

**Offering HIV Post-Exposure Prophylaxis (PEP)  
Following Non-Occupational Exposures  
Recommendations for Health Care Providers in the  
State of California**



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**Table of Contents**

Introduction ..... 1

Organization of this Document ..... 2

Copies of this Document ..... 2

Acknowledgement ..... 2

Executive Summary ..... 3

    Table 1 ..... 7

    Table 2 ..... 8

Scientific Background ..... 9

Who Should be Offered PEP? ..... 11

    Children and Adolescents ..... 13

    Pregnancy ..... 13

    Other Community Exposures ..... 13

    Timing of PEP Initiation ..... 14

    Medications for PEP ..... 15

    HIV Counseling and Testing ..... 17

    Mental Health and Substance Abuse Referrals ..... 17

    Other Laboratory Testing ..... 18

    Clinical Infrastructure Considerations ..... 19

    Clinician Training Resources ..... 20

Appendix A: Sample Patient Information Sheets ..... 25

Appendix B: Sample Scripts of Key Issues to Discuss with Clients ..... 29

Appendix C: Sample Clinical Progress Note ..... 38

Appendix D: Task Force Members ..... 40

References ..... 41

## **Introduction**

Health and Safety Code Section 121348, et seq. (Chapter 746, Koretz, Statutes of 2003), instructs the California Department of Health Services, Office of AIDS (DHS/OA), to appoint and convene a task force to develop recommendations for the use of post-exposure prophylaxis (PEP) for the prevention of HIV infection in the general population. The task force was appointed and convened in November 2003 to develop the recommendations contained in this document.

PEP may be considered for use in the general population in the following circumstances:

- Following consensual sexual exposure;
- Following non-consensual sexual exposure;
- Following exposure through sharing of injection drug use equipment;
- Following exposure through accidental needle sticks or sharps injuries;
- Following occupational exposure in non-health care workers; and
- Following physical assaults involving blood or other infectious body fluids.

Recommendations for the use of PEP following sexual assault can be found at: <http://www.dhs.ca.gov/AIDS/Reports/PDF/HIVProphylaxisFollowingSexualAssault.pdf>.

The recommendations contained in this document primarily refer to individuals who have had a potential exposure to HIV through consensual sexual activity, and secondarily to individuals who may have had an exposure to HIV through sharing of injection drug use equipment.

This document does not address in detail other community exposures (e.g., injuries from discarded needles, non-health care worker exposures, assaults, etc.). However, the same general principles outlined in this document can reasonably be applied to assess the likelihood of acquiring HIV from such exposures, and thus the potential utility of PEP. If a potentially infectious body fluid (e.g., blood or blood products, genital secretions, peritoneal, pleural or cerebrospinal fluids but NOT saliva, tears, or sweat) was in contact with a mucous membrane (e.g., eye, oral, nasal, or genital mucosa) or non-intact skin (punctured, cut or substantially abraded), HIV infection is possible and consideration of PEP is warranted. Although HIV cannot survive in dried blood or body fluids, it can survive in syringes for up to 30 days in some circumstances [1-3].

These recommendations are designed to provide guidance to health care providers who are managing potential non-occupational HIV exposures. The focus is on the following areas:

- Deciding who should be offered PEP based upon the details of the exposure;
- Deciding what medications and services to provide; and
- Determining how to provide these medications and services.

Whenever possible, PEP medications should be provided in association with HIV and sexually transmitted disease (STD) counseling and testing, as well as comprehensive HIV prevention services.

### **Organization of this Document**

The Executive Summary contains the key elements regarding non-occupational PEP use and should be used as a quick reference only. It is not comprehensive.

The remaining chapters include additional detail regarding each of the issues raised in the Executive Summary and should be consulted for a more comprehensive level of information.

The Appendixes contain additional training, clinical management, and patient education resources.

### **Copies of this Document**

Copies of this document may be obtained via the OA web site: [www.dhs.ca.gov/AIDS](http://www.dhs.ca.gov/AIDS). Permission to reproduce this document is hereby granted.

### **Acknowledgement**

Much of the material contained in this document is adapted from: The HIV In-Site Knowledge Base Chapter (April 2003) titled, "Prophylaxis Following Non-Occupational Exposure to HIV," written by Michelle Roland, M.D., University of California, San Francisco. For updates to this chapter and additional information and education resources regarding non-occupational PEP, please refer to: <http://www.hivinsite.org/InSite.jsp?page=kb-07&doc=kb-07-02-07>.

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## **Executive Summary**

### **Who Should Be Offered PEP?**

Refer to Table 1.

PEP is intended for individuals of negative or unknown HIV infection status following potential exposure to HIV. It is the responsibility of the health care provider to help the client who is seeking PEP to realistically assess his/her risk of acquiring HIV infection, to manage their emotional reactions and to make an informed decision about taking PEP. The higher the risk of the exposure (determined by the type of sexual or other activity and the likelihood of HIV infection in the exposure source), the more directive the health care provider should be towards the decision to take PEP. Likewise, the lower the risk of the exposure, the more directive the health care provider should be towards the decision not to take PEP. Ultimately, however, if the client meets these criteria, he/she should be given the opportunity to elect to use PEP. The client should also be encouraged to reevaluate this risk and the decision to use PEP over the subsequent few days. If they do wish to reconsider their initial decision, they should be encouraged to consult with the health care provider about changes in their original decision in order to ensure that the information they are using to change this decision is accurate.

### ***Timing***

Animal models of the natural history of HIV infection following exposure and of PEP interventions suggest that PEP is more effective the sooner it is started [4, 5]. The message to clients, referral sources, and health care providers should be that PEP should be initiated as soon as possible following the exposure. A 72-hour time limit for the initiation of PEP is reasonable given the evidence suggesting that PEP is not effective if initiated more than 72 hours post-exposure in animal models [4, 5].

### ***Exposure Risk***

**EXPOSURE TYPE:** If PEP is effective following mucosal and other non-occupational exposures, then those at highest risk of acquiring HIV infection from their specific exposure would be expected to benefit most from PEP. Health care providers should assist potentially exposed individuals in evaluating their risk, using a hierarchy of risk where receptive anal intercourse is riskier than insertive anal intercourse and receptive vaginal intercourse, which are riskier than insertive vaginal intercourse, which is riskier than receptive oral sex with ejaculation [6-10]. Other mucosal exposures, such as to eyes, and exposures of non-intact skin to potentially infected body fluids, can result in HIV transmission although their position in the risk hierarchy is less well-defined [11]. The average risk of HIV infection from each of these exposure types should be presented within the context of the risk from an occupational needle stick involving a source known to be HIV infected, (i.e., approximately 0.3 percent), for which PEP is often recommended [12, 13]. By comparison, the average per-contact risk of

transmission for unprotected receptive anal intercourse is approximately 1-3 percent; for unprotected insertive anal intercourse and receptive vaginal intercourse this risk is approximately 0.1-1 percent; and for unprotected insertive vaginal intercourse it is less than 0.1 percent [6-10]. The risk associated with receptive oral sex with ejaculation is extremely small, but infections do occur following this activity. The estimated per-contact risk for transmission following mucous membrane exposure to whole blood is 0.09 percent; there are no estimates for transmission rates with other potentially infectious body fluids.

Additional factors that enhance transmission, such as trauma, genital ulcer disease, or cervical ectopy, should also be considered [14]. It should be noted that there is some geographic variation--possibly associated with the distribution of subtypes of HIV-1--in the relative risk of transmission by different routes [15, 16]. For example, men exposed through insertive vaginal intercourse to subtype E (common in Thailand) have a higher per-contact infection rate than men exposed to other subtypes. Injection drug use exposures may carry a higher transmission risk than occupational needle stick injuries, although the viability of HIV in syringes and drug use equipment is difficult to assess [1-3].

**EXPOSURE SOURCE:** To evaluate the likelihood that the source of exposure is HIV infected, local risk demographics must be taken into strong consideration. Exposed individuals who feel safe doing so should be encouraged to speak with their source partner about HIV status and risk. No matter what the risk behavior, if the potential source is truly HIV negative, there is no risk of transmitting HIV. It may be difficult however, particularly in anonymous or casual settings, for a potentially exposed individual to feel confident about a source's claim that he/she is HIV negative. Recently HIV-antibody negative sources with recent HIV exposures may also be in a serologically negative window period of HIV infection. Determining the level of confidence regarding the source's description of his/her HIV status is a shared task of the patient and health care provider.

### **What Interventions Should be Offered and How Should They Be Provided?**

Refer to Table 2.

