasonable suspicion of HIV infection. These recommendations reflect expert opinion and are based on limited data regarding safety, tolerability, efficacy, and toxicity of PEP. If PEP is offered and taken and the source is later determined to be HIV negative, PEP should be discontinued, and no further HIV follow-up testing is indicated for the exposed provider. Because the great majority of occupational HIV exposures do not result in transmission of HIV, the potential benefits and risks of PEP (including the potential for severe toxicity and drug interactions, such as may occur with oral contraceptives, H2-receptor antagonists, and proton pump inhibitors, among many other agents) must be considered carefully when prescribing PEP. HIV PEP medication regimen recommendations are listed in Appendix A, and more detailed information on individual antiretroviral medications is provided in Appendix B. Because of the complexity of selecting HIV PEP regimens, these recommendations should, whenever possible, be implemented in consultation with persons who have expertise in the administration of antiretroviral therapy and who are knowledgeable about HIV transmission. Reevaluation of exposed HCP is recommended within 72 hours after exposure, especially as additional information about the exposure or source person becomes available.

Source Patient HIV Testing

Whenever possible, the HIV status of the exposure source patient should be determined to guide appropriate use of HIV PEP. Although concerns have been expressed about HIV-negative sources who might be in the so-called window period before seroconversion (ie, the period of time between initial HIV infection and the development of detectable HIV antibodies), no such instances of occupational transmission have been detected in the United States to date. Hence, 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. Rapid HIV testing of source patients facilitates timely decision making regarding the need for administration of HIV PEP after occupational exposures to sources whose HIV status is unknown. FDA-approved rapid tests can produce HIV test results within 30 minutes, with sensitivities and specificities similar to those of first- and second-generation enzyme immunoassays (EIAs).\textsuperscript{60} Third-generation chemiluminescent immunoassays, run on automated platforms, can detect HIV-specific antibodies 2 weeks sooner than conventional EIAs\textsuperscript{60} and generate test results in an hour or less.\textsuperscript{61} Fourth-generation combination p24 antigen–HIV antibody (Ag/Ab) tests produce both rapid and accurate results, and their p24 antigen detection allows identification of most infections during the window period.\textsuperscript{62} Rapid determination of source patient HIV status provides essential information about the need to initiate and/or continue PEP. Regardless of which type of HIV testing is employed, all of the above tests are acceptable for determination of source patient HIV status. Administration of PEP should not be delayed while waiting for test results. If the source patient is determined to be HIV negative, PEP should be discontinued, and no follow-up HIV testing for the exposed provider is indicated.

Timing and Duration of PEP

Animal studies have suggested that PEP is most effective when begun as soon as possible after the exposure and that PEP becomes less effective as time from the exposure increases.\textsuperscript{29,30} PEP should be initiated as soon as possible, preferably within hours of exposure. Occupational exposures to HIV should be considered urgent medical concerns and treated immediately. For example, a surgeon who sustains an occupational exposure to HIV while performing a surgical procedure should promptly scrub out of the surgical case, if possible, and seek immediate medical evaluation for the injury and PEP. Additionally, if the HIV status of a source patient for whom the practitioner has a reasonable suspicion of HIV infection is unknown and the practitioner anticipates that hours or days may be required to resolve this issue, antiretroviral medications should be started immediately rather than delayed.

Although animal studies demonstrate that PEP is likely to be less effective when started more than 72 hours after exposure,\textsuperscript{30,85} the interval after which no benefit is gained from PEP for humans is undefined. If initiation of PEP is delayed, the likelihood increases that benefits might not outweigh the risks inherent in taking antiretroviral medications. Initiating therapy after a longer interval (eg, 1 week) might still be considered for exposures that represent an extremely high risk of transmission. The optimal duration of PEP is unknown; however, duration of treatment has been shown to influence success of PEP in animal models.\textsuperscript{29,30,63,64} Because 4 weeks of PEP appeared protective in in vitro, animal,\textsuperscript{29,30,63,64} and occupational\textsuperscript{85} studies, PEP should be administered for 4 weeks, if tolerated.

