

## HIV PROPHYLAXIS FOLLOWING OCCUPATIONAL EXPOSURE

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### What's New — May 2010 Update

**Updated:** Section X: *Occupational PEP for Hepatitis B and C*

#### I. INTRODUCTION

Several clinical studies have demonstrated that HIV transmission can be significantly reduced by the administration of antiretroviral (ARV) agents. A dramatic decline in vertical transmission was observed in the AIDS Clinical Trial Group (ACTG) 076 study,<sup>1</sup> in which pregnant women and their newborns received monotherapy with zidovudine (ZDV), and in the HIVNET 012 study,<sup>2</sup> in which single-dose nevirapine was compared with ZDV. A Centers for Disease Control and Prevention (CDC) retrospective case-control study<sup>3</sup> of ZDV use after occupational HIV exposure in healthcare workers (HCWs) showed an 81% reduction in risk of HIV infection in persons who received ZDV. This study also identified characteristics of both the exposure and the source patient that placed the HCWs at highest risk for HIV acquisition. These studies led to the development of guidelines in 1998 for post-exposure prophylaxis (PEP) after an occupational exposure.

HAART, generally consisting of two nucleoside agents and a protease inhibitor (PI) or non-nucleoside reverse transcriptase inhibitor (NNRTI), has changed the standard of care for patients with chronic, established HIV infection. These potent regimens are used for PEP, although randomized clinical trials on which to base recommendations are unlikely to be conducted. To develop these guidelines for occupational PEP, the New York State Department of Health AIDS Institute (NYSDOH AI) has reviewed the available PEP studies, the current standards for the use of HAART in established HIV infection, and other issues that would affect the timely administration of optimal PEP. These guidelines update the previously issued guidelines of 2003.

Because there are no clinical trials on which to definitively base recommendations, the following NYSDOH AI guidelines are based on best practice evidence and constitute the considered opinion of a group of expert clinicians in the field of adult HIV medicine. New York State recommendations differ from those published by CDC (see Appendix B). The consensus opinion of this Committee continues to support a more aggressive approach to block HIV infection after occupational exposure. The recommendation to initiate PEP must take into account the potential benefit of preventing infection versus the risk of toxicity from the medications used for PEP.

## II. RATIONALE FOR PEP

### RECOMMENDATION:

**The Committee recommends the use of HAART regimens for all significant-risk occupational exposures when the HCW is evaluated within 36 hours of exposure.**

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

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

In vivo evidence from a small study of HCWs who were exposed percutaneously to HIV but who did not seroconvert suggests that limited viral replication may occur without establishment of infection. HIV-specific T-cell proliferative responses were observed in the majority of these individuals. Because the T-cell proliferative response is major histocompatibility complex (MHC) class I specific, limited viral replication within the tissue macrophages is inferred. Acceptance of this sequence of events also carries important implications. If limited HIV replication following exposure is a frequent event, then the argument to use HAART becomes even stronger.

## III. RISK FACTORS ASSOCIATED WITH HIV TRANSMISSION

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

Analysis of the characteristics of an exposure has yielded a hierarchy of relative risk (RR) associated with occupational acquisition of HIV (see Table 1).

**TABLE 1**  
**RELATIVE RISK FACTORS FOR HIV INFECTION AFTER PERCUTANEOUS EXPOSURE TO HIV-INFECTED BLOOD**

<b>Risk Factor</b>	<b>Adjusted Odds Ratio*</b>	<b>(95% CI)</b>
Deep injury	16.1	(6.1-44.6)
Visible blood on device	5.2	(1.8-17.7)
Procedure involving needle placed directly in a vein or artery	5.1	(1.9-14.8)
Terminal illness in source patient	6.4	(2.2-18.9)
Post-exposure use of zidovudine	0.2	(0.1-0.6)

Reprinted from Case-control study of HIV seroconversion in health care workers after percutaneous exposure to HIV-infected blood: France, United Kingdom, and United States, January 1988-August 1994. *MMWR Morb Mortal Wkly Rep* (1995;44:929-933).

\* All values were significant at  $p < 0.01$ .

The mean risk following an occupational percutaneous exposure is roughly 1 in 300 (0.3%). However, the mean risk may be significantly higher in cases in which more than one of the above risk factors is present (e.g., in persons who incur a deep injury with a hollow-bore needle from a patient with HIV who has a high viral load due to ineffective or no ARV therapy).

After a mucous membrane exposure, the average risk of seroconversion is approximately 9 in 10,000 (0.09%). In this analysis, the use of ZDV PEP by HCWs in the CDC study was shown to reduce the risk of HIV acquisition by 81%.<sup>3</sup>

#### IV. RECORDING INFORMATION FOLLOWING OCCUPATIONAL EXPOSURE

##### RECOMMENDATION:

**When an occupational exposure occurs, the following information should be recorded in the HCW's confidential medical record:**

- **Date and time of the exposure**
- **Details of the procedure being performed and the use of protective equipment at the time of the exposure**
- **The type, severity, and amount of fluid to which the HCW was exposed**
- **Details about the exposure source**
- **Medical documentation that provides details about post-exposure management**

Specific OSHA requirements regarding documentation may be found at [www.osha.gov/pls/oshaweb/owadisp.show\\_document?p\\_table=standards&p\\_id=10051](http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=standards&p_id=10051)

## V. GENERAL MANAGEMENT CONSIDERATIONS

### RECOMMENDATIONS:

**Wound and skin sites should be cleansed with soap and water immediately. The HCW should not attempt to squeeze the wound. Exposed mucous membranes should be flushed with water.**

**PEP is recommended for exposure to blood or visibly bloody fluid or other potentially infectious material (e.g., semen; vaginal secretions; and cerebrospinal, synovial, pleural, peritoneal, pericardial, and amniotic fluids) associated with potential HIV transmission and in any of the exposure situations outlined in Table 2.**

**If HIV serostatus of the source is unknown, voluntary HIV testing of the source should be sought. In New York State, specific informed consent for HIV testing is required (see Appendix C).**

**Rapid testing is strongly recommended for the source patient, and for those organizations subject to OSHA regulations, rapid testing is mandated for occupational exposures. Rules regarding confidentiality and consent for testing are identical to those for other HIV tests (see Appendix C for a special consent form for testing the source patient).**

**If the rapid test result is positive, the result should be given to the source patient. To establish a diagnosis of HIV infection, the test must be confirmed by a Western blot assay, which should be performed as soon as possible.**

**If the result from testing the source patient is not immediately available and PEP is indicated based on assessment, the initiation of PEP should not be delayed pending the test result.**

**TABLE 2  
EXPOSURES FOR WHICH PEP IS INDICATED**

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

Rapid testing is strongly recommended for the source patient, and for those organizations subject to OSHA regulations, rapid testing is mandated for occupational exposures. Results from rapid testing are usually available in 30 minutes. If the test result is not immediately available, the initiation of PEP should not be delayed pending the test result. A negative result would indicate that HIV PEP may not be needed. If the result of the HIV test from the source patient is negative, the HCW should be informed of the small chance that it could be a false-negative result if the source patient has been recently infected (during the "window period"). PEP should be recommended in situations when a significant risk exposure has occurred and there is a strong likelihood that the source patient has recently acquired HIV infection.

Unfortunately, the uncertainties occasionally associated with a given exposure may complicate the decision-making process, especially for an inexperienced clinician, and may possibly delay the prompt (within 2 hours) initiation of PEP. Uncertainties may exist about whether or not the source patient is HIV-infected and what constitutes a viable definition of a significant exposure. For the inexperienced clinician, rather than emphasize the relative risk of a particular exposure, the NYSDOH AI Medical Care Criteria Committee believes that the critical decision point should be to determine whether the HCW has had a percutaneous, mucocutaneous, or non-intact skin exposure to potentially HIV-infected blood, visibly bloody fluids, or other potentially infectious material. For these exposures, prompt initiation of PEP followed by telephone or in-person consultation with a clinician experienced in HIV PEP is recommended (see Section XI: *Resources for Consultation*).

## **VI. IMPLEMENTING PEP**

### **RECOMMENDATIONS:**

**PEP should be initiated as soon as possible, ideally within 2 hours and generally no later than 36 hours post-exposure. The prescribing provider should ensure that the HCW has access to the full course of ARV medications.**

**HAART is always recommended for at-risk exposures. Any variance from the recommended regimens should be made in consultation with an HIV Specialist or an occupational health clinician experienced in providing PEP (see [HIV Specialist](#)).**

**ARV medications for PEP should be readily available to HCWs who sustain a known or highly suspect occupational exposure to HIV. In establishing plans for providing PEP, employers should determine the following:**

- **How PEP will be made available within 1 to 2 hours of an exposure**
- **How a 24- to 48-hour supply of PEP will be made available for urgent use**
- **Who will be given authority for releasing drugs for this purpose**
- **How the HCW will obtain PEP drugs to complete the 4-week regimen (some individuals may be reluctant to go to their local pharmacy)**

**Confidential baseline HIV antibody testing of the HCW should be obtained at the time the occupational exposure is reported or within 72 hours of initiating PEP.**

**Confidential HIV testing of the source should be obtained as soon as possible after the exposure. A special consent form for testing the source patient is available and must be used (see Appendix C).**

**If the source patient's HIV test result is negative, the HCW should be informed of the small chance that it could be a false-negative result if the source patient has been recently infected. PEP should be recommended in situations when a significant risk exposure has occurred and the clinician suspects that the source patient has a strong likelihood of having recently acquired HIV infection.**

**If a recommendation to begin PEP is declined, this decision should be documented in the medical record of the HCW.**

**All patients placed on PEP should be re-evaluated within 72 hours of their exposure. This allows for further clarification of the nature of the exposure, review of available source patient serologies, and evaluation of adherence to and toxicities associated with the PEP regimen.**

**A total of 4 weeks of treatment is recommended. This treatment duration is based on animal data and is generally recommended by HIV Specialists.**

**If an HCW presents for evaluation of a high-risk exposure at a time >36 hours after the incident, rather than late initiation of PEP, close monitoring of the HCW for signs and symptoms of acute HIV infection is generally recommended with subsequent introduction of HAART if acute seroconversion occurs.**

Animal models of PEP have shown that effective ARV treatment is most likely to prevent infection when initiated within 24 hours of experimental exposure.<sup>4-8</sup> It is unknown whether initiation of PEP beyond this point confers protection. Most ARV drugs require an intracellular activation step that delays the onset of antiviral activity. Thus, clinicians should begin PEP as soon as possible, ideally within 2 hours and generally not later than 36 hours following exposures that carry the risk of HIV transmission. An absolute elapsed time after which PEP should not be administered, however, cannot be stated with certainty.