### ***Which Medications and for How Long?***

There is no consensus about how many drugs to use for occupational or non-occupational PEP, although the animal data supporting a 28-day course is compelling [5]. Since the effectiveness of zidovudine (ZDV) monotherapy in reducing HIV transmission risk after occupational exposure has been established, it is reasonable to attempt to include ZDV in non-occupational PEP regimens. However, ZDV resistance has emerged since the study was conducted and the impact of resistance should be considered when selecting a PEP regimen. Some experts believe that two drugs will provide adequate potency in a prophylactic setting, which involves an inoculum much smaller than the amount of virus present in an infected individual initiating treatment. Other experts are concerned about providing the maximum potential antiviral potency and advocate the addition of a third drug, despite increased cost and the potential for additional toxicity. Some data

suggest that there is significant toxicity associated with three-drug regimens; one study found two-drug regimens to be generally well tolerated [17, 18]. Severe hepatotoxicity associated with full-course nevirapine has resulted in recommendations against its use in PEP, although short-course nevirapine remains recommended for the prevention of mother-to-child transmission of HIV [19].

It is clear that transmission of drug-resistant HIV occurs. The mechanisms involved in the prophylactic effect of antiviral medications, and the impact resistance may have on its effectiveness, are less clear [20, 21]. To complicate matters, plasma HIV resistance patterns do not always represent the resistance patterns of virus isolated from genital secretions [22-25]. Mother-to-child transmission studies have provided inconsistent results regarding the importance of drug resistance in prophylaxis failures [26-28].

Despite this uncertainty, it is reasonable to assume that antiretroviral resistance may have an impact on effectiveness. Thus, it is important to construct, when possible, a PEP regimen to which the virus involved is unlikely to be resistant. When the source partner's antiretroviral medication history and corresponding HIV viral load measurements are known, PEP medications can be selected based on deductions of existing resistance in the exposure source. A clinician with expertise in antiviral resistance should be consulted immediately when the exposure source's medication history is known. Initiation of a standard PEP regimen should not be delayed more than a few hours (i.e., two to four hours) while attempting to gather relevant information regarding the exposure source and obtaining expert consultation.

### ***Laboratory Testing***

Note that these guidelines differ from the Centers for Disease Control and Prevention (CDC) occupational PEP guidelines related to: 1) frequency of HIV antibody testing, and 2) routine monitoring of laboratory toxicity. CDC guidelines recommend HIV testing at 6, 13, and 24 weeks. As there is not likely to be substantial benefit to more testing, which may cause more anxiety and cost without substantially increasing detection of breakthrough infections, the recommendation is less frequent HIV antibody testing. Patients requesting an additional HIV test should be accommodated. CDC guidelines recommend routine laboratory testing two weeks after PEP initiation. The task force does not believe there are data suggesting that these must be performed. For CDC guidelines, refer to: <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5011a1.htm>.

HIV antibody testing should be performed at the time of presentation and two to three and six months after the exposure. A case of delayed seroconversion in a treated monkey suggests that delayed seroconversion may occur in the context of human PEP, although this has not been reported in either the occupational or non-occupational setting except during co-transmission with hepatitis C [4, 11, 29]. Unless the patient develops symptoms and signs consistent with acute HIV infection, HIV ribonucleic acid (RNA) testing should not be performed, as the specificity characteristics of these tests are not satisfactory in a diagnostic setting [30-32]. The odds of a false-positive test

result are significant in a setting of low pre-test probability and may outweigh any potential benefit of detecting HIV viremia during the brief period prior to seroconversion [33].

Testing for STD and hepatitis should be considered in patients presenting for PEP. Safety laboratory studies, such as a complete blood count and liver enzymes, may be tailored to the specific individual based upon medical history and symptoms since there are no data to suggest they need to be routinely performed.

### ***Other Medical Interventions***

Post-coital contraception should be provided to women who have had vaginal intercourse.

When possible, immunizations for hepatitis A and B should be offered when indicated. If immunizations are not available, referrals should be provided.

### ***Risk Reduction and HIV Pre- and Post-Test Counseling***

The provision of PEP should always include risk-reduction focused HIV pre- and post-test counseling, with an emphasis on identifying the emotional and social factors that may have contributed to the risk-taking activity. It is helpful to explore the incident in contrast to a time when the person was able to maintain lower risk behavior. The second counseling step is to explore the pattern of behavior: Was this an isolated event, episodic, or part of a regular pattern? Developing a specific, client-centered risk-reduction plan and appropriate referrals is the third key counseling component. In follow-up visits, the risk-reduction plan should be reviewed and reevaluated and the outcome of prior referrals assessed. Note that effective risk-reduction counseling may have a greater impact on the overall risk of acquiring HIV infection than that provided by PEP for an isolated exposure.

### ***Adherence Counseling***

Specific adherence counseling must be provided by the health care provider and/or other medical staff. This counseling should include specific information regarding dosing, frequency, what to do if a dose is missed, etc. Exploring anticipated times and cues for taking morning and evening doses is also helpful.

**Table 1: Exposure Characteristics and Indications for PEP**

Exposure Characteristic	Offer PEP:
<p><b>1) Timing.</b></p>	<p>As soon as possible, and no later than 72 hours following exposure.</p> <p style="text-align: center;">- <i>AND IF</i> -</p>
<p><b>2) Exposure type.</b></p>	<ul style="list-style-type: none"> <li>• Receptive anal intercourse; or</li> <li>• Shared injection drug use equipment; or</li> <li>• Insertive anal intercourse; or</li> <li>• Receptive vaginal intercourse; or</li> <li>• Insertive vaginal intercourse; or</li> <li>• Other potentially infectious body fluid on a mucous membrane or non-intact skin; or</li> <li>• Receptive oral intercourse with ejaculation (consider due to lower risk; if oral pathology, risk is higher).</li> </ul> <p style="text-align: center;">- <i>AND IF</i> -</p>
<p><b>3) Exposure source.</b></p> <p><b>(Note: identifying specific risk groups depends upon the local HIV demographics where the exposure occurred.)</b></p>	<ul style="list-style-type: none"> <li>• Known HIV-infected; or</li> <li>• Men who have sex with men (MSM) of unknown HIV status; or</li> <li>• Injection drug user (IDU) of unknown HIV status; or</li> <li>• Anonymous (consider); or</li> <li>• Known but with unknown HIV status and risk factor history (consider).</li> </ul>

**Table 2: PEP Interventions**

Component	Options (*recommended)
<b>Medications.</b>	<ul style="list-style-type: none"> <li>• *Two-nucleoside analogues:               <ul style="list-style-type: none"> <li>○ Preferred regimen is Combivir (ZDV + lamivudine).</li> <li>○ Alternative nucleoside analogue combinations include: stavudine or tenofovir in combination with lamivudine or emtricitabine. Abacavir and didanosine should be avoided unless resistance considerations outweigh potential toxicity (hypersensitivity and pancreatitis, respectively).</li> </ul> </li> <li>• ± Protease inhibitor (Kaletra or others, see “Medications for PEP”) or Efavirenz (consider only when very high-risk exposure and known infected source or resistance characteristics make it difficult to construct a potent two nucleoside regimen).</li> <li>• Full course nevirapine is contraindicated for PEP (per U.S. Public Health Service). Note that short course nevirapine is recommended for the prevention of mother-to-child transmission in resource poor settings.</li> </ul> <p>If the exposure source’s medication history is accessible, obtain expert antiretroviral resistance consultation immediately. If local consultation is unavailable, call the National HIV Telephone Consultation Service at (800) 933-3413. The hours are: 6 a.m.-5 p.m., Pacific Standard Time (PST), Monday-Friday. <i>Note that this service is available for health care providers only.</i> Consider academic hospital infectious disease consultation after hours.</p>
<b>Duration of therapy.</b>	<ul style="list-style-type: none"> <li>• 28 days.</li> </ul>
<b>Follow-up HIV counseling and testing.</b>	<ul style="list-style-type: none"> <li>• *Baseline.</li> <li>• Four to six weeks (consider).</li> <li>• *Two to three months.</li> <li>• *Six months.</li> </ul>
<b>Other testing and interventions.</b>	<ul style="list-style-type: none"> <li>• *STD screening and treatment.</li> <li>• *Hepatitis B screening.</li> <li>• *Hepatitis C screening in at-risk populations.</li> <li>• *Hepatitis A and B immunizations.</li> <li>• *Safety labs per specific medications, medical history, and symptoms at baseline and follow-up (e.g., complete blood count [cbc], hepatic function, renal function, amylase, etc.); routine safety labs are not recommended.</li> <li>• *Post-coital contraception if desired.</li> </ul>
<b>Counseling and referrals.</b>	<ul style="list-style-type: none"> <li>• *Medication adherence counseling.</li> <li>• *Risk-reduction counseling.</li> <li>• *Referrals for substance use and mental health treatment as appropriate.</li> </ul>

## **Scientific Background**

Several programs and observational studies have been designed to offer PEP following exposure to HIV following non-occupational exposures including consensual and nonconsensual sex and injection drug use. In 1998, CDC published guidelines regarding non-occupational PEP that neither recommended nor discouraged its use [34]. Revised guidelines are undergoing review within the Department of Health and Human Services after a May 2001 consultation resulted in draft revisions. Several states have non-occupational PEP policy or guidelines. Massachusetts has policy and procedures in place to provide PEP following all such exposures [35], Rhode Island has recently developed guidelines for non-occupational PEP use [36], and the states of New York and California have guidelines for the use of PEP following sexual assault [37, 38]. Internationally, several countries have official policies recommending non-occupational PEP [39], including France [40], Italy [41], Spain, Switzerland [42], Australia, and South Africa.