Recommendations for the Selection of Drugs for HIV PEP

The PHS no longer recommends that the severity of exposure be used to determine the number of drugs to be offered in an HIV PEP regimen, and a regimen containing 3 (or more) antiretroviral drugs is now recommended routinely for all occupational exposures to HIV. Examples of recommended PEP regimens include those consisting of a dual NRTI backbone plus an INSTI, a PI (boosted with ritonavir), or a NNRTI. Other antiretroviral drug combinations may be indicated for specific cases (eg, exposure to a source patient harboring drug-resistant HIV) but should be prescribed only after consultation with an expert in the use of antiretroviral agents. No new definitive data exist to demonstrate increased efficacy of 3-drug HIV PEP regimens compared with the previously recommended 2-drug HIV PEP regimens for occupational HIV exposures associated with a lower level of transmission risk. The recommendation for consistent use of 3-drug HIV PEP regimens reflects (1) studies demonstrating superior effectiveness of 3 drugs in reducing viral burden in HIV-infected persons compared with 2 agents\textsuperscript{29,65,66} (2) concerns about source patient drug resistance to agents commonly used for PEP,\textsuperscript{67,68} (3) the safety and tolerability of new HIV drugs, and (4) the potential for improved PEP regimen adherence due to newer medications that are likely to have fewer side effects. Clinicians facing challenges such as antiretroviral medication availability, potential adherence and toxicity issues, and others associated with a 3-drug PEP regimen might still consider a 2-drug PEP regimen in consultation with an expert.

The drug regimen selected for HIV PEP should have a favorable side effect profile as well as a convenient dosing schedule to facilitate both adherence to the regimen and completion of 4 weeks of PEP. Because the agents administered for PEP still can be associated with severe side effects, PEP is not justified for exposures that pose a negligible risk for transmission. Expert consultation could be helpful in determining whether an exposure constitutes a risk that would warrant PEP. The preferred HIV PEP regimen recommended in this guideline should be reevaluated and modified whenever additional information is obtained concerning the source of the occupational exposure (eg, possible treatment history or antiretroviral drug resistance) or if expert consultants recommend the modification. Given the complexity of choosing and administering HIV PEP, consultation with an infectious diseases specialist or another physician who is an expert in the administration of antiretroviral agents is recommended whenever possible. Such consultation should not, however, delay timely initiation of PEP.

The PHS now recommends emtricitabine (FTC) plus TDF (these 2 agents may be Dispensed as Truvada, a fixed-dose combination tablet) plus raltegravir (RAL) as HIV PEP for occupational exposures to HIV. This regimen is tolerable, potent, and conveniently administered, and it has been associated with minimal drug interactions. Additionally, al-
Box 1: Situations for Which Expert Consultation for Human Immunodeficiency Virus (HIV) Postexposure Prophylaxis (PEP) Is Recommended

Delayed (ie, later than 72 hours) exposure report
• Interval after which benefits from PEP are undefined

Unknown source (eg, needle in sharps disposal container or laundry)
• Use of PEP to be decided on a case-by-case basis
• Consider severity of exposure and epidemiologic likelihood of HIV exposure
• Do not test needles or other sharp instruments for HIV

Known or suspected pregnancy in the exposed person
• Provision of PEP should not be delayed while awaiting expert consultation

Breast-feeding in the exposed person
• Provision of PEP should not be delayed while awaiting expert consultation

Known or suspected resistance of the source virus to antiretroviral agents
• If source person’s virus is known or suspected to be resistant to 1 or more of the drugs considered for PEP, selection of drugs to which the source person’s virus is unlikely to be resistant is recommended
• Do not delay initiation of PEP while awaiting any results of resistance testing of the source person’s virus

Toxicity of the initial PEP regimen
• Symptoms (eg, gastrointestinal symptoms and others) are often manageable without changing PEP regimen by prescribing antimotility or antiemetic agents
• Counseling and support for management of side effects is very important, as symptoms are often exacerbated by anxiety

Serious medical illness in the exposed person
• Significant underlying illness (eg, renal disease) or an exposed provider already taking multiple medications may increase the risk of drug toxicity and drug-drug interactions

Expert consultation can be made with local experts or by calling the National Clinicians’ Post-Exposure Prophylaxis Hotline (PEPline) at 888-448-4911.

...though we have only limited data on the safety of RAL during pregnancy, this regimen could be administered to pregnant HCP as PEP (see the discussion above). Preparation of this PEP regimen in single-dose “starter packets,” which are kept on hand at sites expected to manage occupational exposures to HIV, may facilitate timely initiation of PEP.

Several drugs may be used as alternatives to FTC plus TDF plus RAL. TDF has been associated with renal toxicity, and an alternative should be sought for HCP who have underlying renal disease. Zidovudine could be used as an alternative to TDF and could be conveniently prescribed in combination with lamivudine, to replace both TDF and FTC, as Combivir. Alternatives to RAL include darunavir plus ritonavir (RTV), etravirine, rilpivirine, atazanavir plus RTV, and lopinavir plus RTV. When a more cost-efficient alternative to RAL is required, saquinavir plus RTV could be considered. A list of preferred alternative PEP regimens is provided in Appendix A.

