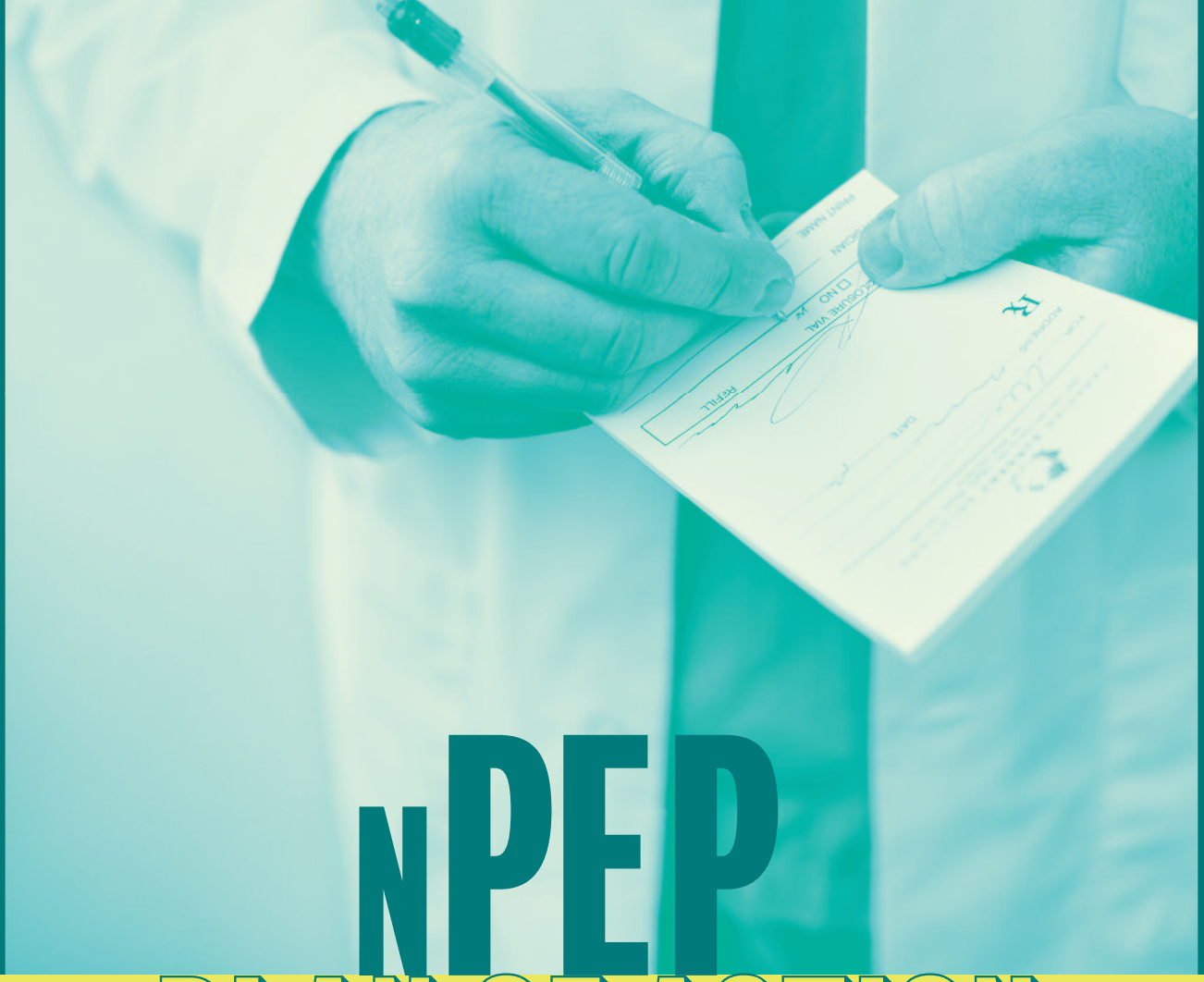

nPEP
PLAN OF ACTION

FOR HEALTH CARE PROVIDERS

Florida HEALTH
HIV/AIDS Prevention


nPEP

NON-OCCUPATIONAL POST-EXPOSURE PROPHYLAXIS (nPEP) PLAN OF ACTION TOOLKIT FOR HEALTH CARE PROVIDERS

Prepared by the Florida Department of Health HIV/AIDS Section's Medical Team

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INTRODUCTION

IF YOU HAVE QUESTIONS REGARDING THE PROVISION OF nPEP, CONTACT THE CLINICIAN CONSULTATION CENTER PEPLINE, 1-888-448-4911, OR THE SOUTHEAST AIDS EDUCATION AND TRAINING CENTER:
NORTH FLORIDA SITE, (352) 273-7845
SOUTH FLORIDA SITE, (305) 582-2233

FOREWORD

This document contains key elements regarding Non-Occupational Post-Exposure Prophylaxis (nPEP) management. Frequent changes in standards of HIV prevention and care require that the guidelines be carefully reviewed by the medical team in your facility to ensure that they conform to acceptable local and current approaches. Medical prevention and treatment updates are posted frequently to several websites, including the websites at www.aidsinfo.nih.gov/ and www.cdc.gov/. It is recommended that every health care provider be familiar with all relevant guidelines.

This document is not intended to replace clinical research literature or current United States Public Health Service (USPHS) Guidelines, and may not include the full range of prevention and treatment options for all patients. If there are questions regarding the provision of nPEP, it is recommended that health care providers contact the Clinician Consultation Center PEPline at 1-888-448-4911.

PEP DEFINITION

Post-exposure Prophylaxis (PEP) is the provision of medications to prevent transmission of a disease or illness following an occupational or non-occupational exposure.

TWO TYPES OF PEP

Non-occupational PEP (nPEP) is taken when an individual is potentially exposed to HIV outside the workplace, for example, during episodes of unprotected sex or needle-sharing/injection drug use. Non-occupational exposure is any direct mucosal, percutaneous or intravenous contact with potentially infectious body fluids.