## ***Efficacy and Related Background Data***

Although there are no efficacy data directly supporting the use of non-occupational PEP for sexual exposures, several related sets of data from an occupational exposure study, mother-to-child transmission studies, and animal studies support its biological plausibility. The validity of generalizing results of PEP following nonmucosal exposures to mucosal exposures in humans remains uncertain because of differences in the immune response. Animal models of mucosal exposures do demonstrate PEP effectiveness.

## ***Occupational Exposure Studies***

The 1987 approval of ZDV was followed by consideration of antiretroviral therapy as prophylaxis following potential exposure to HIV. In 1990, CDC published a statement that neither recommended nor discouraged such use following occupational exposures to HIV. The 1995 presentation of a case-control study in health care workers demonstrating a 79 percent reduction in the likelihood of HIV infection associated with ZDV use following occupational exposure led to the 1996 revision of CDC guidelines to recommend PEP following occupational exposures [43]. The published study ultimately showed an 81 percent reduction in HIV infection associated with ZDV use and raised a number of questions regarding generalizability to non-occupational exposures, the feasibility of providing non-occupational PEP, and its safety and cost-effectiveness [44].

## ***Mother-to-Child Transmission Studies***

Multiple studies of antiretroviral drugs used in pregnant women and/or their newborns have demonstrated efficacy in preventing mother-to-child transmission of HIV infection [45, 46]. Some of these studies have included drugs given to both the mother and the newborn, some just to the mother, and two to just the newborn [47, 48]. A New York

State Department of Health analysis demonstrating efficacy even in those infants who only received ZDV within 48 hours after birth (9.2 percent compared to 26.6 percent transmission without PEP) suggests that there is likely a post- as well as a pre-exposure effect of antiretrovirals used in the prevention of mother-to-child transmission [48]. The first prospective study of antiretrovirals used only in the postnatal period to prevent mother-to-child transmission also demonstrated efficacy in reducing mother-to-child transmission of HIV [47].

### ***Animal Studies***

Results from animal studies of PEP have provided data supportive of its probable efficacy in intravenous, oral, and vaginal simian immunodeficiency virus (SIV) and HIV-2 exposures, and these data have been instructive in terms of timing and duration of therapy. In SIV models, nucleotide and nucleoside analogues have been protective in preventing infection in a majority of intravenously inoculated macaques when given early after exposure (within 24 hours is superior to 48 or 72 hours) and for a 28-day course [5, 49-52]. When provided to macaques following intravaginal exposure to HIV-2, the nucleotide analogue PMPA (tenofovir) was fully protective when treatment was initiated at 12 or 36 hours post-inoculation (zero of eight infected), and only partially effective at 72 hours (one of four treated animals infected; three of four controls infected) [4]. The three control animals seroconverted at two weeks and the experimental animal at 16 weeks post-exposure, raising concerns about the possibility of delayed seroconversion and the need for adequate follow-up HIV antibody testing after administration of PEP. Reassuringly, studies of health care workers who have seroconverted following PEP have not demonstrated delayed seroconversion. Studies in oral mucosal transmission models have shown efficacy of combined pre- and post-exposure interventions, even with antiretroviral-resistant virus, raising questions about the mechanism of action of PEP in this setting [53-55]. Non-nucleoside reverse transcriptase inhibitors (NNRTIs) appear to be at least partially protective PEP agents in primate studies [56, 57].

### ***Observational Studies in Humans***

Only a single study of PEP following non-occupational exposures has been published; there were no seroconversions among 401 enrolled subjects with follow-up six months after PEP initiation [18]. Unpublished studies from the United States, Brazil, Australia, and South Africa report few seroconversions following non-occupational PEP use, although follow-up is often limited [58-62]. A recent unpublished analysis of data from San Francisco, California, demonstrates the difficulty of attributing HIV seroconversions to failure of PEP in the non-occupational context, where the potential infection source is rarely available for testing and additional potential exposures are common [63].

### ***Failure of PEP to Prevent HIV Infection Following Occupational Exposure***

There have been several reports of failure of PEP to prevent HIV infection following occupational exposures [11, 12, 64-67]. While offering some protection, PEP is not expected to be 100 percent effective in any setting. Thus, some failures of PEP are not inconsistent with the efficacy of PEP.

### **Who Should Be Offered PEP?**

PEP should be offered to HIV uninfected or unknown status individuals presenting within 72 hours of a potential exposure to HIV. Assessing the likelihood of HIV infection following exposure includes two factors: 1) did a potentially infectious body fluid from the exposure source come into contact with the exposed individual's mucous membrane or non-intact skin, *and* 2) is the exposure source known to be HIV infected or at risk of having HIV infection?

Individuals at highest risk of acquiring HIV infection from their specific exposure are expected to benefit most from PEP. Potentially exposed individuals should be assisted in evaluating their risk based upon the type of sex or other exposure they had, and the likelihood that the exposure source is HIV infected.

### ***Assessing the Risk of the Exposure***

If a potentially infectious body fluid (e.g., blood or blood products, genital secretions, peritoneal, pleural or cerebrospinal fluids but NOT saliva, tears, or sweat) was in contact with a mucous membrane (e.g., eye, oral, nasal, or genital mucosa) or non-intact skin (punctures, cut or substantially abraded), infection is possible and consideration of PEP is warranted.

The following activities are associated with HIV transmission risk. Note that additional factors that might enhance sexual transmission, such as trauma, genital ulcer disease, or cervical ectopy, should also be considered (92).

- Receptive anal intercourse (1–3 percent per-contact transmission risk).
- Shared injection drug use equipment (0.67 percent per-contact transmission risk).
- Insertive anal intercourse (0.1–1 percent per-contact transmission risk).
- Receptive vaginal intercourse (0.1–1 percent per-contact transmission risk).
- Insertive vaginal intercourse (less than 0.1 percent per-contact transmission risk).
- Other potentially infectious body fluid on a mucous membrane or non-intact skin.
- Receptive oral intercourse with ejaculation (case reports only; consider PEP).

- AND -

### ***Assessing the Likelihood that the Source of Exposure is HIV-Infected***

To evaluate the likelihood that the source of exposure is HIV-infected, local risk demographics must be taken into consideration. Exposed individuals who feel safe doing so should be encouraged to speak with their exposure source about HIV status and risk. In California, when considering indications for PEP, it is reasonable to assume that exposure sources who are MSM or past or present IDUs may have HIV infection. There is a growing incidence of HIV infection among the female sex partners of IDUs or men who deny having sex with men, particularly in some African American and Latino communities. Thus, it is reasonable to consider PEP for women who have unprotected sex with men who are known to them, but whose sexual and injection drug use history is not known with confidence. It is also reasonable to consider PEP for individuals following sexual encounters with anonymous partners.

### ***Source Plasma Viral Load***

An undetectable or low plasma HIV RNA level or plasma viral load does not ensure that genital secretions are not infectious, due to viral compartmentalization.

### ***Source HIV Testing***

If an exposure source of unknown HIV status presents with the potentially exposed client, HIV testing of the source should be encouraged, using a rapid or standard HIV antibody test. If a rapid test is negative, PEP should be deferred unless there is a high index of suspicion that the source may be in the seronegative window period of infection. If using a standard test, PEP can be discontinued when the results come back with the same caveat.