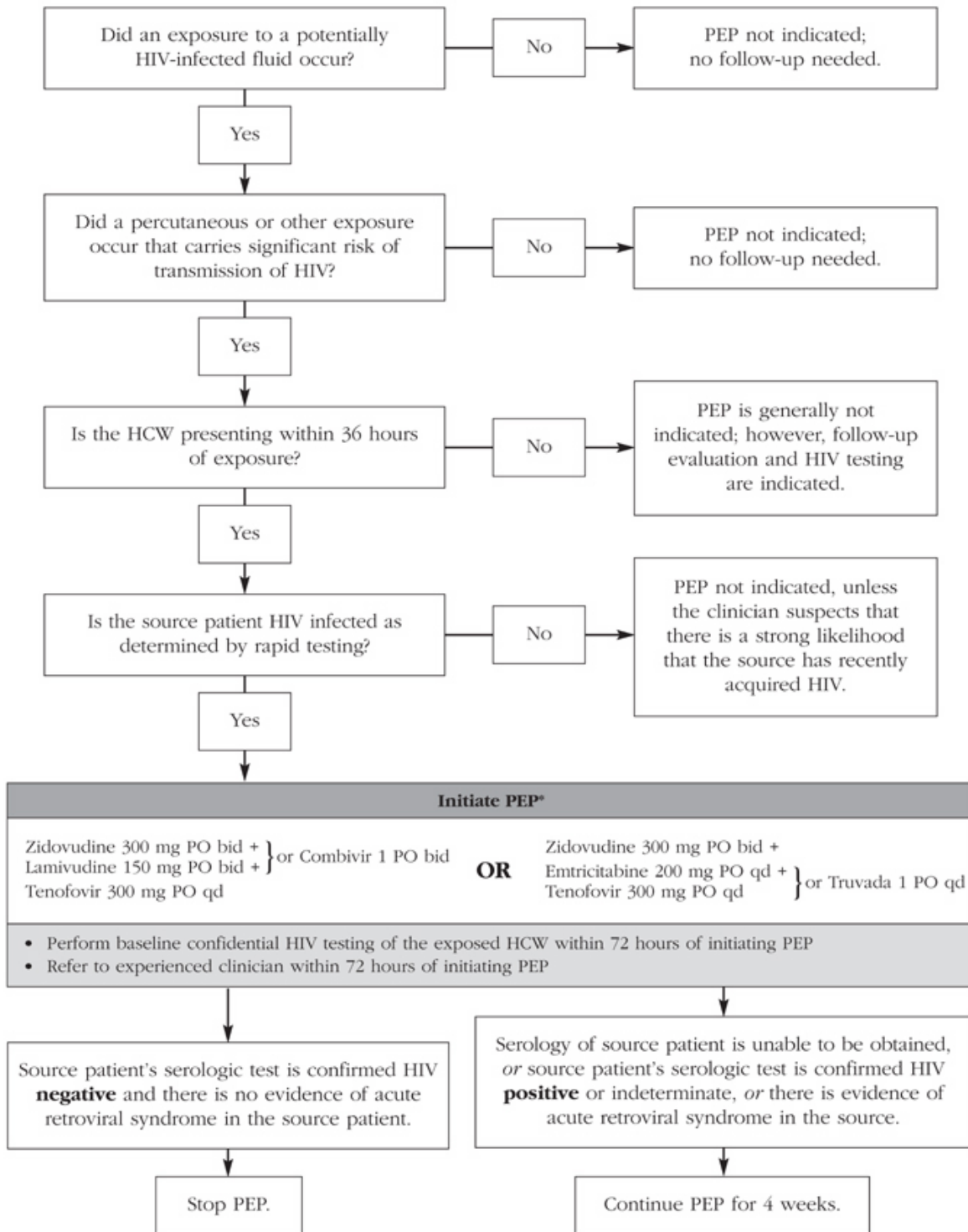
Late initiation of PEP (1-2 weeks after an exposure) may blunt initial viremia and block the clinical signs and symptoms associated with seroconversion, yet rebound of viral replication and the appearance of clinical symptoms would occur with cessation of PEP. If an HCW presents for evaluation of a high-risk exposure at a time >36 hours after the incident, rather than late initiation of PEP, close monitoring of the HCW for signs and symptoms of acute HIV infection is recommended with subsequent introduction of HAART if acute seroconversion occurs. Approximately 50% of persons who become infected with HIV will have a mononucleosis-like illness within 2 to 6 weeks after the exposure.

ARV drugs for PEP should be readily available to HCWs who sustain a known or highly suspected occupational exposure to HIV. The employer should determine who will pay for PEP and whether the Workers' Compensation plan will cover these drugs. HCWs should not be expected to pay out-of-pocket for PEP, even if it is reimbursed at a later date.

The employer of personnel covered by the Bloodborne Pathogen Standard is obligated to provide post-exposure care, including prophylaxis, at no cost to the employee. The employer may subsequently attempt to obtain reimbursement from Workers' Compensation. Appendix F provides information regarding employer issues and responsibilities.

Consultation with an HIV Specialist (see [HIV Specialist](#)) to determine the composition of the PEP regimen is recommended, but if a Specialist is not readily available, the initiation of PEP should not be delayed. Phone consultation with an HIV Specialist or an occupational health clinician experienced in providing PEP would be appropriate. Expert advice may also be obtained from the National Clinicians' Consultation Center PEP line at 1-888-HIV-4911 (1-888-448-4911). Optimal management of the HCW who has had an occupational exposure to a bloodborne pathogen balances the benefits of preventing infection with the risks of medication-induced side effects and toxicity (see Figure 1).

**Figure 1: PEP Following Occupational Exposure**



\* See Appendix A for dosing recommendations in patients with renal impairment.

## VII. RECOMMENDED PEP REGIMENS

### RECOMMENDATIONS:

**Clinicians should initiate three-drug ARV therapy for significant occupational exposures to HIV. The preferred PEP regimen is shown in Table 3. Alternative agents may be used in the setting of drug intolerance or toxicity (see Table 3 and Appendix A).**

**The PEP regimen should be continued for 4 weeks.**

**When the source is known to be HIV infected and information regarding previous ARV therapy, current level of viral suppression, or genotypic/phenotypic resistance profile is available, the clinician, in consultation with an HIV Specialist, should individualize the regimen to more effectively suppress viral replication.**

<b>TABLE 3</b>	
<b>HIV PEP REGIMEN FOLLOWING OCCUPATIONAL EXPOSURE AMONG HCWs<sup>a,b,c</sup></b>	
Zidovudine <sup>d</sup> 300 mg PO bid + Lamivudine 150 mg PO bid	} or Combivir 1 PO bid
<b>plus</b>	
Tenofovir 300 mg PO qd	
<b>OR</b>	
Zidovudine <sup>d</sup> 300 mg PO bid	
<b>plus</b>	
Emtricitabine 200 mg PO qd + Tenofovir 300 mg PO qd	} or Truvada 1 PO qd

#### Notes:

<sup>a</sup> When the source is known to be HIV-infected, past and current ARV therapy experience, viral load data, and genotypic or phenotypic resistance data (if available) may indicate the use of an alternative PEP regimen. Consult an HIV Specialist.

<sup>b</sup> NNRTIs should be considered only when 1) the patient cannot tolerate either tenofovir or a protease inhibitor alternative, or 2) the patient has been exposed to a source with known drug-resistant HIV that is sensitive to NNRTIs. Use of efavirenz should only be considered in men and in women not capable of bearing children because of associations with teratogenicity in animal studies and in anecdotal reports in humans. Initial central nervous system toxicity, often seen with efavirenz, may affect one's ability to work. Nevirapine is not recommended for women with CD4 counts >250 cells/mm<sup>3</sup> or men with CD4 counts >400 cells/mm<sup>3</sup> and should only be used when NRTIs or PIs are not an option and no other hepatic risk (e.g., hepatitis) is present. If nevirapine is used, it is essential that the 14-day lead-in period be strictly followed. Serum liver enzymes should be obtained at baseline, at dose escalation, and 2 weeks after dose escalation.

<sup>c</sup> The dosing interval of lamivudine, emtricitabine, and tenofovir should be adjusted in patients with baseline creatinine clearance <50 mL/min. Because Combivir and Truvada are fixed-dose combinations, clinicians should consider using the individual components (i.e., Combivir = zidovudine + lamivudine; Truvada = emtricitabine + tenofovir) dose adjusted for creatinine clearance (see Appendix A for dosing recommendations in patients with renal impairment). If the combination pills are used in this setting, clinicians should monitor for renal toxicity.

<sup>d</sup> Zidovudine: If the patient is intolerant to zidovudine, stavudine 40 mg PO bid may be substituted (if patient is <60 kg, 30 mg PO bid should be given). Dosing interval of zidovudine should be adjusted in patients with baseline creatinine clearance <15 mL/min (see Appendix A for dosing recommendations in patients with renal impairment).

The Committee chose tenofovir as the third agent because it achieves high intracellular levels and has been effective in trials of PEP in primates. The combination of 2 NRTIs plus tenofovir has high failure rates for treatment of established HIV infection and is only recommended for PEP where the goal is prevention of infection and not treatment.

As experience with occupational PEP continues to accumulate, it has become increasingly clear that non-adherence to PEP is multifactorial. Factors affecting adherence include ARV drug intolerance, regimen complexity, fear, anxiety, expense, frustration, and beliefs that the regimen will not work. Although there are no clinical trial data (other than that on zidovudine), based on post-exposure animal data using tenofovir<sup>9</sup> and its excellent tolerability and simplicity, the Committee now recommends the simpler standard PEP regimen of zidovudine, lamivudine, and tenofovir. Substitutions for tenofovir include the PIs nelfinavir and lopinavir/ritonavir (co-formulated as Kaletra). If these cannot be used, an NNRTI may be considered. In the setting of renal insufficiency, tenofovir and lamivudine may require dose reduction or be contraindicated (see Appendix A). The package insert for these agents should be consulted.

Reports of nevirapine-induced hepatotoxicity among people receiving PEP have led to the recommendation that nevirapine be considered as an alternative component of the PEP regimen only when NRTIs and PIs are not an option.<sup>10</sup> Use of efavirenz in a PEP regimen should only be considered in men and in women not capable of bearing children because it has been associated with teratogenicity in animal studies and in humans anecdotally.

## VIII. MONITORING THE HCW FOLLOWING OCCUPATIONAL EXPOSURE

### RECOMMENDATIONS:

**Clinicians should closely monitor people receiving PEP to detect ARV-induced toxicities** (see [Antiretroviral Therapy](#)<sup>11</sup> for monitoring recommendations).