Occupational PEP (oPEP) is taken when an individual working in a health care setting is potentially exposed to products or material(s) that could be or are known to be infected with HIV.

This document presents a plan of action to enable health care providers to address nPEP, the use of HIV medication to reduce the risk of HIV infection after a possible exposure to HIV. Patients presenting for nPEP should be evaluated as soon as possible so treatment, if indicated, can be initiated within recommended timeframes. To be most effective, evidence suggests a 72-hour timeframe for the initiation of nPEP following possible HIV exposure. nPEP initiation should begin as soon as possible following the exposure.

CHILDREN AND ADOLESCENTS

These guidelines do not specifically address the special needs of children and adolescents. The American Academy of Pediatric's (AAP) guidance, *Postexposure Prophylaxis in Children and Adolescents for Nonoccupational Exposure to Human Immunodeficiency Virus* at http://pediatrics.aappublications.org/content/111/6/1475.

FOUR ACTION STEPS OF nPEP

1. EVALUATION 2. RISK ASSESSMENT 3. TREATMENT 4. REFERRAL, FOLLOW-UP AND MONITORING

1. EVALUATION

Evaluation of the exposed patient should be conducted with the highest level of confidentiality. HIV reporting should take place as required by state laws.

CIRCUMSTANCES OF EXPOSURE AND nPEP MANAGEMENT

The following circumstances of the exposure and nPEP management should be recorded in the medical record with details, including:

EXPOSURE: Date and time of exposure (is it within 72 hours)

EXPOSURE TYPE: Details of the exposure: type and amount of fluid or material and severity of exposure

INCIDENT: Details of the incident: where and how exposure occurred, exposure sites on body

SOURCE: Details about exposure source, if available
- HIV, hepatitis B and hepatitis C status
- If the source is HIV infected, determine the stage of disease, HIV viral load, current and previous antiretroviral therapy and antiretroviral resistance information.