Some antiretroviral drugs are contraindicated as HIV PEP or should be used for PEP only under the guidance of expert consultants (Appendixes A and B). Among these drugs are nevirapine, which should not be used and is contraindicated as PEP because of serious reported toxicities, including hepatotoxicity (with 1 instance of fulminant liver failure requiring liver transplantation), rhabdomyolysis, and hypersensitivity syndrome. Antiretroviral drugs not routinely recommended for use as PEP because of the higher risk for potentially serious or life-threatening adverse events include didanosine and tipranavir. The combination of didanosine and stavudine should not be prescribed as PEP due to increased risk of toxicity (eg, peripheral neuropathy, pancreatitis, and lactic acidosis). Additionally, abacavir should be used as HIV PEP only in the setting of expert consultation, due to the need for prior HLA B57-01 testing to identify individuals at higher risk for a potentially fatal hypersensitivity reaction. The PI enfuvirtide (Fuzeon, T20) is also not generally recommended as PEP, unless its use is deemed necessary during expert consultation, due to its subcutaneous route of administration, significant side effects, and potential for development of anti-T20 antibodies that may cause false-positive HIV antibody tests among uninfected patients.

When the source patient’s virus is known or suspected to be resistant to 1 or more of the drugs considered for the PEP regimen, the selection of drugs to which the source person’s virus is unlikely to be resistant is recommended; again, expert consultation is strongly advised. If this information is not immediately available, the initiation of PEP, if indicated, should not be delayed; the regimen can be modified after PEP has been initiated whenever such modifications are deemed appropriate. For HCP who initiate PEP, reevaluation of the exposed person should occur within 72 hours after exposure, especially if additional information about the exposure or source person becomes available.

Regular consultation with experts in antiretroviral therapy and HIV transmission is strongly recommended. Preferably,
Box 2: Follow-Up of Healthcare Personnel (HCP) Exposed to Known or Suspected Human Immunodeficiency Virus (HIV)—Positive Sources

Counseling (at the time of exposure and at follow-up appointments). Exposed HCP should be advised to use precautions (eg, use of barrier contraception and avoidance of blood or tissue donations, pregnancy, and, if possible, breast-feeding) to prevent secondary transmission, especially during the first 6–12 weeks after exposure.

For exposures for which postexposure prophylaxis (PEP) is prescribed, HCP should be informed regarding the following:

- Possible drug toxicities (eg, rash and hypersensitivity reactions that could imitate acute HIV seroconversion and the need for monitoring)
- Possible drug interactions
- The need for adherence to PEP regimens

Early reevaluation after exposure. Regardless of whether a healthcare provider is taking PEP, reevaluation of exposed HCP within 72 hours after exposure is strongly recommended, as additional information about the exposure or source person may be available.

Follow-up testing and appointments. Follow-up testing at a minimum should include the following:

- HIV testing at baseline and at 6 weeks, 12 weeks, and 6 months after exposure; alternatively, if the clinician is certain that a fourth-generation combination HIV p24 antigen–HIV antibody test is being utilized, then HIV testing could be performed at baseline, 6 weeks after exposure, and 4 months after exposure
- Complete blood counts and renal and hepatic function tests (at baseline and 2 weeks after exposure; further testing may be indicated if abnormalities are detected)

HIV testing results should preferably be given to the exposed healthcare provider at face-to-face appointments.

FOLLOW-UP OF EXPOSED HCP

Importance of Follow-Up Appointments

HCP who have experienced occupational exposure to HIV should receive follow-up counseling, postexposure testing, and medical evaluation regardless of whether they take PEP. Greater emphasis is placed on the importance of follow-up of HCP on HIV PEP within 72 hours of exposure and improving follow-up care provided to exposed HCP (Box 2). Careful attention to follow-up evaluation within 72 hours of exposure can (1) provide another (and perhaps less anxiety-ridden) opportunity to allow the exposed HCP to ask questions and for the counselor to make certain that the exposed HCP has a clear understanding of the risks for infection and the risks and benefits of PEP, (2) ensure that continued treatment with PEP is indicated, (3) increase adherence to HIV PEP regimens, (4) manage associated symptoms and side effects more effectively, (5) provide an early opportunity for ancillary medications or regimen changes, (6) improve detection of serious adverse effects, and (7) improve the likelihood of follow-up serologic testing for a larger proportion of exposed personnel to detect infection. Closer follow-up should in turn reassure HCP who become anxious after these events.73,74 The psychological impact of needlesticks or exposure to blood or body fluid should not be underestimated for HCP. Exposed personnel should be advised to use precautions (eg, use of barrier contraception and avoidance of blood or tissue donations, pregnancy, and, if possible, breast-feeding) to prevent secondary transmission, especially during the first 6–12 weeks after exposure. Providing HCP with psychological counseling should be an essential component of the management and care of exposed HCP.