**Because of the complexity and potential adverse effects of the treatment regimens, longitudinal care of the exposed HCW should be provided either directly by or in consultation with an HIV Specialist or an experienced occupational health clinician who is familiar with the most current PEP guidelines.**

**Sequential confidential HIV testing should be obtained at baseline, 1, 3, and 6 months post-exposure even if PEP is declined (see Table 4). In New York State, if the test result is positive, a Western blot assay must be performed to confirm the diagnosis of HIV infection. See Appendices D and E for specific counseling recommendations.**

**If the HCW presents with signs or symptoms of acute HIV seroconversion, immediate consultation with an HIV Specialist should be sought for optimal diagnostic testing and treatment options.**

**The HCW should be evaluated weekly over the first month to assess PEP adherence, adverse effects of the ARV therapy, interval physical complaints, and emotional status** (see [Antiretroviral Therapy](#)<sup>11</sup> for monitoring recommendations, [Long-Term Complications of Antiretroviral Therapy](#)<sup>12</sup> for adverse drug effects, and [HIV Drug-Drug Interactions](#)<sup>13</sup> for important drug interactions).

**TABLE 4**  
**MONITORING RECOMMENDATIONS AFTER INITIATION OF PEP REGIMENS FOLLOWING OCCUPATIONAL EXPOSURE AMONG HCWS**

	Clinic visit	CBC with differential	Serum liver enzymes	HIV antibody test*
<b>Baseline</b>	X	X	X	X
<b>Week 1</b>	X			
<b>Week 2</b>	X	X	X	
<b>Week 3</b>	X			
<b>Month 1</b>	X	X	X	X
<b>Month 3</b>				X
<b>Month 6</b>				X

\* Recommended even if PEP is declined.

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

Approximately 50% of HCWs for whom PEP is initiated do not complete therapy due to side effects or non-adherence. When an HCW is potentially occupationally exposed to HIV, longitudinal medical follow-up of the HCW is necessary regardless of whether PEP is initiated and/or completed, in order to test sequentially for HIV infection. For HCWs receiving PEP, follow-up is necessary to also monitor for adverse effects of the PEP regimen, and maximize adherence to the prescribed regimen.

When infection occurs, the ELISA will generally be positive within 3 weeks of the onset of symptoms and is virtually always positive within 3 months following exposure. The confirmatory Western blot may yield an indeterminate result during the early stages of seroconversion. Subsequent testing should be performed to confirm definite seroconversion.

Approximately 50% of patients acutely infected with HIV will experience at least some symptoms of the acute retroviral syndrome. Symptoms may include pharyngitis, morbilliform rash, thrush, lymphadenopathy, and hepatosplenomegaly. Acute HIV infection is often not recognized in the primary care setting because of the similarity of the symptom complex with that of the “flu” or other common illnesses. When acute HIV seroconversion is suspected based on the clinical scenario, a plasma HIV RNA assay should be used in conjunction with an HIV-1 antibody test to diagnose acute or primary HIV infection. See [Diagnostic, Monitoring, and Resistance Tests for HIV](#) for further information on HIV testing, and [Diagnosis and Management of Acute HIV Infection](#) for further information on management of acute HIV infection.

## IX. PEP FOR THE PREGNANT HCW

### RECOMMENDATIONS:

**Before administering PEP to a pregnant woman, the clinician should discuss the potential benefits and risks to her and to the fetus. Drugs to avoid during pregnancy are listed in Table 5.**

**Based on increasing clinical experience with HAART, PEP is indicated at any time during pregnancy when a significant exposure has occurred, despite possible risk to the woman and the fetus. Expert consultation should be sought. When PEP is indicated, it should be initiated ideally within 2 hours and generally no later than 36 hours post-exposure.**

**Efavirenz, which has been associated with teratogenicity in monkeys, should not be used in pregnant women.**

**The combination of didanosine and stavudine should be avoided due to an increased risk of mitochondrial toxicity in pregnant women.**

**Unboosted indinavir should not be used in pregnant women in the second or third trimester due to a substantial decrease in antepartum indinavir plasma concentrations.**

**Clinicians should advise women who may have been exposed to HIV through occupational exposure to avoid breastfeeding for 6 months after the exposure.**

<b>Drug(s) to Avoid</b>	<b>Toxicity</b>
Efavirenz	Teratogenicity
Combination of stavudine and didanosine	Mitochondrial toxicity
Unboosted IDV in the 2nd or 3rd trimester	Substantially lower antepartum indinavir plasma concentrations

Initiation of PEP at any time during pregnancy requires a careful discussion of the risks and benefits of this therapy. In addition to the risk of seroconversion for the HCW, there is a high risk of transmission to the fetus or breastfeeding infant, should the pregnant HCW develop the acute retroviral syndrome. Although birth defects and adverse effects on human fetuses have generally not been associated with the currently available ARV agents, exposure of a fetus to ARV agents during pregnancy carries a theoretical risk of teratogenicity.

The recommendation to initiate PEP in the breastfeeding patient presents several concerns. Both HIV and ARV drugs may be found in breast milk. As such, breastfeeding should be avoided for

6 months after the exposure to prevent HIV transmission and potential drug toxicities. Because HIV infection is most often diagnosed within 3 months of exposure, some women may prefer to breastfeed between 3 to 6 months following exposure. Clinicians should discuss the risks and benefits with the HCW. The infant’s pediatrician should be informed of any potential exposure to HIV or ARV medications.

For additional information, refer to NYSDOH guidelines on *Management of the HIV-Infected Pregnant Woman*.<sup>14</sup>

## X. OCCUPATIONAL EXPOSURES TO HEPATITIS B AND C

### RECOMMENDATION:

**When an occupational exposure occurs, the source patient should be evaluated for both hepatitis B and hepatitis C.**

The risk of transmission of HBV and HCV from an occupational exposure is significantly greater than the risk of HIV transmission. The risk of HCV infection following a needlestick is 1.8%, whereas the risk of HBV infection ranges from 1% to 30% depending on the presence of hepatitis e antigen (see Table 6). The risk of transmission of HCV from a single mucous membrane exposure is negligible.

TABLE 6 AVERAGE RISK FOR TRANSMISSION OF HEPATITIS B AND C VIRUSES AFTER NEEDLESTICK (COMPARED WITH HIV)	
Source	Risk
HBV	
HBeAg+	22.0% - 30.0%
HBeAg-	1.0% - 6.0%
HCV+	1.8%
HIV+	0.3%

### A. Hepatitis B Virus Post-Exposure Management

#### RECOMMENDATIONS:

**The hepatitis B vaccine series should be initiated in *non-HBV-immune* HCWs who sustain a blood or body fluid exposure.**

**Administration of prophylactic hepatitis B immune globulin (HBIG) and the initiation of the hepatitis B vaccine series injected at different sites is recommended when the non-HBV-immune HCW sustains a blood or body fluid exposure to a source patient with known acute or active HBV (see Table 7). Both HBIG and the first dose of the hepatitis B vaccine series should be ideally administered within 24 hours of exposure; HBIG should not be given later than 14 days post-exposure. The three-dose HBV vaccine series is given at 0, 1 to 2 months, and 6 months.**

**Needlestick injuries and wounds should be washed with soap and water and should not be squeezed. Mucous membranes should be flushed with water.**

Initiation of the HBV vaccine series within 12 to 24 hours of an exposure has been demonstrated to be 70% to 90% effective in preventing HBV infection. The combination of vaccine and HBIG achieves a similar level of efficacy. Among known non-responders to vaccination, one dose of HBIG is 70% to 90% effective in preventing HBV when administered within 7 days of percutaneous HBV exposure,<sup>15</sup> and multiple doses have been shown to be 75% to 95% effective.<sup>16</sup> Pregnant women can safely receive both the HBV vaccination and HBIG.

When considering PEP for HBV exposures, both the source patient's HBsAg status and the HCW's vaccination status should be considered (see Table 7). Determination of antibody response of previously vaccinated HCWs should be based on information available at presentation. It is not recommended that decision-making be delayed while testing for anti-HBs. If antibody response is unknown, follow recommendations for "antibody response unknown" in Table 7.

Both HBIG and the first dose of the hepatitis B vaccine should be ideally administered within 24 hours of exposure; HBIG should not be given later than 14 days post-exposure. The three-dose HBV vaccine series is given at 0, 1 to 2 months, and 6 months. Hepatitis B antibodies should be obtained 1 to 2 months after completion of the third dose of the vaccine; however, levels may be falsely elevated if the exposed person received HBIG within the past 3 to 4 months.

Even if the risk of exposure to HBV is not deemed significant, HBV vaccination should still be advised for all non-HBV-immune HCWs (see [Hepatitis B Virus](#) guidelines for more information). Household, sex, and needle-sharing contacts of HBsAg-positive individuals should be identified and vaccinated according to the guidelines for patients exposed to known HBsAg-positive individuals.

<b>TABLE 7</b>			
<b>RECOMMENDED POST-EXPOSURE PROPHYLAXIS FOR HEPATITIS B VIRUS</b>			
<b>Vaccination and/or antibody response status of exposed patient<sup>a</sup></b>	<b>Treatment when source patient is:</b>		
	<b>HBsAg positive</b>	<b>HBsAg negative</b>	<b>Source unknown or not available for testing</b>
Unvaccinated/non-immune	HBIG <sup>b</sup> ×1; initiate HB vaccine series	Initiate HB vaccine series	Initiate HB vaccine series
Previously vaccinated, <sup>c</sup> known responder <sup>d</sup>	No treatment	No treatment	No treatment
Previously vaccinated, <sup>c</sup> known non-responder <sup>d</sup>	HBIG <sup>b</sup> ×1 and initiate revaccination <sup>e</sup> or HBIG <sup>b</sup> ×2	No treatment	No treatment unless known high-risk source; if high-risk source, <sup>f</sup> then treat as if source were HBsAg positive
Previously vaccinated, <sup>c</sup> antibody response unknown	Single vaccine booster dose	No treatment	No treatment unless known high-risk source; if high-risk source, <sup>f</sup> then treat as if source were HBsAg positive
If still undergoing vaccination	HBIG <sup>b</sup> ×1; complete series	Complete series	Complete series

HBsAg, hepatitis B surface antigen; HBIG, hepatitis B immune globulin; anti-HBs, antibody to hepatitis B surface antigen.

<sup>a</sup> Persons who have previously been infected with HBV are immune to re-infection and do not require PEP.

<sup>b</sup> Dose 0.06 mL/kg intramuscularly.

<sup>c</sup> Vaccinated with full three-dose series.