PATIENT: Details about the exposed patient
- Hepatitis A and hepatitis B vaccination and vaccine-response status
- Other medical conditions, drug allergies and medications
- Pregnancy and breastfeeding status
- nPEP is not indicated for perceived exposures of negligible or no conceivable risk. Health care providers should be willing to decline requests for nPEP and provide supportive counseling and referrals in these situations.

2. RISK ASSESSMENT

The exposure should be evaluated for the potential to transmit HIV based on (1) the type of body substance involved, (2) the route and (3) HIV status of the source patient.

Decisions should be individualized, weighing the likelihood of transmission against the potential benefits and risks of treatment.

In sexual assault, the decision to initiate nPEP is based on whether a significant exposure has occurred rather than on the risk behavior of the alleged assailant.

If the patient is too distraught to engage in a discussion about and/or commitment to the drug regimen at the initial assessment, the health care provider should offer a first dose of the medication and make arrangements for a follow up within 24 hours to further discuss the indications for nPEP.

NATIONAL SEXUAL ASSAULT HOTLINE: 1-800-656-HOPE (4673)
OFFERS RAPE CRISIS CENTER SERVICES TO MITIGATE SEXUAL ASSAULT TRAUMA.

FLORIDA RAPE CRISIS HOTLINE: 1-888-956-7273

HIV STATUS ASSESSMENT

The likelihood of pre-existing HIV infection should be determined for all individuals presenting for nPEP. The following information should be obtained:

- Has the patient ever been tested, and if so, what was the date and result of their last HIV test?
- The number and types of unprotected exposures since the last HIV test. The likelihood of pre-existing HIV infection should be reviewed with the patient prior to nPEP prescription. If pre-existing HIV infection is likely, this information should be integrated into the risk-benefit assessment.

HIV TESTING OF SOURCE

If the source is available and consents, HIV testing should be completed using an HIV rapid test. If a rapid test is negative or nonreactive for the source, nPEP should be deferred unless there is a high index of suspicion that the source may be in the seronegative window period of infection. The seronegative window is up to three months unless 4th generation or newer technology is used, which reduces the window to 15 days on average following the time of exposure. If using a confirmatory test as a backup, nPEP can be discontinued if the result is negative for the source.

EVALUATE THE SOURCE ONLY IF KNOWN OR AVAILABLE

KNOWN HIV INFECTION	UNKNOWN HIV INFECTION
Obtain history of antiretroviral medication, recent viral load, CD4 cell count and date of results	**Obtain risk history and rapid HIV test (4th generation rapid or serum test preferred)**
Consider evaluation and testing for other sexually transmitted infections, including hepatitis B and hepatitis C	**Consider evaluation and testing for other sexually transmitted infections, including hepatitis B and hepatitis C**

Modified from www.hivguidelines.org.

The document, *Risk of HIV Transmission*, found at www.hivguidelines.org/pep-for-hiv-prevention/ occupational/#tab_1, outlines the probability of acquiring HIV from a known source as well as factors that may increase transmission risk. HIV transmission most frequently occurs during sexual or drug-use exposures; however, there are many factors that can influence transmission risk. The probability of transmission when the source person is in the acute and early stage of HIV infection (first six months) has been shown to be 8- to almost 12-fold higher than exposures that take place after the viral set point due to the presence of high HIV viral load levels. The presence of sexually transmitted infections (STIs) in either the source or exposed person also increases risk. Conversely, transmission risk has been shown to be significantly decreased in source persons who are receiving effective antiretroviral therapy (ART). Review the **CDC HIV Risk Reduction Tool** at www.cdc.gov/hivrisk/estimator.

Adapted from New York State Department of Health AIDS Institute's UPDATE: HIV Prophylaxis Following Non-Occupational Exposure (10-28-2014) at www.hivguidelines.org.