Postexposure Testing

HIV testing should be used to monitor HCP for seroconversion after occupational HIV exposure. After baseline testing at the time of exposure, follow-up testing should be performed at 6 weeks, 12 weeks, and 6 months after exposure. Use of fourth-generation HIV Ag/Ab combination immunoassays allow for earlier detection of HIV infection.60,62,75 If a provider is certain that a fourth-generation combination
HIV Ag/Ab test is used, HIV follow-up testing could be concluded earlier than 6 months after exposure. In this instance, an alternative follow-up testing schedule could be used (eg, testing at baseline and 6 weeks after exposure, then concluding testing at 4 months after exposure). Extended HIV follow-up (eg, for 12 months) is recommended for HCP who become infected with HCV after exposure to a source who is coinfected with HIV and HCV. Whether extended follow-up is indicated in other circumstances (eg, for exposure to a source coinfected with HIV and HCV in the absence of HCV seroconversion or for exposed persons with a medical history suggesting an impaired ability to mount an antibody response to acute infection) is unknown. Although rare instances of delayed HIV seroconversion have been reported, adding to an exposed person’s anxiety by routinely extending the duration of postexposure follow-up is not warranted. However, decisions to extend follow-up in a particular situation should be based on the clinical judgment of the exposed person’s healthcare provider and should not be precluded because of HCP anxiety. HIV tests should also be performed for any exposed person who has an illness compatible with an acute retroviral syndrome, regardless of the interval since exposure. A person in whom HIV infection is identified should be referred to a specialist who has expertise in HIV treatment and counseling for medical management. Healthcare providers caring for persons who have occupationally acquired HIV infection should report these cases to their state health departments and to the CDC’s COPHI coordinator at telephone number 404-639-2050.

Monitoring and Management of PEP Toxicity

If PEP is used, HCP should be monitored for drug toxicity by testing at baseline and again 2 weeks after starting PEP. In addition, HCP taking antiretrovirals should be evaluated if any acute symptoms develop while receiving therapy. The scope of testing should be based on medical conditions in the exposed person and the known and anticipated toxicities of the drugs included in the PEP regimen. Minimally, laboratory monitoring for toxicity should include a complete blood count and renal and hepatic function tests. If toxicities are identified, modification of the regimen should be considered after expert consultation. In addition, depending on the clinical situation, further diagnostic studies may be indicated (eg, monitoring for hyperglycemia in a diabetic whose regimen includes a PI).

Exposed HCP who choose to take PEP should be advised of the importance of completing the prescribed regimen. Information should be provided about potential drug interactions and prescription/nonprescription drugs and nutritional supplements that should not be taken with PEP or require dose or administration adjustments, side effects of prescribed drugs, measures (including pharmacologic interventions) that may assist in minimizing side effects, and methods of clinical monitoring for toxicity during the follow-up period. HCP should be advised that evaluation of certain symptoms (eg, rash, fever, back or abdominal pain, pain on urination or blood in the urine, dark urine, yellowing of the skin or whites of the eyes, or symptoms of hyperglycemia [eg, increased thirst or frequent urination]) should not be delayed. Serious adverse events should be reported to the FDA’s MedWatch program.

RE-EVALUATION AND UPDATING OF HIV PEP GUIDELINES

As new antiretroviral agents for treatment of HIV infection and additional information concerning early HIV infection and prevention of HIV transmission become available, the interagency PHS working group will assess the need to update these guidelines. Updates will be published periodically as appropriate.

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Information included in these recommendations might not represent US Food and Drug Administration (FDA) approval or approved labeling for the particular product or indications in question. Specifically, the terms “safe” and “effective” might not be synonymous with the FDA-defined legal standard for product approval.
APPENDIX A

**Table A1. Human Immunodeficiency Virus (HIV) Postexposure Prophylaxis (PEP) Regimens**

| Preferred HIV PEP Regimen |
|---------------------------|
| Raltegravir (Isentress; RAL) 400 mg PO twice daily |
| Plus |
| Truvada, 1 PO once daily |
| (Tenofvir DF [Viread; TDF] 300 mg + emtricitabine [Emtriva; FTC] 200 mg) |

**Alternative Regimens**

(May combine 1 drug or drug pair from the left column with 1 pair of nucleoside/nucleotide reverse-transcriptase inhibitors from the right column; prescribers unfamiliar with these agents/regimens should consult physicians familiar with the agents and their toxicities)*