<sup>d</sup> Based on information available at presentation. Responder is defined as person with previously documented adequate levels of serum antibody to HBsAg (serum anti-HBs >10mIU/mL); non-responder is a person with previously documented inadequate response to vaccination (serum anti HBs <10mIU/mL). It is not recommended that decision-making be delayed while testing for anti-HBs at presentation.

<sup>e</sup> The option of giving one dose of HBIG and re-initiating the vaccine series is preferred for non-responders who have not completed a second three-dose vaccine series. For persons who previously completed a second vaccine series but failed to respond, two doses of HBIG are preferred.

<sup>f</sup> High-risk is defined as sources who engage in needle-sharing or high-risk sexual behaviors, and those born in geographic areas with HBsAg prevalence of ≥2%.<sup>17</sup>

## B. Hepatitis C Virus Post-Exposure Management

### RECOMMENDATIONS:

**Clinicians should consider concurrent exposure to HCV when HCWs present with an HIV exposure.**

**Neither immunoglobulin nor antiviral agents are recommended for HCV post-exposure prophylaxis.**

**When HCV infection is identified, the HCW should be referred for medical management to a gastroenterologist or other clinician with experience in treating HCV.**

Currently, no effective prophylaxis for HCV has been identified. Immunoglobulin and antiviral agents are not recommended for HCV post-exposure prophylaxis (PEP). However, if an individual becomes acutely infected with hepatitis C and is diagnosed at that time, immediate referral to a gastroenterologist or other specialist experienced in the treatment of hepatitis C is strongly recommended. Recent data suggest that early treatment of acute hepatitis C with interferon is highly effective, perhaps as high as 95%.<sup>18</sup>

### 1. Baseline Management

#### RECOMMENDATIONS:

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

**Once the clinician has determined that exposure to blood or body fluid has occurred, the following baseline tests should be obtained (see Table 8 for follow-up according to baseline results):**

#### **Source Patient:**

- **HCV antibody test (e.g., EIA/ELISA), and if positive, HCV RNA test or RIBA**

#### **Exposed HCW:**

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

If the source patient is tested with an EIA/ELISA and found to be positive, then follow-up testing is necessary to confirm the source patient's status. According to the most recent [\*Updated U.S. Public Health Service Guidelines for the Management of Occupational Exposures to HBV, HCV, and HIV and Recommendations for Postexposure Prophylaxis\*](#) (2001), either HCV RNA or RIBA may be used as the confirmatory test. However, most clinicians currently obtain HCV RNA testing, instead of RIBA, to confirm a positive antibody screening result. When the source patient tests positive by either RIBA or HCV RNA test, the exposed person should be managed as if the source has chronic HCV.

**TABLE 8**  
**HEPATITIS C POST-EXPOSURE MANAGEMENT ACCORDING TO**  
**BASELINE TEST RESULTS**

<b>Clinical Scenario</b>	<b>Follow-Up<sup>a</sup></b>
Source patient is HCV-antibody negative	No further testing or follow-up is necessary for source patient or the exposed HCW <sup>b</sup>
Source patient is unavailable or refuses testing	Exposed HCW: Follow-up HCV antibody at 3 and 6 months <sup>b</sup>
Source patient is HCV-antibody positive and HCV RNA negative	Manage the exposed HCW as if the source patient has chronic hepatitis C (see Section 2: <i>Post-Exposure Follow-Up</i> ) <sup>c</sup>
Source patient is positive for both HCV antibody and HCV RNA <i>and</i> Exposed HCW is HCV-antibody negative	Source patient: Counsel and manage as chronic hepatitis C regardless of status of exposed person Exposed HCW: Follow up as outlined in Section 2: <i>Post-Exposure Follow-Up</i>
Exposed HCW tests positive for both HCV antibody and HCV RNA	Counsel and manage as chronic hepatitis C

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

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

<sup>c</sup> A single negative HCV RNA result does not exclude active infection.

**Clinicians should educate exposed HCWs about the natural history of HCV infection and should counsel exposed HCWs about the following:**

- **Avoidance of alcohol and, if possible, medications that may be toxic to the liver.**
- **Risk of transmission related to:**
  - Blood-to-blood contact, including sharing personal care items that may have come in contact with another person’s blood, such as razors or toothbrushes; occupational needlestick injuries; and sharing needles, syringes, or other equipment to inject drugs
  - Sexual activity
  - Donating blood, plasma, organs, tissue, or semen
  - Perinatal transmission
- **Hepatitis C virus is not spread via food or water and is not transmitted by:**
  - Sharing eating utensils
  - Hugging, kissing, or holding hands
  - Coughing or sneezing
  - Breastfeeding: HCV is not transmitted by breastfeeding; however, clinicians should advise women who may have been exposed to HIV to avoid breastfeeding for 6 months after the exposure.

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

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

### **RECOMMENDATIONS:**

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

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

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

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

For HCWs exposed to hepatitis C-infected source patients, regular follow-up with HCV RNA testing is recommended in addition to HCV antibody testing, because HCV RNA testing can identify acute infection within 2 weeks of exposure, whereas accuracy of the antibody test can be delayed up to several months after acute infection (i.e., “window period”). Seroconversion with the ELISA antibody test occurs in 50% of patients within 9 weeks of exposure, in 80% of patients within 15 weeks of exposure, and in at least 97% of patients within 6 months of exposure.<sup>19</sup> The ELISA test is highly sensitive but relatively nonspecific, resulting in a low positive predictive value in low-prevalence populations. Positive HCV ELISA antibody test results require confirmation by a quantitative viral load assay, such as HCV PCR.

## **XII. RESOURCES FOR CONSULTATION**

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

The following resources are the preferred initial contacts for expert consultation:

- The National Clinicians' Consultation Center PEP line at 1-888-HIV-4911 (1-888-448-4911).
- For further education of health providers or for consultation regarding setting up PEP services, contact: [CEI PEP, Testing and Diagnosis Center](#)
- The AIDS Institute is a secondary resource for consultation and referrals. The Institute (212-417-4536) is open between 8:30 AM and 5:00 PM. At other hours, a NYSDOH operator at 518-465-9720 will connect the caller with the Department of Health Duty Officer who can refer the caller to an appropriate resource in his/her geographic area.

Appendix F provides information regarding employer issues and responsibilities.

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## APPENDIX A

### ANTIRETROVIRAL DRUGS

The tables that follow include antiretroviral agents recommended for PEP (zidovudine, lamivudine, tenofovir) as well as alternative antiretroviral drugs because the recommended regimen may require alteration based on factors such as prior use of antiretroviral therapy in the person who is the source of the exposure. For information on all antiretroviral medications, see [Antiretroviral Therapy](#).

The following tables indicate dosage, toxicity, and dose adjustment recommendations for a 4-week course of prophylaxis. Because there are toxicity and dose adjustment considerations for all of these medications when used for chronic treatment, other references should also be consulted. The tables also include letters that reference FDA pregnancy categories as described below.

#### FDA Pregnancy Categories

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

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

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

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

**X** Studies in animals or reports of adverse reactions have indicated that the risk associated with the use of the drug for pregnant women clearly outweighs any possible benefit.

<b>ZIDOVUDINE (ZDV)</b> (Updated February 2009)							
<b>Trade Name</b>	Retrovir						
<b>Classification</b>	Nucleoside Reverse Transcriptase Inhibitor						
<b>Form</b>	100-mg capsules, 300-mg tablets, 10-mg/mL IV solution, 10-mg/mL oral solution Each Combivir tablet contains ZDV 300 mg and 3TC 150 mg Each Trizivir tablet contains ZDV 300 mg, 3TC 150 mg, and ABC 300 mg						
<b>Dosing Recommendations</b>	200 mg tid or 300 mg bid <i>or</i> with 3TC as Combivir, <sup>a</sup> 1 bid <i>or</i> with ABC and 3TC as Trizivir, <sup>a,b</sup> 1 bid						
<b>Hepatic Impairment Dosing</b>	Use with close monitoring						
<b>Renal Impairment Dosing</b>	<table border="1"> <thead> <tr> <th>CrCl (mL/min)</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td>&lt;15</td> <td>100 mg q6-8h (or 300 mg qd)</td> </tr> <tr> <td>Hemodialysis</td> <td>100 mg q6-8h (or 300 mg qd)</td> </tr> </tbody> </table>	CrCl (mL/min)	Dose	<15	100 mg q6-8h (or 300 mg qd)	Hemodialysis	100 mg q6-8h (or 300 mg qd)
CrCl (mL/min)	Dose						
<15	100 mg q6-8h (or 300 mg qd)						
Hemodialysis	100 mg q6-8h (or 300 mg qd)						
<b>Food Effect</b>	Absorption similar with or without food. Fatty food may decrease bioavailability (clinical significance unknown)						
<b>Oral Bioavailability</b>	60%						
<b>Serum Half-life</b>	1.1 hour						
<b>Intracellular Half-life</b>	3 hours						
<b>Elimination</b>	Metabolized to AZT glucuronide (GAZT); renal excretion of GAZT						
<b>Adverse Events</b>	GI intolerance, headache, insomnia, asthenia, lipoatrophy  Bone marrow suppression: anemia, neutropenia, and, less commonly, thrombocytopenia  Lactic acidosis with hepatic steatosis is a rare but potentially life-threatening toxicity						
<b>FDA Pregnancy Category</b>	C (no maternal toxicity or fetal defects noted with long-term follow-up)						
<b>Long-Term Animal Carcinogenicity Studies</b>	Positive (rodent, non-invasive vaginal epithelial tumors)						
<b>Animal Teratogen Studies</b>	Negative (mice and rabbits)						
<b>Black Box Warnings</b>	Zidovudine may be associated with hematologic toxicities, including granulocytopenia and severe anemia, particularly in advanced HIV-infected patients.  Prolonged zidovudine use has been associated with symptomatic myopathy.  Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination.						
<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Stavudine  Doxorubicin (additive bone marrow suppression)						

<b>Cautious Use or Dose Adjustment</b>	
<b>Antivirals</b>	<p><b>Ganciclovir:</b> Additive bone marrow suppression</p> <p><b>Ribavirin:</b> Additive anemia – May require use of EPO</p>
<b>Erythropoiesis-stimulating agents (ESAs)</b>	<b>Hold dose when Hgb &gt;13 g/dL, and reinitiate with a 25% reduction or when Hgb &lt;12 g/dL. Monitor Hct q1-2 wk until maintenance dose established</b>
<p><sup>a</sup> Combivir and Trizivir should not be used in patients with renal insufficiency. Separate components and dose based on glomerular filtration rate (GFR).</p> <p><sup>b</sup> HLA-B*5701 is a pharmacogenetic test (HLA-B*5701) used to identify patients who are predisposed to abacavir hypersensitivity. Clinicians should perform HLA-B*5701 testing before initiating abacavir-based therapy.</p>	