SEXUAL ASSAULT OR INTRAVENOUS DRUG USERS (IDU)

All exposures sustained during sexual assault should be considered at risk for HIV. nPEP should be considered in all cases of sexual assault, especially in cases where the assailant is unknown. It is reasonable to offer nPEP to patients who have been sexually assaulted by persons who are known to them, but whose sexual and injection drug use history is not known. Multiple other factors can be considered to determine the likelihood that the source of exposure is HIV infected.

For local service information in Florida, see the **Florida Council Against Sexual Violence**: www.fcasv.org/information/find-your-local-center or visit www.fcasv.org.

3. nPEP TREATMENT

ADULTS, PREGNANT WOMEN AND ADOLESCENTS AGED 13 YEARS AND OLDER, WITH NORMAL RENAL FUNCTION (CREATININE CLEARANCE ≥ 60 ML/MIN)

RECOMMENDED nPEP REGIMEN

TENOFOVIR DF 300 mg/*EMTRICITABINE 200 mg fixed dose combination (FDC) (TRUVADA®) PO daily
with
RALTEGRAVIR (ISENTRESS®) 400 mg twice daily
or
DOLUTEGRAVIR (TIVICAY®) 50 mg once daily

Duration of therapy: 28-day course of nPEP is recommended.

*Lamivudine 300 mg PO daily may be substituted for emtricitabine. An FDC is available when tenofovir is used with emtricitabine.

ALTERNATIVE nPEP REGIMEN

TENOFOVIR DF 300 mg/*EMTRICITABINE 200 mg fixed dose combination (FDC) (TRUVADA®) once daily
with
DARUNAVIR 800 mg (as two, 400 mg tablets) (PREZISTA®) once daily
and
RITONAVIR 100 mg once daily

Duration of therapy: 28-day course of nPEP is recommended.

*Lamivudine 300 mg PO daily may be substituted for emtricitabine. An FDC is available when tenofovir is used with emtricitabine.

RENAL INSUFFICIENCY

The dosing of tenofovir and emtricitabine or lamivudine should be adjusted in patients with baseline creatinine clearance <50 mL/min. Tenofovir should be used with caution in exposed persons with renal insufficiency or who are taking concomitant nephrotoxic medications. Fixed-dose combinations should not be used in patients who need dose adjustment due to renal failure.

View complete guidleines at www.cdc.gov/hiv/pdf/programresources/cdc-hiv-npep-guidelines.pdf.

More about alternative nPEP regimens at nccc.ucsf.edu/wp-content/uploads/2014/04/CCC_PEP_Quick_Guide_Alternative_Regimen_and_Dosing_and_Toxicity_Tables.pdf.

PREGNANCY PEP OPTIONS

If PEP is started for a pregnant exposed person, the recommendation is to call the Clinician Consultation Center at (888) 448-8765 (24 hours, seven days a week) to speak with consultant on Perinatal HIV/AIDS for the most updated options related to pregnancy and breastfeeding.

PEP OPTIONS

Other PEP options may be considered in the event of intolerance, source patient with resistant virus, ARV access, or exposed person (EP) preference. In these instances, health care providers should seek expert consultation. The National HIV/AIDS Clinicians' Consultation Center is accessible at nccc.ucsf.edu/clinical-resources/pep-resources/pep-quick-guide/, or by calling 1-888-448-4911.

STD AND HEPATITIS TREATMENT AND VACCINATION

Based upon the 2015 CDC Treatment Guidelines, assessment for STDs may be deferred per the option of the treatment health care provider and patient. Many specialists recommend preventative therapy at initial examination because follow-up with patients can be difficult.

For STD treatment and screening guidelines, please see www.nycptc.org/x/STD_TreatmentTable_2015.pdf. For STD screening recommendations, review www.nycptc.org/x/STD_Screening_chart_2015.pdf.