- **Raltegravir (Isentress; RAL)**
- **Darunavir (Prezista; DRV) + ritonavir (Norvir; RTV)**
- **Etravirine (Intélence; ETR)**
- **Rilpivirine (Edurant; RPV)**
- **Atazanavir (Reyataz; ATV) + ritonavir (Norvir; RTV)**
- **Lopinavir/ritonavir (Kaletra; LPV/RTV)**

The following alternative is a complete fixed-dose combination regimen, and no additional antiretrovirals are needed: Stribild (elvitegravir, cobicistat, tenofovir DF, emtricitabine)

**Alternative 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; ddl)
- Nelfinavir (Viracept; NFV)
- Tipranavir (Aptivus; TPV)

**Antiretroviral Agents Contraindicated as PEP**

- Nevirapine (Viramune; NVP)

**Note.** For consultation or assistance with HIV PEP, contact the National Clinicians’ Post-Exposure Prophylaxis Hotline at telephone number 888-448-4911 or visit its website at http://www.nccc.ucsf.edu/about_nccc/pepline/. DF, disoproxil fumarate; PO, per os.

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

**Appendix B**

**Table B1. Information on Human Immunodeficiency Virus (HIV) Postexposure Prophylaxis (PEP) Medications**

| Drug name (Brand; Abbreviation) | Drug class | Dosing (dosage form) | Advantages | Disadvantages |
|---------------------------------|------------|----------------------|------------|---------------|
| Abacavir (Ziagen; ABC) | Nucleoside reverse-transcriptase inhibitor (NRTI) | ABC: 300 mg daily, available as 300-mg tablet | Take without regard for food | Potential for life-threatening ABC hypersensitivity reaction (rash, fever, nausea, vomiting, diarrhea, abdominal pain, malaise, respiratory symptoms) in patients with HLA-B*5701; requires patient testing prior to use, which may not be available or practical prior to initiating PEP |
| Drug name          | Drug class                       | Dosing (dosage form)                                                                 | Advantages             | Disadvantages                                                                 |
|--------------------|----------------------------------|-------------------------------------------------------------------------------------|------------------------|-------------------------------------------------------------------------------|
| Atazanavir (Reyataz; ATV) | Protease inhibitor (PI)          | ATV: 300 mg + RTV: 100 mg once daily (preferred dosing for PEP<sup>1</sup>)          | Well tolerated         | Indirect hyperbilirubinemia and jaundice common                                |
|                    |                                  | ATV: 400 mg once daily without RTV (alternative dosing—may not be used in combination with TDF) |                        | Rash                                                                          |
|                    |                                  | Available as 100-, 150-, 200-, and 300-mg capsules                                   |                        | Nephrolithiasis                                                               |
|                    |                                  |                                                                                     |                        | Potential for serious or life-threatening drug interactions that may affect dosing |
|                    |                                  |                                                                                     |                        | Absorption depends on low pH; caution when coadministered with H<sub>2</sub> antagonists, antacids, and proton pump inhibitors |
|                    |                                  |                                                                                     |                        | PR interval prolongation                                                       |
|                    |                                  |                                                                                     |                        | Caution in patients with underlying conduction defects or on concomitant medications that can cause PR prolongation |
|                    |                                  |                                                                                     |                        | Must be given with food                                                        |
|                    |                                  |                                                                                     |                        | Rash (DRV has sulfonamide moiety)                                              |
|                    |                                  |                                                                                     |                        | Diarrhea, nausea, headache                                                    |
|                    |                                  |                                                                                     |                        | Hepatotoxicity                                                                |
|                    |                                  |                                                                                     |                        | Potential for serious or life-threatening drug interactions that may affect dosing |
|                    |                                  |                                                                                     |                        | Must be given with food and with RTV                                           |
| Darunavir (Prezista; DRV) | PI                             | DRV: 800 mg once daily + RTV: 100 mg once daily (preferred dosing for PEP<sup>1</sup>) | Well tolerated         | Indirect hyperbilirubinemia and jaundice common                                |
|                    |                                  | DRV: 600 mg twice daily + RTV: 100 mg twice daily (alternative dosing)                |                        | Rash                                                                          |
|                    |                                  | Available as 75-, 150-, 400-, and 600-mg tablets                                     |                        | Nephrolithiasis                                                               |
|                    |                                  |                                                                                     |                        | Potential for serious or life-threatening drug interactions that may affect dosing |
| Efavirenz (Sustiva; EFV) | Nonnucleoside reverse-transcriptase inhibitor (NNRTI) | EFV: 600 mg daily; available as 50- and 200-mg capsules and 600-mg tablets          | Available as a complete regimen dosed once per day |                          |
|                    |                                  | Also available as component of fixed-dose combination Atripla, dosed daily (200 mg of FTC + 300 mg of TDF + 600 mg of EFV) |                        | Rash                                                                          |
|                    |                                  |                                                                                     |                        | Neuropsychiatric side effects (eg, dizziness, somnolence, insomnia, abnormal dreaming) common; severe psychiatric symptoms possible (dosing before bedtime might minimize these side effects); use with caution in shift workers |
|                    |                                  |                                                                                     |                        | Do not use during pregnancy; teratogen in nonhuman primates                  |
|                    |                                  |                                                                                     |                        | Potential for serious or life-threatening drug interactions that may affect dosing |
|                    |                                  |                                                                                     |                        | May cause false-positive results with some cannabinoid and benzodiazepine screening assays |
| Elvitegravir (EVG) | Integrase strand transfer inhibitor (INSTI) | Available as a component of fixed-dose combination Stri­bild, dosed daily (150 mg of EVG + 150 mg of cobicistat + 300 mg of TDF + 200 mg of FTC) | Well tolerated         | Indirect hyperbilirubinemia and jaundice common                                |
|                    |                                  |                                                                                     | Available as a complete regimen dosed once per day | Rash                                                                          |
|                    |                                  |                                                                                     |                        | Nephrotoxicity; should not be administered to individuals with acute or chronic kidney injury or those with eGFR <70 |
|                    |                                  |                                                                                     |                        | Cobicistat is a pharmacokinetic enhancer to increase EVG exposures and has no antiviral activity but is a potent CYP3A inhibitor |
|                    |                                  |                                                                                     |                        | Potential for serious or life-threatening drug interactions                  |
|                    |                                  |                                                                                     |                        | Must be given with food                                                        |
### TABLE B1 (Continued)