### ***Multiple Exposures***

Some individuals will present for PEP following a series of exposures, some of which are within, and others outside, the 72 hour cut-off. It will be up to the judgment of the individual health care provider to determine when PEP should be offered and when it should not be offered in such circumstances. It is not unreasonable to offer PEP, however, the reduced likelihood of being able to prevent HIV infection because of the earlier exposures should be explained to the patient.

### ***Assessing the Likelihood of Pre-existing HIV Infection***

All individuals presenting for PEP should be evaluated for the likelihood of pre-existing HIV infection. The following information should be obtained: 1) date of last HIV test, and 2) the number and type of unprotected exposures since the last test. The likelihood of pre-existing HIV infection should be reviewed with the patient prior to PEP prescription. If pre-existing HIV infection is likely, this information should be integrated into the risk-benefit assessment when the patient is deciding about using PEP. In

addition, if the likelihood of pre-existing HIV infection is high, a three-drug regimen should be considered.

### ***Who Should Not be Offered PEP?***

PEP is not indicated for perceived exposures of negligible or no conceivable risk (e.g., kissing, oral-anal contact, mutual masturbation without skin breakdown, bites not involving blood, cunnilingus not involving blood exposure, unprotected receptive oral intercourse without ejaculation [although pre-ejaculate in the presence of oral pathology may carry some risk], unprotected insertive oral sex, etc.). PEP is also not indicated for high-risk behaviors with a person of extremely low likelihood of being HIV infected. Clinicians should be willing to decline requests for PEP and provide supportive counseling and referrals in these situations. In some situations (e.g., a needle stick from a discarded syringe) the risk is simply not known, and individual judgment must be used.

### **Children and Adolescents**

These guidelines do not specifically address the special needs of children and adolescents.

For more information, please refer to:

Havens, P.L. and the Committee on Pediatric AIDS. Post-Exposure Prophylaxis in Children and Adolescents for Non-Occupational Exposure to Human Immunodeficiency Virus. *Pediatrics*, 2003 June;111(6): 1475 – 1489.

Merchant, R.C. and Keshavarz, R. Human Immunodeficiency Virus Post-Exposure Prophylaxis for Adolescents and Children. *Pediatrics*, 2001 Aug;108(2):E38 [68].

AAP 2000 Red Book: Report of the Committee on Infectious Diseases, 25<sup>th</sup> Edition, American Academy of Pediatrics.

### **Pregnancy**

Pregnant women can receive PEP but should not be given Efavirenz or didanosine.

For more information about antiretroviral use in pregnancy, refer to the Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the United States at:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/00053202.htm>.

### **Other Community Exposures**

This document does not address in detail other community exposures, e.g., injuries from discarded needles, non-health care worker exposures, assaults, etc. However, the

same general principles outlined in this document can reasonably be applied to assess the likelihood of acquiring HIV from such exposures, and thus the potential utility of PEP. If a potentially infectious body fluid (e.g., blood or blood products, genital secretions, peritoneal, pleural or cerebrospinal fluids but NOT saliva, tears, or sweat) was in contact with a mucous membrane (e.g., eye, oral, nasal, or genital mucosa) or non-intact skin (punctured, cut or substantially abraded), HIV infection is possible and consideration of PEP is warranted.

Although HIV cannot survive in dried blood or body fluids, it can survive in syringes for up to 30 days in some circumstances [1-3]. There are no reported cases of transmission from this route of exposure. It is a frequent exposure type, so if transmission were possible, it would have been likely to have been reported. In addition, there is no data on medication toxicities in HIV-negative children or children taking other medications. In conclusion, PEP use should be discouraged, but not refused, following discarded needle exposures.

For further discussion regarding injuries from discarded needles in the community, please refer to the AAP 2000 Red Book: Report of the Committee on Infectious Diseases, 25<sup>th</sup> Edition, American Academy of Pediatrics.

### **Timing of PEP Initiation**

Animal models of the natural history of HIV acquisition following exposure and of PEP interventions suggest that PEP will be more effective the sooner it is started [4, 5]. Clients and health care providers should strive to initiate PEP as early as possible after the exposure. After initial telephone assessment of HIV risk and explanation of the risks and benefits of PEP, an initial prescription can be called in to a local pharmacy to last until the client can be seen and evaluated in person, preferably within three days.

A 72-hour time limit for the initiation of PEP is reasonable given the evidence suggesting that PEP is not effective if initiated more than 72 hours post-exposure in animal models, and our understanding of the timing of the establishment of infection following exposure. The risks of providing PEP after it is likely to be effective in preventing transmission include: 1) the development of drug resistance if a two-drug regimen is used and it is not fully suppressive; 2) the risk of further development of resistance if resistant virus was transmitted; and 3) the emotional difficulty patients may have discontinuing medication once it has been started if they do become HIV infected.

There is no human evidence that suggests that PEP alters the natural history of breakthrough infections.

## **Medications for PEP**

### ***Length of Therapy and Amount Dispensed***

The total PEP treatment course is 28 days. PEP should not be provided for fewer than 28 days unless: 1) the potential exposure source is determined to be HIV uninfected; 2) the exposed individual is determined to be HIV infected; 3) the exposed individual changes his or her mind about PEP after reevaluation of the risks and benefits; or 4) there are intolerable side effects and no alternatives are available. A shorter course should not be considered potentially effective at this time.

Individual health care providers and systems should determine a schedule for dispensing PEP medications. Dispensing the entire 28-day course at once may result in wasted medications should side effects warrant medication changes or if the client elects to discontinue PEP. Dispensing an initial week supply of medications and making a follow-up appointment for the remainder will allow staff to assess symptoms and provide additional risk-reduction counseling when the client may still be in a highly motivated and receptive state of mind. This is a convenient schedule when standard HIV testing is used as the second set of medications can be provided at the post-test visit.

### ***Considering Two versus Three Antiretroviral Agents***

There is no consensus among experts about whether two or three antiretroviral drugs should be used for PEP. Arguments for two drugs include the following: 1) the inoculum of virus is small following non-occupational exposure compared with the amount of virus requiring potent antiretroviral therapy for full suppression in an HIV-infected individual; 2) single agent PEP resulted in an 81 percent reduction in the risk of HIV infection in a study of occupational exposures; 3) increased side effects and/or more difficult dosing schedules may result in decreased adherence; and 4) there is a significant cost differential when a third drug is added. Routine three-drug regimens are advocated by those who value the increased antiviral potency.

### ***Initial Medication Choices and When to Consult an Expert***

In the absence of information about the exposure source's antiretroviral history, or if the exposure source is naive to antiretroviral medication, the preferred double nucleoside analogue combination regimen is Combivir (ZDV + lamivudine), one pill twice a day.

Alternative nucleoside analogue combinations include stavudine (40 mg for patients weighing greater than 60 kg and 20 mg for those weighing less than 60 kg, one pill twice a day) or tenofovir, 300 mg once a day, in combination with lamivudine 150 mg twice a day or 300 mg once a day or emtricitabine 300 mg a day. A fixed dose combination pill containing tenofovir and emtricitabine, called Truvada, is available for once daily dosing. Abacavir and didanosine should be avoided unless resistance considerations outweigh potential toxicity.

If the exposure source's medication and/or drug resistance history is accessible, health care providers without expertise in antiretroviral resistance should access expert antiretroviral resistance consultation immediately. If local consultation is not available, call the National HIV Telephone Consultation Service at (800) 933-3413. The hours are: 6 a.m. to 5 p.m., PST, Monday - Friday (*for health care providers only*). Please consider academic hospital infectious disease consultation after hours. PEP medication initiation should not be delayed by more than approximately two to four hours while accessing pertinent information and consultation; combivir or an alternative two-nucleoside regimen should be initiated if a delay of greater than two to four hours is unavoidable. The medication regimen can be changed once this information is available.

When resistance characteristics make it difficult to construct a potent two-nucleoside regimen, a protease inhibitor or Efavirenz 600 mg at bedtime (qHS) can be added to the regimen. The recommended first-line protease inhibitor in this circumstance is lopinavir/ritonavir 133/33 mg (Kaletra), three pills twice a day. Alternative protease inhibitors include nelfinavir 1,250 mg twice a day (bid), indinavir, atazanavir, fosamprenavir, and others. Saquinavir is not a good choice due to pill burden and, with Invirase, absorption issues. If one of these agents is prescribed by a health care provider without expertise in antiretroviral drug management, expert consultation regarding dosing and side effects should be obtained. Drug interactions are also important with these agents. Review of all medications is important if a protease inhibitor or efavirenz are prescribed. Full course nevirapine is contraindicated for PEP.