Hepatitis:

- Post-exposure hepatitis B vaccination, without HBIG, should adequately protect against HBV infection.
- Hepatitis B vaccination should be administered to patients at the time of the initial examination if they have not been previously vaccinated.
- Follow-up doses of vaccine should be administered following recommendations by the Centers for Disease Controland Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP) at www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf.
- Hepatitis C testing

EMERGENCY CONTRACEPTION (EC)

EC should be offered if an exposure could result in pregnancy.

PREGNANCY TESTING

- All women of child-bearing potential should be tested for pregnancy.
- If the presenting exposure is vaginal, patient should return for repeat testing if her menstrual cycle is delayed.
- Pregnant women can receive nPEP but should not be given efavirenz or didanosine plus stavudine.
- For more information about antiretroviral use 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* at www.aidsinfo.nih.gov/guidelines/ or https://aidsinfo.nih.gov/contentfiles/lvguidelines/Peri_Recommendations.pdf.

PATIENTS WITH MULTIPLE EXPOSURES

Following a series of exposures, some individuals will present for nPEP both within and outside of the 72-hour nPEP treatment window. It is the decision of the health care provider to determine whether nPEP should or should not be offered in such circumstances.

STARTER PACK

A starter pack of the preferred regimen should be provided at the time of initial evaluation. A starter pack usually consists of a three- to five-day supply. Medications can be changed at follow up if appropriate based on source patient resistance (if available), efficacy data, toxicity, pill burden/ease of dosing, potential drug interactions, cost and pregnancy risk. Prophylactic antiemetic and antidiarrheal agents can be used if necessary for control of side effects.

LENGTH OF THERAPY AND AMOUNT DISPENSED

The total nPEP treatment is 28 days and should NOT be administered for less than 28 days unless:

- The source is determined to be uninfected via confirmatory HIV test.
- The exposed individual is determined to be HIV infected per confirmatory test.
- There are intolerable side effects and no alternative medications are available.

OR

- The exposed individual changes their mind about nPEP after re-examining the risks and benefits.
- The exposed individual's health care provider determines a customized schedule for dispensing nPEP.
- Three or more days of nPEP are missed consecutively, and the exposed individual is advised to discontinue the medication course.

HEALTH CARE PROVIDER CONSULTATION WITH A SPECIALIST IS RECOMMENDED

If consultation is not immediately available, nPEP should not be delayed; changes can be made as needed after nPEP has been initiated. If the source is found to be HIV negative or nonreactive, nPEP should be discontinued. Delaying nPEP therapy in order to obtain resistance test results (genotyping or phenotyping) for the purpose of selecting more specific therapy is not advised. Exposed persons are frequently unable to complete nPEP regimens due to side effects. Providing prophylactic symptom management can improve adherence.