<b>LAMIVUDINE (3TC)</b> (Updated January 2007)													
<b>Trade Name</b>	Epivir												
<b>Classification</b>	Nucleoside Reverse Transcriptase Inhibitor												
<b>Form</b>	150-, 300-mg tablets; 10-mg/mL oral solution Each Combivir tablet contains ZDV 300 mg and 3TC 150 mg Each Trizivir tablet contains ZDV 300 mg, 3TC 150 mg, and ABC 300 mg Each Epzicom tablet contains ABC 600 mg and 3TC 300 mg												
<b>Dosing Recommendations</b>	150 mg bid or 300 mg qd <50 kg: 2 mg/kg bid <i>or</i> with ZDV as Combivir, <sup>a</sup> 1 bid <i>or</i> with ZDV and ABC as Trizivir, <sup>a,b</sup> 1 bid <i>or</i> with ABC as Epzicom, <sup>b</sup> 1 qd												
<b>Renal Impairment Dosing</b>	<table border="1"> <thead> <tr> <th>CrCl (mL/min)</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td>30-49</td> <td>150 mg qd</td> </tr> <tr> <td>15-29</td> <td>150 mg first dose, then 100 mg qd</td> </tr> <tr> <td>5-14</td> <td>150 mg first dose, then 50 mg qd</td> </tr> <tr> <td>&lt;5</td> <td>50 mg first dose, then 25 mg qd</td> </tr> <tr> <td>Hemodialysis</td> <td>No data</td> </tr> </tbody> </table>	CrCl (mL/min)	Dose	30-49	150 mg qd	15-29	150 mg first dose, then 100 mg qd	5-14	150 mg first dose, then 50 mg qd	<5	50 mg first dose, then 25 mg qd	Hemodialysis	No data
CrCl (mL/min)	Dose												
30-49	150 mg qd												
15-29	150 mg first dose, then 100 mg qd												
5-14	150 mg first dose, then 50 mg qd												
<5	50 mg first dose, then 25 mg qd												
Hemodialysis	No data												
<b>Food Effect</b>	No food effect												
<b>Oral Bioavailability</b>	86%												
<b>Serum Half-life</b>	5-7 hours												
<b>Intracellular Half-life</b>	18 hours												
<b>Elimination</b>	Renal excretion												
<b>Adverse Events</b>	Minimal toxicity for adults Lactic acidosis with hepatic steatosis is a rare but potentially life-threatening toxicity												
<b>FDA Pregnancy Category</b>	C												
<b>Long-Term Animal Carcinogenicity Studies</b>	Negative (no tumors, lifetime rodent study)												
<b>Animal Teratogen Studies</b>	Negative												
<b>Black Box Warnings</b>	Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination.  Epivir tablets and oral solution (used to treat HIV infection) contain a higher dose of lamivudine than Epivir-HBV tablets and oral solution (used to treat chronic hepatitis B). Patients with HIV infection should receive only doses and formulations appropriate for treatment of HIV infection.												

<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Abacavir + tenofovir Emtricitabine Tenofovir + didanosine
<p><sup>a</sup> Combivir and Trizivir should not be used in patients with renal insufficiency. Separate components and dose based on glomerular filtration rate (GFR).</p> <p><sup>b</sup> HLA-B*5701 is a pharmacogenetic test (HLA-B*5701) used to identify patients who are predisposed to abacavir hypersensitivity. Clinicians should perform HLA-B*5701 testing before initiating abacavir-based therapy.</p>	

<b>EMTRICITABINE (FTC)</b> (Updated January 2007)											
<b>Trade Name</b>	Emtriva										
<b>Classification</b>	Nucleoside Reverse Transcriptase Inhibitor										
<b>Form</b>	200-mg capsules Each Truvada tablet contains TDF 300 mg and FTC 200 mg Each Atripla tablet contains EFV 600 mg, FTC 200 mg, and TDF 300 mg										
<b>Dosing Recommendations</b>	200 mg qd <i>or</i> with TDF as Truvada, 1 qd <i>or</i> with EFV and TDF as Atripla, 1 qd										
<b>Renal Impairment Dosing</b>	<table border="1"> <thead> <tr> <th>CrCl (mL/min)</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td>30-49</td> <td>200 mg q48h</td> </tr> <tr> <td>15-29</td> <td>200 mg q72h</td> </tr> <tr> <td>&lt;15</td> <td>200 mg q96h</td> </tr> <tr> <td>Hemodialysis</td> <td>200 mg q96h; dose after dialysis on day of dialysis</td> </tr> </tbody> </table>	CrCl (mL/min)	Dose	30-49	200 mg q48h	15-29	200 mg q72h	<15	200 mg q96h	Hemodialysis	200 mg q96h; dose after dialysis on day of dialysis
CrCl (mL/min)	Dose										
30-49	200 mg q48h										
15-29	200 mg q72h										
<15	200 mg q96h										
Hemodialysis	200 mg q96h; dose after dialysis on day of dialysis										
<b>Food Effect</b>	No food effect										
<b>Oral Bioavailability</b>	93%										
<b>Serum Half-life</b>	10 hours										
<b>Intracellular Half-life</b>	39 hours										
<b>Elimination</b>	Renal excretion 86%										
<b>Adverse Events</b>	Minimal toxicity for adults  Lactic acidosis with hepatic steatosis is a rare but potentially life-threatening toxicity										
<b>FDA Pregnancy Category</b>	B										
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed										
<b>Animal Teratogen Studies</b>	Negative (mice and rabbits)										
<b>Black Box Warnings</b>	Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogues alone or in combination with other antiretrovirals.										
<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Lamivudine										

<b>TENOFOVIR (TDF)</b> (Updated January 2007)									
<b>Trade Name</b>	Viread								
<b>Classification</b>	Nucleotide Reverse Transcriptase Inhibitor								
<b>Form</b>	300-mg tablets Each Truvada tablet contains TDF 300 mg and FTC 200 mg Each Atripla tablet contains EFV 600 mg, FTC 200 mg, and TDF 300 mg								
<b>Dosing Recommendations</b>	300 mg qd <i>or</i> with FTC as Truvada, 1 qd <i>or</i> with EFV and FTC as Atripla, 1 qd								
<b>Renal Impairment Dosing</b>	<table border="1"> <thead> <tr> <th>CrCl (mL/min)</th> <th>Dose</th> </tr> </thead> <tbody> <tr> <td>30-49</td> <td>300 mg q48h</td> </tr> <tr> <td>10-29</td> <td>300 mg bi wk</td> </tr> <tr> <td>ESRD</td> <td>300 mg q wk</td> </tr> </tbody> </table>	CrCl (mL/min)	Dose	30-49	300 mg q48h	10-29	300 mg bi wk	ESRD	300 mg q wk
CrCl (mL/min)	Dose								
30-49	300 mg q48h								
10-29	300 mg bi wk								
ESRD	300 mg q wk								
<b>Food Effect</b>	Fatty meal ↑ TDF AUC 40%  Co-administration of TDF + ddI buffered tablets should be on an empty stomach  TDF + ddI EC may be taken on an empty stomach or with a light meal								
<b>Oral Bioavailability</b>	25% in fasting state; 39% with high fat meal								
<b>Serum Half-life</b>	17 hours								
<b>Intracellular Half-life</b>	10-50 hours								
<b>Elimination</b>	Renal excretion								
<b>Adverse Events</b>	Asthenia, headache, diarrhea, nausea, vomiting, flatulence  Although there have been no cases of lactic acidosis reported with TDF use, lactic acidosis with hepatic steatosis is a rare but potentially life-threatening toxicity with the use of NRTIs  Rare reports of renal insufficiency								
<b>FDA Pregnancy Category</b>	B (one study showed normal growth; however, there was a decrease in fetal bone porosity and insulin-like growth factor was observed)								
<b>Long-Term Animal Carcinogenicity Studies</b>	Negative (rats); in female mice, liver adenomas were increased at exposures 16 times that in humans								
<b>Animal Teratogen Studies</b>	Negative (osteomalacia when given to juvenile animals at high doses)								
<b>Black Box Warnings</b>	Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of nucleoside analogs alone or in combination with other antiretrovirals.								

	Viread has in vitro activity against HBV but is not indicated for the treatment of chronic hepatitis B virus (HBV) infection and the safety and efficacy of Viread have not been established in patients co-infected with HBV and HIV. Severe acute exacerbations of hepatitis B have been reported in patients who are co-infected with HBV and HIV and have discontinued Viread. Hepatic function should be monitored closely with both clinical and laboratory follow-up for at least several months in patients who discontinue Viread and are co-infected with HIV and HBV. If appropriate, initiation of anti-hepatitis B therapy may be warranted.
<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Atazanavir without ritonavir Didanosine + delavirdine Didanosine + efavirenz Didanosine + nevirapine Lamivudine + abacavir Lamivudine + didanosine
<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<b>Atazanavir + ritonavir:</b> ATV AUC ↓ 25%, Cmin ↓ 23% – Use ATV 300 mg + RTV 100 mg qd  <b>Didanosine:</b> ddI AUC ↑ 44%, Cmax ↑ 28% – Monitor for ddI-associated toxicities; for patients ≥60 kg, ↓ ddI EC dose to 250 mg qd; for patients <60 kg ↓ ddI EC to 200 mg qd. Avoid combination in patients with renal failure
<b>Antivirals</b>	<b>Cidofovir, ganciclovir, valganciclovir:</b> May ↑ serum concentration of these drugs and/or TDF – Monitor for dose-related toxicities
<b>Uricosuric agents</b>	<b>Trimethoprim, probenecid:</b> May ↑ serum concentration of these drugs and/or TDF – Monitor for dose-related toxicities