Some health care providers will elect to use a third drug even when drug resistance is not suspected. In such circumstances, a three-drug regimen should only be considered following a very high-risk exposure with a known HIV-infected exposure source.

### ***Managing Side Effects, Including Medication Changes***

Patients should be given information about how to get medical assistance in the case of side effects. Common side effects seen with Combivir include nausea, fatigue, and headaches. Since Combivir has not been studied in a randomized trial of PEP, it is not clear how much these symptoms are a result of medication toxicity and how much they result from the emotional impact of the situation. Taking the pills with food often reduces nausea. Anti-emetics and analgesics can be prescribed as indicated; there are no important drug interactions with the nucleoside analogues. In some cases, PEP regimen will need to be modified. Combivir can be replaced with stavudine or tenofovir in combination with lamivudine.

### ***Missed Doses and Adherence Counseling***

Adherence counseling should be provided to all patients. Patients should be instructed to take a missed dose if it is recognized within approximately six hours of when the dose was scheduled for a bid medication, or 12 hours for a once a day (qD) medication. If

three or more days of medication are missed consecutively, the patient should be advised to discontinue PEP medication course.

### ***Post-Coital Contraception***

Post-coital contraception should be offered when indicated. In order to reduce the cumulative nausea effect of these medications, it is suggested that the post-coital contraceptive be delayed for at least one hour after the initial dose of Combivir. Pre-medicating with an anti-emetic is an option.

## **HIV Counseling and Testing**

### ***Rapid and Standard Testing***

HIV testing should be provided as is routine in the health care setting, using either rapid or standard testing. Patients seeking PEP are likely to fall into a high-risk category for previous HIV infection. In this setting, the positive rapid test has a very high positive predictive value and thus deferring PEP in individuals with a positive result is reasonable. Individuals testing positive on a rapid test should, however, be given the option of initiating PEP pending the results of the confirmatory test. In this case, a three-drug regimen should be used.

### ***HIV Testing for the Exposure Source***

HIV testing of the source of exposure should be encouraged. If an exposure source tests HIV-negative, PEP should be deferred or discontinued unless there is a very high likelihood of pre-seroconversion acute HIV infection.

### ***Timing of Initial and Follow-Up Testing***

An HIV antibody test should be obtained upon presentation for PEP. If PEP medications are provided by telephone prior to an in-person appointment, no more than three to four days of medication should be provided prior to HIV antibody testing. Repeat testing should be encouraged at two to three and six months following the exposure.

## **Mental Health and Substance Abuse Referrals**

Mental health and substance abuse problems may contribute significantly to the risk of subsequent exposures. Thus, PEP should be provided together with services that address the ongoing needs of clients regarding HIV risk behaviors. Health care providers should be aware of local resources for mental health care and substance abuse treatment for individuals presenting for PEP. Primary care referrals should also be available when indicated.

## **Other Laboratory Testing**

### ***Routine Testing for Toxicity***

Routine baseline and follow-up laboratory studies to assess for toxicity are not indicated unless there is a specific clinical concern based upon medical history and/or signs and symptoms.

### ***HIV RNA Testing***

HIV RNA testing should not be used to diagnose HIV infection in the absence of signs or symptoms suggestive of HIV seroconversion.

### ***Evaluation of Acute or Primary HIV Infection***

Patients with signs or symptoms concerning for acute HIV infection should be referred for expert assessment when PEP is provided outside such an expert clinical context. Given the nonspecific nature of the signs and symptoms associated with acute HIV infection, the threshold for referral should be low. Signs and symptoms seen in individuals with acute HIV infection can include: low- or high-grade fever, pharyngitis, oral candidiasis, oral or genital ulcers, lymphadenopathy, a macular rash above the groin, diarrhea, abdominal pain, myalgias, arthralgias, headache, stiff neck, or photophobia starting more than three days after a potential exposure to HIV. Note that many of these signs and symptoms are nonspecific. Laboratory findings often seen in acute HIV infection include lymphocytopenia, mild-to-moderate thrombocytopenia, and mild transaminitis.

### ***STD and Hepatitis Screening, Treatment, and Vaccination***

When possible, patients presenting for PEP should be screened for urethral, rectal and pharyngeal gonorrhea, and chlamydia based upon their sexual history, as well as for syphilis. When possible, they should also be screened for hepatitis B and C infection. Vaccination against hepatitis A and B, or referrals for vaccination, should be provided as indicated. Patients testing positive for hepatitis C antibodies or hepatitis B surface antigen should be referred for primary care.

### ***Pregnancy Testing***

All women of child-bearing potential should receive pregnancy testing. If the presenting exposure is vaginal, they should be advised to return for repeat testing if their menstrual cycle is delayed. Pregnant women can receive PEP but should not be given:  
1) Efavirenz or 2) didanosine plus stavudine.

For more information about antiretroviral use in pregnancy, refer to the Public Health Service Task Force Recommendations for the Use of Antiretroviral Drugs in Pregnant Women Infected with HIV-1 for Maternal Health and for Reducing Perinatal HIV-1 Transmission in the U.S. at: <http://www.cdc.gov/mmwr/preview/mmwrhtml/00053202.htm>

## **Clinical Infrastructure Considerations**

When occupational PEP was first integrated into the health care system, significant resources were required in order to provide information to exposed individuals about the resources available to them, to educate health care providers to develop the expertise required to provide the service, to develop systems to provide rapid access to medications, and to provide follow-up services. Similar resources will be required in the non-occupational setting. Health care provider training regarding PEP is available (see Clinician Training Resources).

Unless a specific system is in place to respond to requests for PEP, all health care systems will face the challenge of responding rapidly to this need in the context of a busy work environment. Triage decisions and staff training are challenging, particularly when PEP requests are infrequent. Ideally, health care providers and systems in local communities should work together to identify a single or multiple sites where comprehensive PEP services will be provided. Providing such services requires significant human resources. Once such a site or sites are identified, likely sources of entry (e.g., emergency departments, urgent care centers, HIV clinics, public health clinics, etc.) should be notified about how to make referrals. In many cases, initial assessment and treatment should be provided at the point of entry, with referral for comprehensive and ongoing care to the identified site or sites that provide PEP services within a day or so.

### ***Emergency Departments and Urgent Care Clinics***

Emergency departments and urgent care clinics should work with local public health, STD, and/or HIV clinics to establish systems for the initial assessment and prescription of PEP followed by rapid access (preferably the same or next day, always within three to four days) to a provider for HIV counseling and testing and the provision of the remainder of the PEP course. Note that challenging triage decisions will need to be made in order to initiate PEP within a reasonable timeframe (e.g., no longer than two to four hours from presentation).

### ***Health Department STD Clinics***

STD clinics are ideally suited to provide PEP within a comprehensive assessment and risk-reduction program. The main limitation of many STD clinics is the lack of experience with antiretroviral drug resistance issues. When patients present with exposure sources with known antiretroviral medication histories, clinicians in these settings should seek expert consultation with local colleagues with expertise in antiretroviral resistance or through the National HIV Telephone Consultation Service at (800) 933-3413. The hours are: 6 a.m.–5 p.m., PST, Monday-Friday. <http://www.ucsf.edu/hivcntr/Warmline/index.html>. *Note that this service is available for health care providers only.*

### ***HIV Specialty Care Clinics***

Clinicians in HIV clinics will need to integrate a number of resources that they may not normally have (e.g., HIV counseling and testing, routine STD testing, hepatitis immunizations, etc.) in order to provide comprehensive PEP services in this setting. Staff requiring training and additional human resources are often necessary to provide comprehensive services.

### **Clinician Training Resources**

The AIDS Education and Training Centers (AETC) Program of the Ryan White CARE Act supports 11 regional centers (and more than 130 associated sites) that conduct multidisciplinary education and training programs for health care providers treating persons with and at risk for HIV/AIDS. AETC programs are administered by the Health Resources and Services Administration (HRSA), HIV/AIDS Bureau. AETC's focus is on training clinicians in primary health care (physicians, physician assistants, nurses, dentists, pharmacists). Training activities are based upon assessed local needs. Emphasis is placed on interactive, hands-on training and clinical consultation. Below are AETCs in California. Clinicians should call for training about PEP as well as other HIV-related topics.