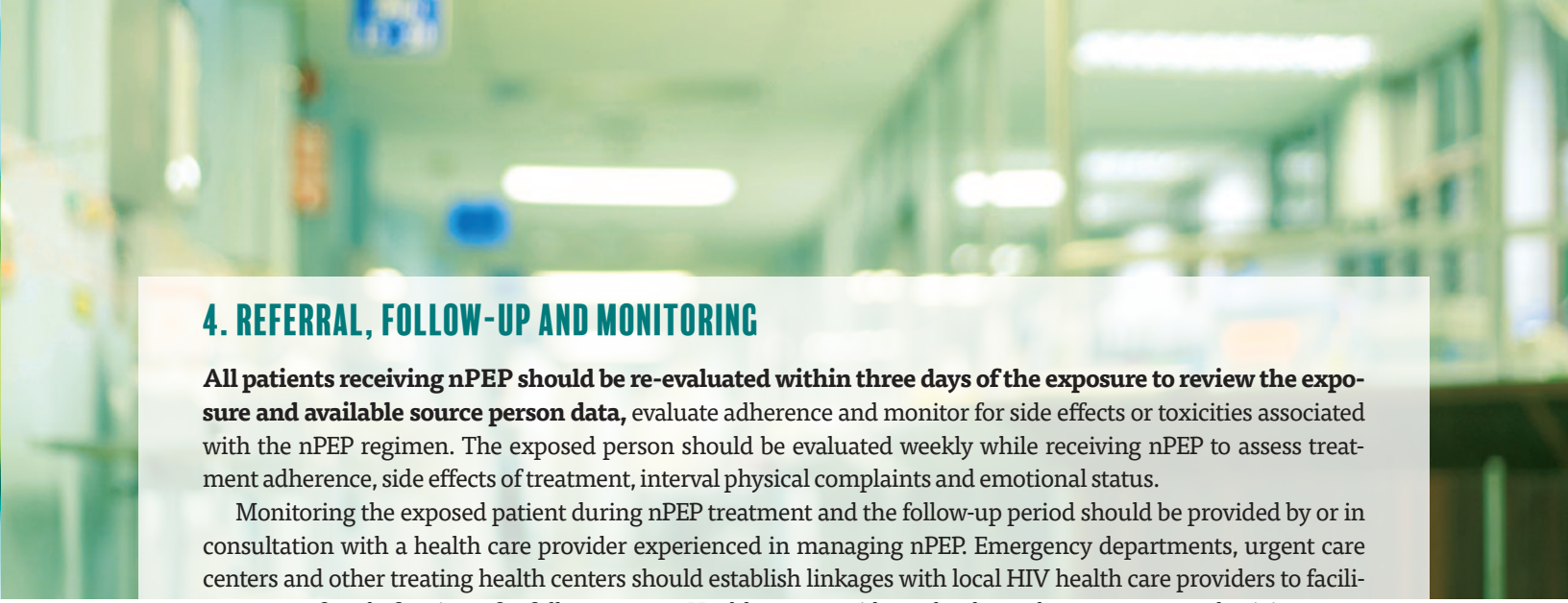
ADDITIONAL RESOURCES FOR HEALTH CARE PROVIDERS

NCCC nPEP Hotline: 1-888-448-4911

CDC HOTLINE: 1-800-232-4636

Southeast AIDS Education and Training Center: aidsetc.org/directory/regional/southeast-aids-education-and-training-center

Vanderbilt Comprehensive Care Clinic: mainline, (615) 875-7873 or (352) 273-7845; administrator's direct line, (305) 582-2233



4. REFERRAL, FOLLOW-UP AND MONITORING

All patients receiving nPEP should be re-evaluated within three days of the exposure to review the exposure and available source person data, evaluate adherence and monitor for side effects or toxicities associated with the nPEP regimen. The exposed person should be evaluated weekly while receiving nPEP to assess treatment adherence, side effects of treatment, interval physical complaints and emotional status.

Monitoring the exposed patient during nPEP treatment and the follow-up period should be provided by or in consultation with a health care provider experienced in managing nPEP. Emergency departments, urgent care centers and other treating health centers should establish linkages with local HIV health care providers to facilitate easy referral of patients for follow-up care. Health care providers who do not have access to a physician experienced in nPEP should use the HIV Clinician Consultation Center PEPline at 1-888-448-4911 for phone consultation. Hours of operation are: 9:00 a.m.–2:00 a.m. EST, seven days a week.