| Drug name          | Drug class | Dosing (dosage form)                                                                 | Advantages                                           | Disadvantages                                                                 |
|--------------------|------------|--------------------------------------------------------------------------------------|------------------------------------------------------|-------------------------------------------------------------------------------|
| Emtricitabine      | NRTI       | 200 mg once daily; available as 200-mg capsule                                        | Well tolerated                                       | Rash perhaps more frequent than with 3TC                                      |
| (Emtriva; FTC)     |            | Also available as component of fixed-dose combination                                  | Minimal toxicity                                     | Hyperpigmentation/skin discoloration                                            |
|                    |            | Atripla, dosed daily (200 mg of FTC + 300 mg of TDF + 600 mg of EFV)                   | Minimal drug interactions                            | If the PEP recipient has chronic hepatitis B, withdrawal of this drug may cause an acute hepatitis exacerbation |
|                    |            | Complera, dosed daily (25 mg of RPV + 300 mg of TDF + 200 mg of FTC)                   | Take without regard for food                         |                                                                               |
|                    |            | Strivid, dosed daily (150 mg of EVG + 150 mg of cobicistat + 300 mg of TDF + 200 mg of FTC) |                                                                      |                                                                               |
|                    |            | Truvada, dosed daily (200 mg of FTC + 300 mg of TDF)                                   |                                                                      |                                                                               |
|                    |            | Available as single-dose vial, reconstituted to 90 mg/mL                               |                                                                      |                                                                               |
| Enfuvirtide        | Fusion inhibitor (FI) | T20: 90 mg (1 mL) twice daily by subcutaneous injection; available as single-dose vial, reconstituted to 90 mg/mL |                                                                      | Local injection-site reactions occur in almost 100% of patients |
| (Fuzeon; T20)      |            |                                                                      |                                                                      | Never studied among antiretroviral-naive or HIV-negative patients |
|                    |            |                                                                      |                                                                      | False-positive EIA HIV antibody tests might result from formation of anti-T20 antibodies that cross-react with anti-gp41 antibodies |
|                    |            |                                                                      |                                                                      | Twice-daily injection                                                        |
|                    |            |                                                                      |                                                                      | Rash (including SJS) and hypersensitivity (sometimes with organ dysfunction, including hepatic failure) |
|                    |            |                                                                      |                                                                      | Nausea                                                                       |
|                    |            |                                                                      |                                                                      | Potential for serious or life-threatening drug interactions that may affect dosing |
|                    |            |                                                                      |                                                                      | Must be given with food                                                     |
|                    |            |                                                                      |                                                                      | Diarrhea, nausea, vomiting, headache, rash (FOSAPV has sulfonamide moiety)  |
|                    |            |                                                                      |                                                                      | Potential for serious or life-threatening drug interactions that may affect dosing |
|                    |            |                                                                      |                                                                      | Oral contraceptives decrease FOSAPV concentrations                           |
|                    |            |                                                                      |                                                                      | Take with food if given with RTV                                             |
|                    |            |                                                                      |                                                                      | If the PEP recipient has chronic hepatitis B, withdrawal of this drug may cause an acute hepatitis exacerbation |
| Etravirine         | NNRTI      | 200 mg twice daily; available as 100- and 200-mg tablets                          | Well tolerated and has not had the same frequency of CNS side effects reported as EFV |                                                                               |
| (Intelence; ETR)  |            |                                                                      |                                                                      |                                                                               |