#### **Pacific AETC**

Department of Family and Community Medicine, University of California, San Francisco

*Address:*

74 New Montgomery Street, Suite 600

San Francisco, CA 94105-3444

*Phone:* (415) 597-8198

*Fax:* (415) 597-9386

*Web site:* <http://www.ucsf.edu/paetc>

*Newsletter:* NewsBrief

#### **San Joaquin Valley AETC**

San Joaquin Valley Health Consortium

*Address:*

2109 West Bullard Avenue, Suite 149

Fresno, CA 93711

*Phone:* (559) 446-2323, ext. 4

*Fax:* (559) 446-2327

*Web site:* <http://www.sjvhc.org/programs/sjvaetc.htm>

*Contacts:*

Mary C. Wallace, Director

*E-mail:* [maryw@sjvhc.org](mailto:maryw@sjvhc.org)

Andres Alba, Program Manager

*E-mail:* [andya@sjvhc.org](mailto:andya@sjvhc.org)

**University of Southern California AETC**

Keck School of Medicine, University of Southern California (USC)

*Address:*

1420 San Pablo Street, PMB B205

Los Angeles, CA 90089-9049

*Phone:* (323) 442-1846

*Fax:* (323) 442-1843

*Web site:* <http://www.paetc.com>

AETC at USC also maintains the HIV Tools web site at: <http://hivtools.com/>

*Contacts:*

Jerry D. Gates, Ph.D., Director

*E-mail:* [jd gates@hsc.usc.edu](mailto:jd gates@hsc.usc.edu)

Sue A. Lemme, M.A., Co-Director

*E-mail:* [lemme@hsc.usc.edu](mailto:lemme@hsc.usc.edu)

**University of California, Los Angeles AETC**

Center for Health Promotion and Disease Prevention, University of California, Los Angeles

*Address:*

10833 LeConte Avenue, CHS, Room 61-236

Los Angeles, CA 9005-1772

*Phone:* (310) 794-7821

*Fax:* (310) 206-5717

*Contacts:*

Tom Donohoe, M.B.A.

Principal Investigator/Director

*E-mail:* [donohoe@ucla.edu](mailto:donohoe@ucla.edu)

**Drew University AETC**

Charles R. Drew University of Medicine and Science

*Address:*

1731 East 120th Street, MP No. 11

Los Angeles, CA 90059

*Phone:* (310) 668-4758

*Fax:* (310) 763-8929

*Contacts:*

Allen S. Funnyé, M.D., Director

*E-mail:* [alfunnye@cdrewu.edu](mailto:alfunnye@cdrewu.edu)

Nanette Marchand, Program Administrator

*E-mail:* [mamarcha@cdrewu.edu](mailto:mamarcha@cdrewu.edu)

**East Bay AETC**

Alameda County Medical Center HIV Services

*Address:*

470 27th Street

Oakland, CA 97612

*Phone:* (510) 437-5172

*Fax:* (510) 271-4366

*Contacts:*

Kathleen A. Clanon, M.D., F.A.C.P., Director

*E-mail:* [kclanon@ACMedCtr.org](mailto:kclanon@ACMedCtr.org)

Mario Ruberte, Office Manager

*E-mail:* [mruberte@ACMedCtr.org](mailto:mruberte@ACMedCtr.org)

**University of California, Irvine AETC**

University of California, Irvine

*Address:*

101 City Drive South, Route 81, Building 53

Orange, CA 92868

*Phone:* (714) 456-5134

*Fax:* (714) 456-8325

*Contacts:*

Jeremiah Tilles, M.D., Director

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**University of California, Davis AETC**

University of California, Davis

*Address:*

4150 V Street, PSSB 3100

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**University of California, San Diego AETC**

University of California, San Diego

*Address:*

200 West Arbor Drive

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*Phone:* (619) 543-2415

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Chris Mathews, M.D., Director

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**University of California, San Francisco AETC**

University of California, San Francisco, Department of Family and Community  
Medicine at San Francisco General Hospital

*Address:*

Box 1365

San Francisco, CA 94143-1365

*Phone:* (415) 476-7059

*Fax:* (415) 476-3454

*Web site:* <http://www.ucsf.edu/sfaetc>

*Contacts:*

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Robert Teague, M.S.S.W., Training Director

*E-mail:* [bteague@itsa.ucsf.edu](mailto:bteague@itsa.ucsf.edu)

**San Jose AETC**

*Address:*

2400 Moorpark Avenue, Suite 205

San Jose, CA 95128

*Phone:* (408) 881-0230

*Fax:* (408) 881-0239

*Contacts:*

Esperanza Garcia Walters, R.N., M.P.H., Director

*E-mail:* [espwalters@aol.com](mailto:espwalters@aol.com)

Jennifer Shockey, Program Coordinator

*E-mail:* [jenhetc@aol.com](mailto:jenhetc@aol.com)

**North Coast Area AETC**

Sonoma County Academic Foundation for Excellence in Medicine

*Address:*

3324 Chanate Road

Santa Rosa, CA 95404

*Phone:* (707) 527-6223

*Fax:* (707) 576-4087

*Web site:* <http://members.aol.com/scafem/northcos.html>

*Contacts:*

Danielle Jones, Program Coordinator

Marshall Kubota, M.D., Site Director

## **Appendix A: Sample Patient Information Sheets**

### ***What is PEP and how does this program work?***

#### **What is PEP?**

PEP stands for post-exposure prophylaxis or post-exposure prevention. It is a program meant to help people who may have been exposed to HIV through sex or injection drug use in the past 72 hours to try to prevent HIV infection. The program includes HIV testing, a 28-day course of anti-HIV medications, and counseling and referrals to help people stay safe and HIV negative in the future.

#### **How risky was my exposure?**

It is hard to know exactly what the chance of becoming HIV infected (HIV positive) is from a single exposure to HIV. The information we have comes from research studies of people who were HIV negative and then became HIV positive. Even though the average risk of infection from one exposure is relatively small, there is no way to know the actual risk of any specific exposure. Unfortunately, people do get HIV from a single episode of unprotected sex or shared injection drug use equipment.

Average risks for a single exposure are approximately: receptive anal intercourse 1-3 percent; insertive anal intercourse 0.1–1 percent (1 of 1,000 to 1 of 100); receptive vaginal intercourse (the woman) 0.1–1 percent (1 of 1,000 to 1 of 100); insertive vaginal intercourse (the man); and, receptive oral sex with ejaculation almost zero, although it can happen. These numbers are very small, but health care workers who get a needle stick have a risk of 0.3 percent (3 of 1,000) of getting infected, and PEP is recommended for them. For those who get blood splashed in the eye or mouth, PEP is offered but not recommended. The risk from that kind of exposure is about 0.03 percent (3 of 10,000).

#### **What do we know about the effectiveness of PEP medications?**

There are no studies in people who have had sexual or injection drug use exposures to HIV, so we do not know for sure if PEP will work in these cases. There are some related situations where it has been effective. For health care workers who have had a needle stick injury, using AZT after the incident reduced the risk of getting HIV infection by about 80 percent. Babies whose mothers took AZT while they were pregnant were about two-thirds less likely to get HIV. Even babies whose mothers did not take any medicines, but the babies did, were less likely to become infected. Some tests in animals have shown good effect from these medications. It looks like the best effect occurs when the medicines are started as soon as possible. There is likely to be no benefit to using PEP medications if the exposure happened more than 72 hours before.

### **How else can I stay HIV negative?**

Since the chance of getting HIV from one exposure is relatively low, the most important thing you can do is to avoid being exposed again. Each time you have unprotected sex or share needles with someone who may have HIV infection, it is like playing a game of Russian Roulette. It is just a matter of time before luck runs out, and you become infected.

### **How does this program work? [Modify per local program]**

The first time we see you, we will ask you questions to make sure you might benefit from PEP. We will then talk to you about HIV testing, and about what was going on for you when you got exposed. A health care provider (doctor, nurse practitioner, or physician assistant) will talk to you about your medical history, examine you, and recommend specific medications. We will ask you questions about HIV medicines your partner has used to help us decide which medicines to recommend for you. We will give you a prescription to last until your next appointment, which will be in the next ten days. Over the next week to ten days, you will need to follow up with the HIV counselor to get your HIV test results and talk more about staying safe, and with a health care provider who specializes in PEP to make sure you are taking your medication correctly and tolerating them well. That health care provider will review all your other blood and urine test results with you (we will test you for other sexually transmitted diseases and hepatitis) and will give you a prescription for the rest of the 28 days of medications. You may also be referred to see our social worker so you can get more counseling or other referrals that might help you to stay safe and HIV negative. If you need or want to, you can see the social worker or health care provider again.

We would like you to come back to have another HIV test in two to three months and again in six months. We want to make sure you have stayed HIV negative, and to offer you medical care and support if you become HIV positive.