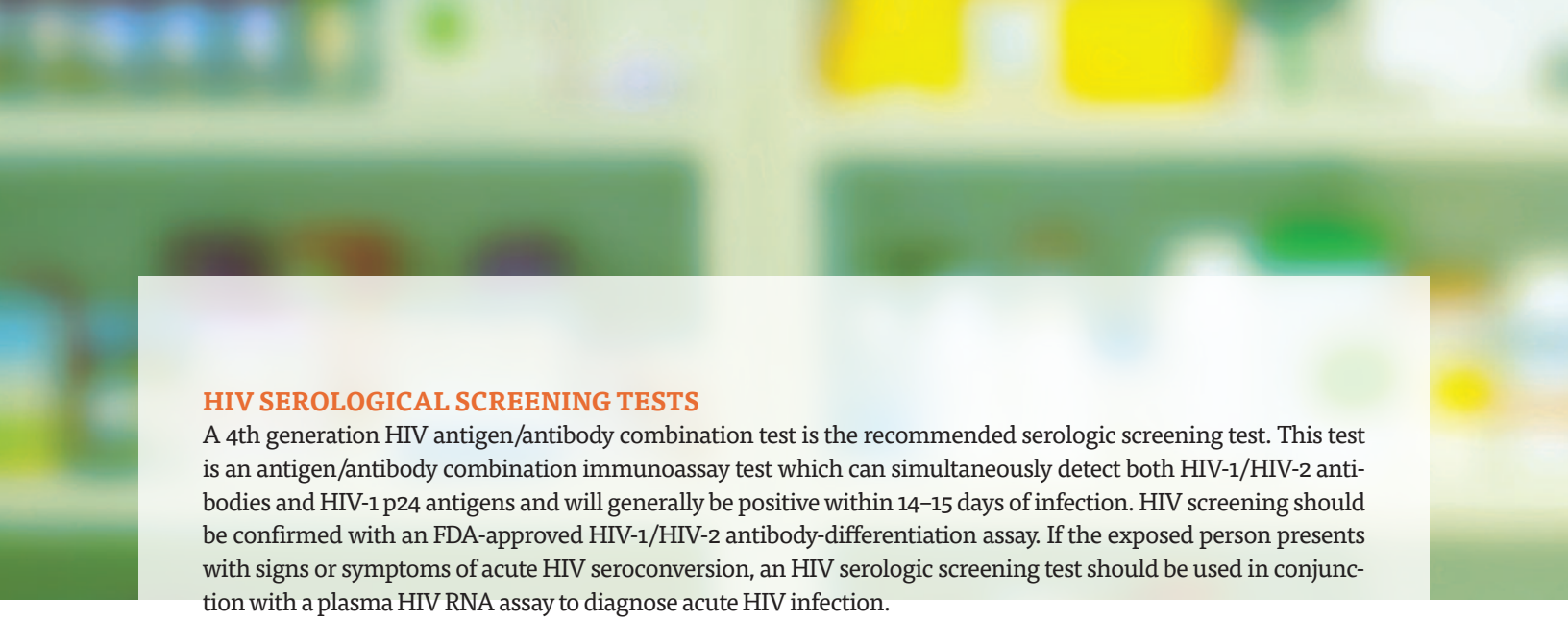
MONITORING RECOMMENDATIONS AFTER INITIATION OF nPEP REGIMENS FOLLOWING NON-OCCUPATIONAL EXPOSURES

	Baseline	Week 1	Week 2	Week 3	Week 4	Week 12
Clinic Visit	√	√ Or by phone	√ Or by phone	√ Or by phone	√	
Pregnancy Test	√					
Serum liver enzymes, BUN, Creatinine, CBC[a]	√		√		√	
HIV Screening Test[b]	√				√	√
STI Screening[b] **GC/CT NAAT (based on site of exposure)** **RPR (see *HIV Prophylaxis for Victims of Sexual Assault* for recommendations in cases of sexual assault)**	√		√ *consider*			
Hepatitis B and C[b]	**For post-exposure management, see Section IX: *Non-Occupational Exposures to Hepatitis B and C***					

a—CBC should be obtained for all exposed persons at baseline. Follow-up CBC at Week 2 and Week 4 is indicated only for those receiving a zidovudine-containing regimen.

b —Recommended even if nPEP is declined.

During the treatment period, other blood tests may be indicated to monitor for side effects of treatment. The timing and specific testing indicated varies based on the nPEP regimen used. Health care providers should be aware of the resources available within the community that offer medical and supportive counseling/adherence services following non-occupational exposure. Patients with signs or symptoms of acute HIV infection should be referred for further assessment when nPEP is provided outside of an expert clinical context.