<b>STAVUDINE (D4T)</b> (Updated February 2009)			
<b>Trade Name</b>	Zerit		
<b>Classification</b>	Nucleoside Reverse Transcriptase Inhibitor		
<b>Form</b>	15-, 20-, 30-, 40-mg capsules; 1 mg/mL for oral solution		
<b>Dosing Recommendations</b>	≥60 kg: 40 mg bid <60 kg: 30 mg bid		
<b>Hepatic Impairment Dosing</b>	No adjustment. Use with close monitoring		
<b>Renal Impairment Dosing</b>	<b>CrCl (mL/min)</b>	<b>Weight</b>	<b>Dose</b>
	26-50	<60 kg ≥60 kg	15 mg q12h 20 mg q12h
	10-25	<60 kg ≥60 kg	15 mg q24h 20 mg q24h
	Hemodialysis	Same dose as CrCl 10-25 mL/min; dose after dialysis on day of dialysis	
<b>Food Effect</b>	No food effect		
<b>Oral Bioavailability</b>	86%		
<b>Serum Half-life</b>	1.0 hour		
<b>Intracellular Half-life</b>	3.5 hours		
<b>Elimination</b>	Renal excretion 50%		
<b>Adverse Events</b>	Peripheral neuropathy (most common), pancreatitis, lipodystrophy, rapidly progressive ascending neuromuscular weakness (rare)  Lactic acidosis with hepatic steatosis is a rare but potentially life-threatening toxicity		
<b>FDA Pregnancy Category</b>	C (may be at increased risk of lactic acidosis)		
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed		
<b>Animal Teratogen Studies</b>	Negative (but sternal bone calcium decreases in rodents)		
<b>Black Box Warnings</b>	<p>Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, have been reported with the use of antiretroviral nucleoside analogues alone or in combination.</p> <p>Fatal lactic acidosis has been reported in pregnant women who received a combination of stavudine and didanosine with other ARV combinations. Stavudine and didanosine combination should only be used during pregnancy if the potential benefit clearly outweighs the potential risks.</p> <p>Fatal and non-fatal pancreatitis have occurred when stavudine was part of a combination regimen with didanosine with or without hydroxyurea.</p>		

<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Zidovudine
<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<b>Didanosine:</b> Peripheral neuropathy, lactic acidosis, and pancreatitis have been reported with this combination – Use only if benefits clearly outweigh risks

<b>EFAVIRENZ (EFV)</b> (Updated April 2010)	
<b>Trade Name</b>	Sustiva
<b>Classification</b>	Non-nucleoside Reverse Transcriptase Inhibitor
<b>Form</b>	50-, 200-mg capsules; 600-mg tablets Each Atripla tablet contains EFV 600 mg, FTC 200 mg, and TDF 300 mg
<b>Dosing Recommendations</b>	600 mg once daily, preferably at bedtime on an empty stomach <i>or</i> with FTC and TDF as Atripla, 1 once daily
<b>Hepatic Impairment Dosing</b>	Monitor serum liver enzymes before and during treatment in patients with underlying hepatic disease, including hepatitis B or C co-infection, marked transaminase elevations, or who are taking medications associated with liver toxicity
<b>Food Effect</b>	Take on an empty stomach. Avoid meals with >40-60 g fat. Fatty meal ↑ EFV AUC 28%. Most experts recommended taking on an empty stomach during the first 2 weeks to minimize CNS side effects, but co-administration with food after 2 weeks is acceptable.
<b>Oral Bioavailability</b>	Data not available
<b>Serum Half-life</b>	40-55 hours
<b>Elimination</b>	Metabolized by cytochrome P450 2B6>3A4 (3A4 mixed inducer/inhibitor <i>in vitro</i> , but 3A4 inducer <i>in vivo</i> ); 14%-34% excreted in urine (glucuronidated metabolites, <1% unchanged), 16%-61% in feces
<b>Adverse Events</b>	Rash, <sup>a</sup> central nervous system symptoms (dizziness, somnolence, insomnia, abnormal dreams, confusion, impaired concentration, amnesia), <sup>b</sup> psychiatric symptoms (agitation, depression, depersonalization, hallucinations, euphoria, suicidal ideation)  Increased transaminase levels  False-positive cannabinoid test
<b>FDA Pregnancy Category</b>	D (reported cases of neural tube defect in human fetuses). Birth defects occurred in 14 of 501 live births (first trimester exposure) and 2 of 55 live births (second/third-trimester exposure)
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed
<b>Animal Teratogen Studies</b>	Positive (cynomolgus monkey-anencephaly, anophthalmia, microphthalmia)
<b>Black Box Warnings</b>	None
<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Unboosted atazanavir (for therapy-experienced patients) Fosamprenavir without ritonavir Any other NNRTIs (e.g., DLV, ETR, NVP)  Astemizole, bepridil, cisapride, ergot derivatives, garlic supplements, midazolam, <sup>c</sup> pimozone, rifampentine, St. John's Wort, terfenadine, triazolam
<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<b>Atazanavir:</b> For therapy-naïve patients – Use ATV 400 mg + RTV 100 mg once daily with food

	<p><b>Darunavir:</b> DRV Cmin ↓ 31%; EFV AUC and Cmin ↑ 21% and 17%, respectively – Studied dose lower than FDA approved dose. Consider using DRV/r 600/100 mg twice daily with EFV 600 mg qhs <i>or</i> DRV/r 900/100 mg once daily with EFV 600 mg qhs (based on PK data)</p> <p><b>Fosamprenavir:</b> FPV Cmin ↓ 36% when dosed at FPV 1400 mg + RTV 200 mg once daily – Use FPV 700 mg + RTV 100 mg twice daily, or FPV 1400 mg + RTV 300 mg once daily</p> <p><b>Indinavir:</b> IDV ↓ 31% – ↑ IDV dose to 1000 mg q8h, or consider IDV 800 mg + RTV 200 mg q12h</p> <p><b>Lopinavir/ritonavir:</b> LPV AUC ↓ 40% – ↑ LPV/r dose to 500/125 mg twice daily with food</p> <p><b>Maraviroc:</b> ↓ MVC AUC – ↑ MVC dose to 600 mg twice daily (if not co-administered with a PI)</p> <p><b>Saquinavir:</b> SQV ↓ 62%; EFV ↓ 12% – Use SQV 1000 mg + RTV 100 mg q12h</p> <p><b>Tipranavir/ritonavir:</b> Use TPV 500 mg + RTV 200 mg twice daily</p>
<b>Anticoagulants</b>	<b>Warfarin:</b> Potential ↑ or ↓ warfarin levels – Monitor warfarin levels
<b>Anticonvulsants</b>	<b>Carbamazepine, phenobarbital, phenytoin:</b> Unknown – Avoid co-administration. If no alternatives available, use with close monitoring of anticonvulsant levels
<b>Antifungals</b>	<p><b>Itraconazole, ketoconazole:</b> ↓ itra/keto – Consider alternative antifungal</p> <p><b>Voriconazole:</b> ↑ voriconazole to 400 mg q12h plus EFV 300 mg qhs. EFV should not be co-administered with voriconazole at the standard doses. In severe cases of invasive aspergillosis, consider voriconazole therapeutic drug monitoring</p> <p><b>Posaconazole</b> – avoid concomitant use unless benefit outweighs risk. Monitor posaconazole serum concentrations with co-administration</p>
<b>Antimycobacterials</b>	<p><b>Clarithromycin:</b> CL ↓ 39% – Monitor for efficacy; or, if possible, use alternative agent, such as azithromycin</p> <p><b>Rifabutin:</b> RFB ↓ 35% – ↑ RFB dose to 450-600 mg once daily or 600 mg 3x/wk</p> <p><b>Rifampin:</b> EFV ↓ 22% – Consider ↑ EFV dose to 800 mg once daily in persons &gt;60 kg</p>
<b>Calcium Channel Blocker</b>	<b>Diltiazem:</b> ↓ diltiazem – Diltiazem dose adjustment should be guided by clinical response
<b>Oral Contraceptives</b>	<b>Ethinyl estradiol:</b> EE ↑ 37% – Use alternative barrier form or additional method of contraception. Monitor for contraceptive adverse drug reactions
<b>Selective Serotonin Reuptake Inhibitors (SSRIs)</b>	<b>Sertraline:</b> ↓ sertraline – Sertraline dose adjustment should be guided by clinical response
<b>Synthetic Narcotics</b>	<b>Methadone:</b> ↓ methadone levels significantly – Monitor and titrate dose to effect
<p><sup>a</sup> In clinical trials, EFV was discontinued because of rash in 1.7% of patients. Rare cases of Stevens-Johnson syndrome have been reported.</p> <p><sup>b</sup> Symptoms usually subside spontaneously after 2-4 weeks.</p> <p><sup>c</sup> Patients experiencing serious psychiatric symptoms should be evaluated to assess whether symptoms may be related to EFV. If so, the clinician should discontinue use of EFV if the risks outweigh the benefits.</p>	

<b>NEVIRAPINE (NVP)</b> (Updated February 2009)	
<b>Trade Name</b>	Viramune
<b>Classification</b>	Non-nucleoside Reverse Transcriptase Inhibitor
<b>Form</b>	200-mg tablets; 50 mg/5 mL oral suspension
<b>Dosing Recommendations</b>	200 mg qd x 14 days, then 200 mg bid with or without food
<b>Hepatic Impairment Dosing</b>	Should not be administered in patients with moderate to severe hepatic impairment; patients with hepatic fibrosis or cirrhosis may be at risk for drug accumulation
<b>Food Effect</b>	No food effect
<b>Oral Bioavailability</b>	>90%
<b>Serum Half-life</b>	25-30 hours
<b>Elimination</b>	Metabolized by cytochrome P450 (3A4 inducer); 80% excreted in urine (glucuronidated metabolites, <5% unchanged), 10% in feces
<b>Adverse Events</b>	Rash,* fever, nausea, headache Increased transaminase levels, symptomatic hepatitis, including hepatic necrosis
<b>FDA Pregnancy Category</b>	C (no fetal defect was found in HIVNET 006 trial)
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed
<b>Animal Teratogen Studies</b>	Negative
<b>Black Box Warnings</b>	<p>Severe, life-threatening, and in some cases fatal hepatotoxicity, including fulminant and cholestatic hepatitis, hepatic necrosis and hepatic failure, has been reported in patients treated with nevirapine. In some cases, patients presented with non-specific prodromal signs or symptoms of hepatitis and progressed to hepatic failure. These events are often associated with rash. Women and patients with higher CD4 counts are at increased risk of these hepatic events. Women with CD4 counts &gt;250 cells/mm<sup>3</sup>, including pregnant women receiving chronic treatment for HIV infection, are at considerably higher risk for these events. Patients with signs or symptoms of hepatitis must discontinue nevirapine and seek medical evaluation immediately.</p> <p>Severe, life-threatening skin reactions, including fatal cases, have occurred in patients treated with nevirapine. These have included cases of Stevens-Johnson syndrome, toxic epidermal necrolysis, and hypersensitivity reactions characterized by rash, constitutional findings, and organ dysfunction. Patients developing signs or symptoms of severe skin reactions or hypersensitivity reactions must discontinue nevirapine and seek medical evaluation immediately.</p> <p>It is essential that patients be monitored intensively during the first 18 weeks of therapy with nevirapine to detect potentially life-threatening hepatotoxicity or skin reactions. The greatest risk of severe rash or hepatic events (often associated with rash) occurs in the first 6 weeks of therapy. However, the risk of any hepatic event, with or without rash, continues past this period, and monitoring should continue at frequent intervals. In some cases, hepatic injury has progressed despite discontinuation of treatment. Nevirapine should not be restarted following severe hepatic, skin or hypersensitivity reactions. In addition, the 14-day lead-in period with nevirapine 200 mg daily dosing must be strictly followed.</p>