### **What other resources are available to me? [Modify per local program]**

We have a number of counseling, substance use, mental health, and other resource referrals. Please let us know if there is any other way we can help you. Also, if you do not already have a health care provider, we can get you a regular, primary provider.

### **If You Have Questions:**

To schedule or reschedule an appointment, call the clinic at [Modify per local program].

For questions or problems related to this program or your medicines, call [Modify per local program].

For general information, call the California AIDS Hotline at: (800) 367-2437.

## **Combivir™ Information Sheet**

### **What is PEP?**

PEP is medication that helps to prevent HIV infection after sexual or injection drug use exposures. It stands for post-exposure prophylaxis. “Post-Exposure” means after a possible exposure to HIV and “prophylaxis” means medicines that prevent infection.

### **Does PEP prevent people from getting HIV after being exposed to HIV?**

PEP *may* be helpful in preventing people from getting HIV after these exposures, but we do not know for sure.

### **Which PEP medication will I be taking?**

PEP medication you will be taking is called Combivir. Combivir is a combination pill containing two medicines, AZT and 3TC.

### **How should I take my medication?**

Combivir may be taken with or without food, but probably causes less upset stomach if it is taken with food. One pill is taken twice a day, in the morning and in the evening, for 28 days. Be sure to drink plenty of fluids with the pills.

### **Why is it important to take my medications correctly?**

The medication must be in the blood stream for it to work to prevent HIV infection. Also, if the medication does not work to prevent HIV infection, drug resistance might develop if the medication is not taken correctly. Drug resistance means that HIV is able to overcome a drug that was at one time working well to keep it from spreading. HIV can develop resistance to PEP medications when they are used at doses lower than the recommended dose, or when doses are skipped. That is why it is especially important to take these medications correctly.

### **What are the possible side effects of Combivir?**

The most common side effects are fatigue or tiredness, nausea, and headache. About half of people who take this medicine might have one or more of these symptoms for a few days. They usually go away on their own. It is often hard to know if these symptoms are caused by the medicine or by being upset and worried, which is normal. We can help you treat these symptoms if they are bothering you. Other unusual side effects may include blood test abnormalities of the red blood cells (anemia, can make you feel weak or out of breath), the white blood cells (that fight infections) or the liver. It would be very rare for these to happen with just 28 days of medication, and if they do, they will almost always get better once the medicine is stopped.

**Does Combivir interact with other drugs?**

It does not interact with any common medications.

**What should I do if I have problems with the medications or questions?**

With the start of PEP, there may be temporary side effects such as headache, fatigue, or a general sense of feeling ill. These side effects are likely to get better or even disappear over time. If the side effects are severe report immediately to the emergency department. If they are not severe, please call [Modify per local program].

**Appendix B: Sample Scripts of Key Issues to Discuss with Clients**

Note that these scripts are intended for use by health care providers as they contain technical information.

1. *Your Risk of Acquiring HIV.*
2. *Does PEP Work? What Do We Know and Not Know?*
3. *Medication Side Effects.*
4. *Baseline and Follow-Up HIV Testing.*
5. *What If I Am Already HIV Positive?*

**Sample Script 1: Your Risk of Acquiring HIV**

[This sample script is general in its content and can be tailored for the individual client and their risk factors.

Additional factors that will increase the risk of acquiring HIV infection include sexually transmitted diseases in either partner and cervical ectopy in adolescent girls. These factors should be discussed if relevant.]

In order to make an informed decision about whether or not to use PEP medications, it is important for you to make an assessment of the risks and benefits. The benefits of using PEP, assuming that PEP works to prevent HIV infection, are directly proportional to the risk of acquiring HIV infection from the exposure that you had. Your risk of acquiring HIV infection from the exposure that you had is related to two key factors: first, the type of sex that you had, and second is the likelihood that the person that you had sex with has HIV infection.

Let's talk about **the risk of acquiring HIV from different types of sex**. First, it is important to understand that there are limitations to the information that is available to help us understand the risk of acquiring HIV from a single episode of unprotected sex. These data come from where HIV-negative people are followed over time and tested, usually every six months, for new HIV infection. Questionnaires are used to record the number of episodes of unprotected sex that the person had in the interval between HIV testing. Mathematical models are applied to try to predict the risk of acquiring HIV infection from a single episode of unprotected sex.

Based on these types of studies we believe that the risk of acquiring HIV infection from a single episode of unprotected receptive anal intercourse is somewhere between about 1 and 5 percent (1 to 5 in 100), the risk of acquiring HIV infection from a single episode of insertive anal sex as well as receptive vaginal sex is less than 0.1 (1 of 1,000) to less than 1 percent (1 of 100), and the risk of acquiring HIV infection from a single episode of insertive vaginal sex is less than 0.1 percent (1 of 1,000). The risk of acquiring HIV infection from oral sex with ejaculation is confusing. Although statistically it appears that there is no risk, there are numerous case reports that document transmission of HIV infection through this route. Many sexual assaults will involve more than one perpetrator and more than one type of sexual activity. Thus, the risk of acquiring HIV infection from specific types of sexual activity during sexual assault must be evaluated in this context. In addition, the likelihood of trauma associated with sexual assault is significant and there is no information to help us understand the increased risk associated with this trauma.

The second factor involved in determining the risk of getting HIV infection is **the likelihood that the person you had sex with has HIV infection**. It is important to understand the local patterns and rates of HIV infection where your exposure occurred. In general in California, people considered to be at high risk of having HIV infection include MSM, past or present injection drug users, and sex partners of these two

groups. If your exposure happened in another country, or even in another part of the United States, other groups of people might also be at high risk of having HIV infection (for example, sex workers and young African American and Latino men and women).

Now that we have discussed the type of sex you had and the likelihood of the person you had sex with being HIV positive, you should be in a better position to assess your risk of acquiring HIV infection from this exposure. This will help you to make a decision about whether or not you want to accept the risks associated with PEP (discussed in script 3). But first... go to script 2 – Does PEP Work? What Do We Know and Not Know?

**Sample Script 2: Does PEP Work? What Do We Know and Not Know?**

When making a decision about whether or not to use PEP medications it is important to understand what is known and not known about whether PEP works, and how well it works in different circumstances. The first key point to understand is that there is no direct evidence that PEP works to prevent HIV infection when it is used following sexual exposures. However, there are **four related areas** where antiviral (or anti-HIV) medications have been used that all point in the direction suggesting that PEP should be at least partially effective in preventing HIV infection when used following sexual exposures. These include: 1) health care workers who have had needle stick injuries; 2) babies who have been born to HIV-positive mothers who did not receive any medications but the babies did; 3) animal models of intravenous and sexual exposures; and 4) and observational studies in humans following sexual exposures.

The only direct evidence that we have in adults that PEP is effective comes from **health care workers who have had needle sticks**. One study showed an 81 percent reduction in the risk of getting HIV infection in those health care workers who used AZT following their exposure as compared to those health care workers who did not use any medications.

Initial studies of the **prevention of mother-to-child transmission of HIV infection** in the United States included a combination of medications given during pregnancy, labor, and after the baby was born. The first published study demonstrated a two-thirds reduction in the likelihood of infants acquiring HIV infection using this strategy. At that time it was difficult to know whether the effect of the AZT was a pre-exposure or a post-exposure effect. Since then, we have learned that even those infants who received AZT or other medications within the first couple of days of life had a significant reduction in the likelihood of acquiring HIV infection compared to infants who did not receive any PEP.

The third area that supports the concept of PEP is **animal studies**. Some of these studies use intravenous virus. Other studies used oral and vaginal exposure models more similar to human sexual exposures. These studies showed differing degrees of efficacy of PEP.

Finally, there are several **observational studies** in the United States, Brazil, Australia, South Africa, and elsewhere that suggest that the new HIV infection rate among sexually exposed individuals who receive PEP is very low, and is often associated with late initiation or incomplete adherence to PEP.

**The bottom line is that we do not have direct evidence that PEP works following sexual exposure. But we do have a lot of information all pointing in the direction suggesting it may be partially effective.** We will probably never have direct evidence for two main reasons. The first is that many believe it is unethical to randomly assign half of exposed individuals to receive no treatment. Even if it were ethically possible to do this, the feasibility concerns are overwhelming. It would require thousands and

thousands of people in both arms of the study to be able to demonstrate a difference since the transmission rates are so low even without the use of PEP. This is similar to the challenges faced in a vaccine study. In addition to those challenges, sexual exposures tend not to be an isolated experience, thus adding a whole additional level of complexity to the interpretation of such a study.