HIV SEROLOGICAL SCREENING TESTS

A 4th generation HIV antigen/antibody combination test is the recommended serologic screening test. This test is an antigen/antibody combination immunoassay test which can simultaneously detect both HIV-1/HIV-2 antibodies and HIV-1 p24 antigens and will generally be positive within 14–15 days of infection. HIV screening should be confirmed with an FDA-approved HIV-1/HIV-2 antibody-differentiation assay. If the exposed person presents with signs or symptoms of acute HIV seroconversion, an HIV serologic screening test should be used in conjunction with a plasma HIV RNA assay to diagnose acute HIV infection.

HIV SEROCONVERSION

If HIV infection develops after an exposure, it will generally occur within two to four weeks of exposure. HIV testing at baseline, 4 weeks, and 12 weeks is recommended after significant exposures, regardless of whether the individual accepts or declines PEP treatment. Point-of-care HIV tests (rapid tests) are less sensitive than laboratory-based HIV tests; therefore, exposed persons should be tested with laboratory-based HIV tests whenever possible.

Patients acutely infected with HIV will often experience at least some symptoms of the acute retroviral syndrome. Fever and flu-like symptoms are common in acute HIV infection but are nonspecific. Rash, mucocutaneous ulcers, oropharyngeal candidiasis and meningismus are more specific. Symptoms may also include fatigue or malaise, joint pain, headache, loss of appetite, night sweats, myalgias, lymphadenopathy, oral and/or genital ulcers, nausea, diarrhea or pharyngitis. Acute HIV infection is often not recognized in the primary care setting because of the similarity of the symptom complex with that of the flu or other common illnesses.

REFERRALS

nPEP should be provided with services that address ongoing needs of patient risk behaviors.

- Health care providers should be aware of local resources for mental health and substance abuse treatment; mental health and substance abuse may contribute significantly to the risk of subsequent exposures.
- HIV Hotline for patients in need of HIV-specific support: 1-800-CDC-INFO.
- Primary care referrals should also be available when indicated.
- National Sexual Assault Telephone Hotline: rape crisis center services to mitigate sexual assault trauma, 1-800-656-HOPE.
- For information about rape crisis services concerned with HIV prophylaxis for victims of sexual assault: www.hivguidelines.org/clinical-guidelines/post-exposure-prophylaxis/hiv-prophylaxis-for-victims-of-sexual-assault/.

REFERRALS FOR nPEP FOLLOW UP

Option 1: The initial facility's (clinic) health care provider performing an examination, including sexual assault exams, should solicit and establish a relationship with a qualified physician who is knowledgeable about HIV treatment and nPEP, and has the ability to receive patients within three to five days of the initial exam and referral.

Option 2: The initial facility's HIV treatment physician may have the patient return to the facility for follow-up treatment if no other option is available.

Option 3: If the initial facility does not have an established relationship and/or there is no local HIV treatment physician, sexual assault victims who have been assessed by a physician and who have met the criteria for nPEP, can be referred to another primary care or infectious disease physician.

PHARMACY CONSIDERATIONS

Pharmacists play a role in the dispensation of nPEP regimens. In order to ensure more timely access of nPEP medications to patients, health care providers should be aware that the use of "phone-in" oral prescriptions may result in faster dispensing and avoid situations where drug access might be limited. When nPEP is prescribed to a patient receiving other prescription and non-prescription medications, a complete drug profile review should take place to assess for any drug interactions. No medications should be dispensed as part of an nPEP regimen if all medications are unavailable at the same time.

It is beneficial to coordinate with local pharmacies in determining which ones have nPEP medications in stock or can order them quickly. Health care providers can discuss the treatment with local pharmacies and the need for an urgent response when prescribing nPEP medications. Pharmacists with specific questions regarding nPEP therapy are welcome to contact the PEP Hotline at (888) 448-4911, available seven days a week from 9:00 a.m.–2:00 a.m. EST.