<b>Drugs to Avoid</b>	<p><b>As part of ARV regimen:</b>  Atazanavir  Other NNRTIs (e.g., ETR, EFV, and DLV)</p> <p>Garlic supplements, ketoconazole, rifampin, rifapentine, St. John's Wort</p>
<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<p><b>Indinavir:</b> IDV ↓ 28% – ↑ IDV dose to 1000 mg q8h, or consider IDV 800 mg + RTV 100 mg bid</p> <p><b>Lopinavir/ritonavir:</b> LPV Cmin ↓ 55% – ↑ LPV/r dose to 600/150 mg (3 tabs or 7.5 mL) bid with food</p> <p><b>Saquinavir:</b> SQV ↓ 25% – Use SQV 1000 mg + RTV 100 mg bid</p>
<b>Anticonvulsants</b>	<b>Carbamazepine, phenobarbital, phenytoin:</b> Unknown – Avoid co-administration. If no alternatives available, use with close monitoring of anticonvulsant levels
<b>Antifungals</b>	<p><b>Fluconazole:</b> Significant ↑ in NVP not observed – Monitor for NVP-associated adverse effects</p> <p><b>Voriconazole:</b> Potential for bi-directional inhibition; may significantly ↓ voriconazole – Monitor voriconazole serum concentrations and nevirapine toxicities</p>
<b>Antimycobacterials</b>	<b>Clarithromycin:</b> NVP ↑ 26%; CL ↓ 31% – Monitor for efficacy or use alternative agent (azithromycin)
<b>Oral Contraceptives</b>	<p><b>Ethinyl estradiol:</b> EE ↓ ~20% – Use alternative or additional method of contraception</p> <p><b>Norethindrone:</b> ↓ norethindrone – Use alternative or additional method of contraception</p>
<b>Synthetic Narcotics</b>	<b>Methadone:</b> ↓ methadone levels significantly – Monitor and titrate dose to effect
* In clinical trials, NVP was discontinued because of rash in 7% of patients. Rare cases of Stevens-Johnson syndrome have been reported.	

NELFINAVIR (NFV) (Updated March 2008)	
<b>Trade Name</b>	Viracept
<b>Classification</b>	Protease Inhibitor
<b>Form</b>	250-, 625-mg tablets, 50 mg/g oral powder
<b>Dosing Recommendations</b>	750 mg tid or 1250 mg bid
<b>Hepatic Impairment Dosing</b>	Should not be used or used with caution in patients with moderate to severe hepatic impairment
<b>Food Effect</b>	Levels increase 2- to 3-fold; take with meal or snack To increase absorption, take with meal containing 500-1000 kcal (20-50% fat)
<b>Oral Bioavailability</b>	20-80%
<b>Serum Half-life</b>	3.5-5 hours
<b>Route of Metabolism</b>	P450 cytochrome 3A4 inhibitor (less than ritonavir)
<b>Storage</b>	Room temperature
<b>Adverse Events</b>	Diarrhea (most common), hyperglycemia, <sup>a</sup> serum transaminase elevation, fat redistribution and lipid abnormalities <sup>b</sup>  Possible increased bleeding episodes in patients with hemophilia
<b>FDA Pregnancy Category</b>	B (of 757 births reported to the Registry, the rate of birth defects was comparable to the general population)
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed
<b>Animal Teratogen Studies</b>	Negative
<b>Black Box Warnings</b>	None
<b>Drugs to Avoid</b>	<b>As part of the ARV regimen:</b> Etravirine Tipranavir/ritonavir  Alprazolam, amiodarone, astemizole, cisapride, ergot derivatives, garlic supplements, lovastatin, midazolam, <sup>c</sup> pimozone, proton pump inhibitors, quinidine, rifampin, rifapentine, simvastatin, St. John's Wort, terfenadine, triazolam
<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<b>Indinavir:</b> Not recommended because of high pill burden  <b>Maraviroc:</b> ↑ MVC AUC – ↓ MVC dose to 150 mg bid  <b>Ritonavir:</b> NFV ↑ 1.5-fold – Consider NFV 500-750 mg + RTV 400 mg bid (limited data; only a modest benefit with RTV boosting)  <b>Saquinavir:</b> Not recommended because of high pill burden

<b>Anticonvulsants</b>	<b>Carbamazepine, phenobarbital, phenytoin:</b> May ↓ NFV levels substantially – Monitor anticonvulsant levels and virologic response. Consider obtaining NFV levels (target C <sub>min</sub> >0.8)
<b>Antifungals</b>	<b>Voriconazole:</b> Potential for bi-directional inhibition – Monitor for toxicities
<b>Antimycobacterials</b>	<b>Azithromycin:</b> ↑ azithromycin – Monitor for adverse effects  <b>Rifabutin:</b> NFV AUC ↓ 32%; RFB ↑ 207% – ↓ RFB dose to 150 mg qd or 300 mg 3x/wk. <sup>d</sup> ↑ NFV dose to 1000 mg q8h. If NFV is boosted with RTV, use RFB 150 mg qod + NFV 500-750 mg bid + RTV 400 mg bid (limited data)
<b>Erectile Dysfunction Agents</b>	<b>Sildenafil:</b> Sildenafil AUC ↑ 2- to 11-fold – Use cautiously, start with reduced dose of 25 mg q48h and monitor for adverse effects  <b>Tadalafil:</b> Substantial ↑ in tadalafil AUC and half-life – Start with a 5-mg dose; do not exceed a single 10-mg dose of tadalafil in 72 hours  <b>Vardenafil:</b> May ↑ vardenafil AUC – Start with 2.5-mg dose; do not exceed a single 2.5-mg dose of vardenafil in 72 hours
<b>Lipid-Lowering Agents</b>	<b>Atorvastatin:</b> ATO AUC ↑ 74% – Use lowest possible starting dose of ATO with careful monitoring
<b>Oral Contraceptives</b>	<b>Ethinyl estradiol:</b> EE ↓ 47% – Use alternative or additional method of contraception <b>Norethindrone:</b> ↓ 18% – Use alternative or additional method of contraception
<b>Synthetic Narcotics</b>	<b>Methadone:</b> May ↓ methadone levels – Monitor and titrate dose if needed. No significant change in the R-methadone (active). No withdrawal symptoms observed
<p><sup>a</sup> Cases of worsening glycemic control in patients with preexisting diabetes, and cases of new-onset diabetes including diabetic ketoacidosis have been reported with the use of all protease inhibitors.</p> <p><sup>b</sup> Patients with hypertriglyceridemia or hypercholesterolemia should be evaluated for risks for cardiovascular events and pancreatitis.</p> <p><sup>c</sup> Can be used with caution as a single dose in a monitored situation for procedural sedation.</p> <p><sup>d</sup> Rifabutin 3x/wk is recommended if CD4 cell count &lt;100 cells/mm<sup>3</sup>.</p>	

INDINAVIR (IDV) (Updated November 2009)	
<b>Trade Name</b>	Crixivan
<b>Classification</b>	Protease Inhibitor
<b>Form</b>	100-, 200-, 333-, 400-mg capsules
<b>Dosing Recommendations</b>	800 mg q8h <i>or</i> IDV 800/RTV 100 mg twice daily <i>or</i> IDV 400/RTV 400 mg twice daily
<b>Hepatic Impairment Dosing</b>	Mild to moderate hepatic impairment due to cirrhosis: 600 mg q8h
<b>Food Effect</b>	<p><b>Unboosted:</b> Take on empty stomach 1 hour before or 2 hours after meals; food ↓ AUC 77%. May take with skim milk or low-fat meal. Drink plenty of fluids (8-10 cups/day)</p> <p>Grapefruit juice ↓ IDV AUC 26%<sup>a</sup>; 1 g/day of Vitamin C ↓ IDV AUC 14%, ↓ C<sub>min</sub> 32%</p> <p><b>Boosted:</b> No food effect</p>
<b>Oral Bioavailability</b>	65% (on empty stomach)
<b>Serum Half-life</b>	1.5-2 hours
<b>Route of Metabolism</b>	P450 cytochrome 3A4 inhibitor and substrate
<b>Storage</b>	Room temperature
<b>Adverse Events</b>	<p>GI intolerance, nausea, headache, asthenia, blurred vision, dizziness, rash, metallic taste, alopecia, paronychia</p> <p>Nephrolithiasis, hyperglycemia,<sup>b</sup> fat redistribution and lipid abnormalities,<sup>c</sup> thrombocytopenia, hemolytic anemia, possible increased bleeding episodes in patients with hemophilia, increased indirect bilirubinemia (inconsequential)</p>
<b>FDA Pregnancy Category</b>	C (potential ↑ bilirubin and nephrolithiasis in neonates)
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed
<b>Animal Teratogen Studies</b>	Negative (but extra ribs in rodents)
<b>Black Box Warnings</b>	None
<b>Drugs to Avoid</b>	<p><b>As part of the ARV regimen:</b>            Atazanavir (potential for additive increased indirect bilirubin)            Etravirine            Tipranavir/ritonavir</p> <p>Alprazolam, astemizole, cisapride, ergot derivatives, garlic supplements, lovastatin, midazolam,<sup>d</sup> pimozone, ranolazine, rifampin, rifapentine, simvastatin, St. John's Wort, terfenadine, triazolam</p>