**Sample Script 3: Medication Side Effects**

**It is important for you to understand the possible side effects** that you might experience from taking these medications before you make your decision about taking them.

**For Individuals Receiving AZT-Containing Regimens:**

About half of people will experience one or more of the following: fatigue (or tiredness), nausea, or headache. For most people these symptoms are relatively mild and improve within a few days. However, for some people the symptoms can be really bad. It is important for you to let us know if you have significant symptoms, or symptoms that are concerning to you, because we can make recommendations that might reduce these symptoms or possibly make changes in your medication regimen. Our goal is not for you to feel sick from these medications, so please do tell us if you are having problems! Sometimes it is complicated to try to understand how much these symptoms are related to the medication and how much they are related to the stress that you are probably experiencing following your possible exposure.

There are two more serious potential side effects that would be extremely unusual with 28 days of medication but that you need to be aware of BEFORE you take this medication. These include inflammation of the liver, which is called a drug induced hepatitis, and suppression of the bone marrow, which can cause decreases in your red or white blood cell count. A decrease in red blood cells is called anemia and can cause fatigue and shortness of breath. A decrease in white blood cells is called neutropenia and can make you more susceptible to certain kinds of infections. Both of these side effects would be extremely unusual with 28 days of medication, and we would expect that they would get better when the medications were stopped. However, it is important for you to understand that we cannot give you a 100 percent guarantee that you will not have serious side effects from these medications. There are no long-term side effects that have been described with a 28-day course of medications.

**For Individuals Receiving d4T-Containing Regimens:**

This medication rarely causes side effects when used for 28 days. The main side effect that you need to be aware of and that we need to watch for is numbness, tingling, or burning in the tips of the fingers and the tips of the toes. This is called peripheral neuropathy. If you experience this symptom for more than a day we want you to let us know. This is important because we can lower the dose of the medication and reduce the likelihood of this symptom continuing. The longer this symptom is present the more likely it is that it will not go away when the medications are stopped. So, it is very important for you to let us know if you are having numbness or tingling in the tips of your toes or fingers.

**For Individuals Receiving ddl-Containing Regimens:**

Common side effects include nausea and abdominal discomfort. It is critical that this medication be taken on an empty stomach (which is two hours after you last ate and one hour before you eat again). Take this medication with water only; not even juice is okay. There is one serious potential side effect with this medication called pancreatitis or inflammation of the pancreas. The pancreas is an organ that is located in the middle upper part of your abdomen. Pancreatitis can be very, very serious, leading to hospitalization, and even at times to death. You will need to weigh your risk of acquiring HIV infection against your risk of developing pancreatitis from ddl (e.g., Videx). Although this risk is very, very small it is of course very important.

**For Individuals Receiving Tenofovir-Containing Regimens:**

Common side effects include nausea and abdominal discomfort. Tenofovir can cause some problems with the kidneys, but this would be very unusual with a 28-day course. If you are using Videx with tenofovir, the dose of Videx must be reduced.

**For Individuals Receiving a Third Antiretroviral Agent:**

The specific side effects of that drug should be described.

**Sample Script 4: Baseline and Follow-Up HIV Testing**

**It is important to know if you are already HIV positive** before making a decision to use PEP medications, or as soon as possible after you start PEP. We will give you an HIV test at the time that you receive your initial PEP prescription or at your first follow-up visit if we only provide a starter pack. This first HIV test will not tell us anything about the current exposure that you just had. What it will tell us is if you are already HIV infected from a previous exposure. If you are already HIV positive, you will not be provided with PEP medications. This is because using 28 days of medication if you are already HIV positive will not give you any benefit. In fact, it could cause some harm, because your HIV could develop some resistance to these medications, making future treatment less effective. The results of your first HIV test will be available within [fill in minutes or days depending on your testing set-up]. We will provide you with your results as well as counseling about the meaning of your HIV test results.

**It is important that you receive follow-up HIV testing** after you complete your course of PEP medications, or even if you decide not to use PEP or if you stop your medications before you complete a full 28-day course. The follow-up HIV test will tell you whether you did get HIV infection from either your exposure or from another exposure in the previous few months. We will be able to refer you to services if you test HIV positive. We strongly recommend that you get a follow-up HIV test in two to three months, and again in six months following your exposure.

**Sample Script 5: What If I Am Already HIV Positive?**

If you are already HIV positive you will not be provided with PEP medications (or, if you have been started on PEP medications and your initial HIV test comes back positive we will ask you to discontinue taking those medications). This is because using 28 days of medication if you are already HIV positive will not provide you with any benefit. In fact, it could cause some harm, because your HIV could develop some resistance to these medications, making future treatment potentially less effective.

**In the case of a rapid HIV test:** It is very important to understand that a positive result on a rapid HIV test might not mean that the person is really HIV positive. The rapid test is very accurate but an initial positive test will need to be confirmed with a standard test. It will take [complete per your system] days for the second test to come back. You may choose to take PEP while you await the confirmatory test result.

**In the case of a standard test:** It will take [complete per your system] days for the test results to come back. If your HIV test is positive you will be asked to stop your PEP medications and you will be referred to services for people with HIV infection.

**Appendix C: Sample Clinical Progress Note**

This sample Progress Note is provided for adaptation by health care providers for use in their specific clinical setting. The sample contains the key elements of the history, examination, assessment, and plan required to responsibly provide PEP. It is not meant to be used as a data collection tool.

A note like this may be used at the initial point of care and then faxed to the follow-up provider with the patient's permission.

Additional information may be added to an adapted Progress Note, including vaccinations, follow-up of abnormal test results, etc.

Offering HIV Post-Exposure Prophylaxis (PEP) Following Non-Occupational Exposures

Date:   /   /      
 MM DD Y

AGE: \_\_\_\_\_ Gender:  F  M

EXPOSURE & HIV INFORMATION
<p><b>Date of Exposure:</b>  <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/></p> <p><b>Time of Exposure (range):</b>  <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/> - <input type="text"/> <input type="text"/> : <input type="text"/> <input type="text"/></p> <p><b>Hours Between Exposure &amp; PEP:</b> _____</p> <p><b>Exposure Description:</b>  <input type="checkbox"/> Receptive Vaginal <input type="checkbox"/> Receptive Anal  <input type="checkbox"/> Insertive Vaginal <input type="checkbox"/> Insertive Anal  <input type="checkbox"/> Receptive Oral with Ejaculation  <input type="checkbox"/> Other – Describe: _____</p> <p><b>Source HIV Status</b>  <input type="checkbox"/> Known Positive <input type="checkbox"/> Unknown</p> <p><b>Source ARV History:</b>  <input type="checkbox"/> None or unknown <input type="checkbox"/> Yes – Describe: _____</p> <p><b>Date last HIV Test:</b> <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> / <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/></p> <p><b>Result last HIV Test:</b> <input type="checkbox"/> Positive <input type="checkbox"/> Negative</p> <p><b>Other Exposures in past 6 months (# and type):</b>                  _____                  _____</p>

SYMPTOMS
<p><b>Sx of Possible Acute HIV (Include duration):</b>                  _____                  _____                  _____</p> <p><b>Referred for evaluation:</b> <input type="checkbox"/> Yes <input type="checkbox"/> No</p>

Physical Assessment
<p><b>Thrush:</b> <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><b>LAN:</b> <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><b>KS</b> <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p><b>Other</b> _____                  _____</p>

Pregnancy Test Result
<p><input type="checkbox"/> Positive <input type="checkbox"/> Negative <input type="checkbox"/> NA</p>

Assessment and Plan
<p>Possible HIV Exposure Seeking PEP                  PEP Meds  <input type="checkbox"/> Combivir 1 po b.i.d. or <input type="checkbox"/> Other _____</p> <p><input type="checkbox"/> Reviewed with patient: Drug information sheet, adverse events, emergency phone numbers, medication adherence, use of alcohol.</p> <p><input type="checkbox"/> Follow-up appointment made</p> <p>Labs ordered: HIV test <input type="checkbox"/>, hepatitis serologies <input type="checkbox"/>, pregnancy test <input type="checkbox"/></p>

**Notes:**  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_  
 \_\_\_\_\_

MEDICAL HISTORY
<p><b>Pertinent Past Medical History:</b>                  _____                  _____</p> <p><b>Alcohol:</b> _____</p> <p><b>Drug Allergies:</b> <input type="checkbox"/> NKDA <u>or</u> <input type="checkbox"/> Yes:                  Specify: _____                  _____</p> <p><b>Current Meds:</b> _____</p>

Signature \_\_\_\_\_ Date \_\_\_\_\_

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