| Fosamprenavir      | PI         | FOSAPV: 1,400 mg daily + RTV: 100 mg once daily (preferred dosing for PEP)            | Well tolerated                                       |                                                                               |
| (Lexiva; FOSAPV)  |            | FOSAPV: 1,400 mg twice daily without RTV (alternative dosing)                      |                                                                      |                                                                               |
|                    |            | Available as 700-mg tablet                                                          |                                                                      |                                                                               |
| Lamivudine         | NRTI       | 3TC: 300 mg once daily (preferred dosing for PEP)                                   | Well tolerated                                       |                                                                               |
| (Epivir; 3TC)     |            | 3TC: 150 mg twice daily (alternative dosing)                                        | Minimal toxicity                                      |                                                                               |
|                    |            | Available as 150- and 300-mg tablets                                                 | Minimal drug interactions                             |                                                                               |
|                    |            | Also available as component of fixed-dose combination generic lamivudine/zidovudine, dosed twice daily (150 mg of 3TC + 300 mg of AZT) | Take without regard for food                         |                                                                               |
|                    |            | Combivir, dosed twice daily (150 mg of 3TC + 300 mg of AZT)                          |                                                                      |                                                                               |
|                    |            | Epzicom, dosed daily (300 mg of 3TC + 600 mg of ABC)                                 |                                                                      |                                                                               |
|                    |            | Trizivir, dosed twice daily (150 mg of 3TC + 300 mg of ABC + 300 mg of AZT)         |                                                                      |                                                                               |
| Drug name                  | Drug class | Dosing (dosage form)                                                                 | Advantages                                         | Disadvantages                                      |
|---------------------------|------------|-------------------------------------------------------------------------------------|----------------------------------------------------|---------------------------------------------------|
| Lopinavir/ritonavir        | PI         | Kaletra: 400/100 mg = 2 tablets twice daily (preferred dosing for PEP)               | Take without regard for food                       | GI intolerance, nausea, vomiting, diarrhea are common |
|                           |            | Kaletra: 800/200 mg = 4 tablets once daily (alternative dosing)                      |                                                    | PR and QT interval prolongation have been reported; use with caution in patients at risk of cardiac conduction abnormalities or receiving other drugs with similar effect |
|                           |            | Available as 200/50-mg tablets                                                      |                                                    | Potential for serious or life-threatening drug interactions that may affect dosing |
| Maraviroc                 | CCR5 coreceptor antagonist | MVC: 300 mg twice daily (if on concomitant CYP3A inducers, dose may need adjustment by expert consultant); available as 150- and 300-mg tablets | Well tolerated                                     | Abdominal pain, cough, dizziness, musculoskeletal symptoms, pyrexia, rash, orthostatic hypotension Hepatotoxicity that may present with an allergic reaction, including rash Requires HIV tropism testing of source virus before treatment to ensure CCR5-tropic virus and efficacy, which may not be available or practical prior to initiating PEP Potential for serious or life-threatening drug interactions that may affect dosing Dose adjustments for MVC required when given with potent CYP3A inhibitors or inducers |
| Raltegravir               | INSTI      | 400 mg twice daily; available as 400-mg tablet                                       | Well tolerated                                     | Insomnia, nausea, fatigue, headache, and severe skin and hypersensitivity reactions have been reported |
| Rilpivirine               | NNRTI      | 25 mg once daily; available as 25-mg tablet                                            | Well tolerated and fewer rashes and discontinuations for CNS adverse effects compared with EFV Available as a complete regimen dosed once per day | Depression, insomnia, rash, hypersensitivity, headache Potential for serious or life-threatening drug interactions that may affect dosing Caution when coadministered with H2 antagonists and antacids Coadministration with proton pump inhibitors is contraindicated Use RPV with caution when coadministered with a drug having a known risk of torsades de pointes Must be given with food |
| Saquinavir                | PI         | SQV: 1,000 mg + RTV: 100 mg twice daily (preferred dosing for PEP); available as 500 mg tablet | Well tolerated, although GI events common          | GI intolerance, nausea, diarrhea, headache Pretreatment ECG recommended SQV/r is not recommended for patients with any of the following: (1) congenital or acquired QT prolongation, (2) pretreatment ECG >450 msec, (3) receiving concomitant therapy with other drugs that prolong QT interval, (4) complete AV block without implanted pacemakers, and (5) risk of complete AV block PR and QT interval prolongations, torsades de pointes has been reported Potential for serious or life-threatening drug interactions that may affect dosing Must be given with food |
**TABLE B1 (Continued)**

| Drug name            | Drug class | Dosing (dosage form)                                                                 | Advantages                                      | Disadvantages                                                                 |
|----------------------|------------|-------------------------------------------------------------------------------------|------------------------------------------------|-------------------------------------------------------------------------------|
| **Stavudine**        | NRTI       | d4T: 40 mg twice daily if body weight is >60 kg                                      | Take without regard for food                    | GI side effects include diarrhea and nausea                                   |
| (Zerit; d4T)         |            | d4T: 30 mg twice daily if body weight is <60 kg                                      |                                                | Hepatotoxicity, neurologic symptoms (eg, peripheral neuropathy), pancreatitis |
|                      |            | Available as 15-, 20-, 30-, and 40-mg tablets                                        |                                                |                                                                                |
|                      |            | 300 mg once daily; available as 300-mg tablet                                        | Well tolerated                                   |                                                                                |
|                      |            | Also available as component of fixed-dose combination                                 |                                                |                                                                                |
|                      |            | Atripla, dosed daily (200 mg of FTC + 300 mg of TDF + 600 mg of EFV)                  |                                                |                                                                                |
|                      |            | Complera, dosed daily (25 mg of RPV + 300 mg of TDF + 200 mg of FTC)                 |                                                |                                                                                |
|                      |            | Stribild, dosed daily (150 mg of EVG + 150 mg of cobicistat + 300 mg of TDF + 200 mg of FTC) |                                                |                                                                                |
|                      |            | Truvada, dosed daily (200 mg of FTC + 300 mg of TDF)                                  |                                                |                                                                                |
| **Tenofovir DF**     | NRTI       |                                                                                                |                                                |                                                                                |
| (Viread; TDF)        |            | 300 mg once daily; available as 300-mg tablet                                        | Take without regard for food                    |                                                                                |
|                      |            | Also available as component of fixed-dose combination                                 |                                                |                                                                                |
|                      |            | Atripla, dosed daily (200 mg of FTC + 300 mg of TDF + 600 mg of EFV)                  |                                                |                                                                                |
|                      |            | Complera, dosed daily (25 mg of RPV + 300 mg of TDF + 200 mg of FTC)                 |                                                |                                                                                |
|                      |            | Stribild, dosed daily (150 mg of EVG + 150 mg of cobicistat + 300 mg of TDF + 200 mg of FTC) |                                                |                                                                                |
| **Zidovudine**       | NRTI       | AZT: 300 mg twice daily; available as 100-mg capsule or 300-mg tablet                | Take without regard for food                    | Side effects (especially nausea, vomiting, headache, insomnia, and fatigue) common and might result in low adherence |
| (Retrovir; ZDV; AZT) |            | Also available as component of fixed-dose combination generic lamivudine/zidovudine, dosed twice daily (150 mg of 3TC + 300 mg of AZT) |                                                |                                                                                |
|                      |            | Combivir, dosed twice daily (150 mg of 3TC + 300 mg of AZT)                           |                                                |                                                                                |
|                      |            | Trizivir, dosed twice daily (150 mg of 3TC + 300 mg of ABC + 300 mg of AZT)           |                                                |                                                                                |

**NOTE.** This appendix does not provide comprehensive information on each individual drug. For detailed information, please refer to individual drug package inserts. AV, atrioventricular; CNS, central nervous system; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; EIA, enzyme immunoassay; GI, gastrointestinal; SJS, Stevens-Johnson syndrome.

* Certain antiretroviral agents, such as PIs, have the option of once- or twice-daily dosing depending on treatment history and use with ritonavir. For PEP, the selection of dosing and schedule is to optimize adherence while minimizing side effects where possible. This table includes the preferred dosing schedule for each agent, and in all cases with the exception of Kaletra the once-daily regimen option is preferred for PEP. Twice-daily administration of Kaletra is better tolerated with respect to GI toxicities compared with the once-daily regimen. Alternative dosing and schedules may be appropriate for PEP in certain circumstances and should preferably be prescribed by individuals experienced in the use of antiretroviral medications.

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