<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<p><b>Darunavir:</b> DRV AUC and C<sub>min</sub> ↑ 24% and 44%, respectively; IDV AUC and C<sub>min</sub> ↑ 23% and 125% respectively. Dose not established. Co-administration may ↑ risk of nephrolithiasis</p> <p><b>Delavirdine:</b> ↑ IDV – ↓ IDV dose to 600 mg q8h</p> <p><b>Didanosine:</b> IDV AUC ↓ 84% – Take IDV 1 hour before or after buffered ddi on an empty stomach (no interaction with ddi EC)</p> <p><b>Efavirenz:</b> IDV ↓ 31% – ↑ IDV dose to 1000 mg q8h, or consider IDV 800 mg + RTV 200 mg q12h</p> <p><b>Lopinavir/ritonavir:</b> ↑ IDV – ↓ IDV dose to 600 mg twice daily or 666 mg twice daily</p> <p><b>Maraviroc:</b> ↑ MVC AUC – ↓ MVC dose to 150 mg twice daily</p> <p><b>Nelfinavir:</b> IDV ↑ 50%; NFV ↑ 80% – Consider IDV 1200 mg + NFV 1250 mg twice daily (limited data)</p> <p><b>Nevirapine:</b> IDV ↓ 28% – ↑ IDV dose to 1000 mg q8h, or consider IDV + RTV</p> <p><b>Ritonavir:</b> IDV ↑ 2- to 5-fold – Use IDV 800 mg + RTV 100 mg twice daily; renal events may be increased with higher IDV C<sub>max</sub></p>
<b>Anticonvulsants</b>	<b>Carbamazepine:</b> Markedly ↓ IDV – Consider phenytoin, phenobarbital, valproic acid, levetiracetam, or topiramate
<b>Antidepressants</b>	<b>Trazodone:</b> May lead to substantial ↑ in trazodone – Consider ↓ dose of trazodone
<b>Antifungals</b>	<p><b>Itraconazole:</b> ↓ unboosted IDV dose to 600 mg tid – Do not exceed 200 mg itraconazole twice daily</p> <p><b>Ketoconazole:</b> IDV ↑ 68% – ↓ IDV dose to 600 mg tid</p> <p><b>Voriconazole:</b> No interaction with IDV but when IDV is boosted with RTV, potential for bi-directional inhibition – Monitor for toxicities</p>
<b>Antimycobacterials</b>	<b>Rifabutin:</b> IDV ↓ 32%; RFB ↑ 204% – ↓ RFB dose to 150 mg once daily or 300 mg 3x/wk. <sup>e</sup> ↑ IDV dose to 1000 mg q8h. If IDV is boosted with RTV, use RFB 150 mg qod + IDV 400 mg + RTV 400 mg twice daily
<b>Erectile Dysfunction Agents</b>	<p><b>Sildenafil:</b> Sildenafil AUC ↑ 3-fold – Use cautiously, start with reduced dose of 25 mg q48h and monitor for adverse effects</p> <p><b>Tadalafil:</b> Substantial ↑ in tadalafil AUC and half-life – Start with a 5-mg dose, and do not exceed a single dose of 10 mg in 72 hours</p> <p><b>Vardenafil:</b> Vardenafil ↑ 16-fold; IDV (unboosted) ↓ 30% – For unboosted IDV, consider using sildenafil instead; for IDV + RTV, do not exceed 2.5 mg vardenafil in 72 hours</p>
<b>Lipid-Lowering Agents</b>	<b>Atorvastatin:</b> Potential for ATO AUC ↑ – Use lowest possible starting dose of ATO with careful monitoring (consider pravastatin or rosuvastatin)

- <sup>a</sup> Contrary to package insert, one study found no effect on IDV pharmacokinetics when given with orange juice or grapefruit juice (Penzak SR, et al. *J Clin Pharmacol* 2002;42:1165).
- <sup>b</sup> Cases of worsening glycemic control in patients with preexisting diabetes, and cases of new-onset diabetes including diabetic ketoacidosis have been reported with the use of all protease inhibitors.
- <sup>c</sup> Discontinuation of PIs may be required to reverse fat redistribution. Patients with hypertriglyceridemia or hypercholesterolemia should be evaluated for risks for cardiovascular events and pancreatitis.
- <sup>d</sup> Can be used with caution as a single dose in a monitored situation for procedural sedation.
- <sup>e</sup> Rifabutin 3x/wk is recommended if CD4 count <100 cells/mm<sup>3</sup>.

LOPINAVIR/RITONAVIR (LPV/R) (Updated January 2010)	
<b>Trade Name</b>	Kaletra
<b>Classification</b>	Protease Inhibitor
<b>Form<sup>a</sup></b>	LPV 200 mg/RTV 50 mg film-coated tablets LPV 100 mg/RTV 25 mg film-coated tablets LPV 80 mg/RTV 20 mg per mL oral solution (contains 42% alcohol)
<b>Dosing Recommendations</b>	<p><b>For therapy-naïve patients:</b>  LPV 400 mg/RTV 100 mg (2 tablets) twice daily with or without food <i>or</i>  LPV 800 mg/RTV 200 mg (4 tablets) once daily with or without food<sup>b</sup> <i>or</i>  LPV 400 mg/RTV 100 mg (5 mL) twice daily with food <i>or</i>  LPV 800 mg/RTV 200 mg (10 mL) once daily with food<sup>b</sup></p> <p><b>For therapy-experienced patients:</b>  LPV 400 mg/RTV 100 mg (2 tablets) twice daily with or without food <i>or</i>  LPV 400 mg/RTV 100 mg (5 mL) twice daily with food</p> <p><i>(Once-daily administration is not recommended in therapy-experienced patients)</i></p>
<b>Hepatic Impairment Dosing</b>	Use with caution in patients with hepatic impairment
<b>Food Effect</b>	<p><b>Tablets:</b> May take with or without food; swallow whole</p> <p><b>Oral solution:</b> Must take with food. To increase absorption by 50%-80%, take with meal containing &gt;15 g of fat</p>
<b>Oral Bioavailability</b>	Not determined in humans
<b>Serum Half-life</b>	5-6 hours
<b>Route of Metabolism</b>	P450 cytochrome 3A4 inhibitor and substrate (may be an inducer at steady-state)
<b>Storage</b>	<p><b>Tablets:</b> store at room temperature. Do not expose to high humidity outside original container for longer than 2 weeks</p> <p><b>Refrigerated oral solution:</b> stable until expiration date on label. If stored at room temperature, stable for 2 months</p>
<b>Adverse Events</b>	<p>GI intolerance, nausea, vomiting, diarrhea, asthenia</p> <p>Rare: Pancreatitis, including marked triglyceride elevations; in some cases, fatalities have been observed</p> <p>PR interval prolongation may occur. Second- and third-degree AV block have been reported. Use with caution in patients with underlying structural heart disease, preexisting conduction system abnormalities, ischemic heart disease or cardiomyopathies, as these patients may be at increased risk for developing cardiac conduction abnormalities. The impact on the PR interval of co-administration of LPV/r with other drugs that prolong the PR interval (including calcium channel blockers, beta-adrenergic blockers, digoxin and atazanavir) has not been evaluated; co-administration of LPV/r with these drugs should be undertaken with caution, particularly with those drugs metabolized by CYP3A.</p>

	<p>QT interval prolongation and torsade de pointes have been reported. Avoid use in patients with congenital long QT syndrome, those with hypokalemia, and with other drugs that prolong the QT interval.</p> <p>Elevated serum transaminase, hyperglycemia,<sup>c</sup> fat redistribution and lipid abnormalities,<sup>d</sup> possible increased bleeding episodes in patients with hemophilia</p> <p>Increased potential for sildenafil-associated adverse events such as visual abnormalities, hypotension, prolonged erections, and syncope when co-administered when sildenafil is used for the treatment of pulmonary arterial hypertension. Avoid high-dose sildenafil and use with caution.</p>
<b>FDA Pregnancy Category</b>	C
<b>Long-Term Animal Carcinogenicity Studies</b>	Not completed
<b>Animal Teratogen Studies</b>	Negative (but delayed skeletal ossification and increase in skeletal variations in rats at maternally toxic doses)
<b>Black Box Warnings</b>	None
<b>Drugs to Avoid</b>	<p><b>As part of the ARV regimen:</b>  Darunavir/ritonavir  Tipranavir/ritonavir</p> <p>Alfuzosin, alprazolam, astemizole, cisapride, ergot derivatives, flecainide, fluticasone, garlic supplements, lovastatin, midazolam,<sup>e</sup> pimozone, propafenone, ranolazine, rifampin,<sup>f</sup> rifapentine, high-dose sildenafil, salmeterol, simvastatin, St. John's Wort, terfenadine, triazolam</p>
<b>Cautious Use or Dose Adjustment</b>	
<b>Antiretrovirals</b>	<p><b>Atazanavir:</b> ATV 300 mg once daily plus LPV/r 400/100 mg twice daily. Monitor for PR interval prolongation</p> <p><b>Efavirenz:</b> LPV AUC ↓ 40% – ↑ LPV/r dose to 500/125 mg twice daily with food</p> <p><b>Etravirine:</b> Use standard dose</p> <p><b>Fosamprenavir:</b> Not recommended by some. Consider FPV 1400 mg twice daily plus LPV/r 600/150 mg twice daily. Consider therapeutic drug monitoring</p> <p><b>Indinavir:</b> ↑ IDV – ↓ IDV dose to 600 mg twice daily or 666 mg twice daily</p> <p><b>Maraviroc:</b> ↑ MVC AUC – ↓ MVC dose to 150 mg twice daily</p> <p><b>Nevirapine:</b> LPV C<sub>min</sub> ↓ 55% – ↑ LPV/r dose to 500/125 mg twice daily with food</p> <p><b>Raltegravir:</b> Use standard dose</p> <p><b>Saquinavir:</b> SQV AUC and C<sub>min</sub> ↑ – Use SQV 1000 mg twice daily</p>
<b>Antiarrhythmics</b>	<b>Amiodarone, bepridil, lidocaine (systemic), quinidine:</b> ↑ antiarrhythmics – Use with caution. Monitor concentrations of antiarrhythmics

<b>Anticonvulsants</b>	<p><b>Carbamazepine, phenobarbital, phenytoin:</b> Levels ↑ when co-administered with RTV – Use with caution; monitor anticonvulsant levels</p> <p><b>Valproic acid:</b> May ↓ valproic acid. LPV AUC ↑ 75%</p> <p><b>Lamotrigine:</b> LPV not affected, but lamotrigine AUC ↓ 50%. Titrate to effect</p>
<b>Antidepressants</b>	<p><b>Trazodone:</b> Trazodone AUC ↑ 240%, Cmax ↑ 34% – Use lowest dose; monitor for CNS and CV adverse effects</p> <p><b>Bupropion:</b> Bupropion AUC ↓ 46%. Titrate to effect</p>
<b>Antifungals</b>	<p><b>Itraconazole:</b> Itraconazole ↑ – Use with caution, do not exceed 200 mg itraconazole daily</p> <p><b>Ketoconazole:</b> LPV AUC ↓ 13%; keto ↑ 3-fold – Use with caution, do not exceed 200 mg keto daily</p> <p><b>Voriconazole:</b> Potential for bi-directional inhibition; when boosted with RTV, may significantly ↓ voriconazole – Monitor for toxicities and voriconazole serum concentrations (target trough &gt;2 mcg/mL)</p>
<b>Antihypertensive</b>	<p><b>Beta-blocker:</b> May ↑ PR interval; use with close monitoring</p> <p><b>Calcium channel blocker:</b> May ↑ PR interval; use with close monitoring</p>
<b>Antimycobacterials</b>	<p><b>Clarithromycin:</b> CL AUC ↑ 77% – Adjust CL dose for moderate and severe renal impairment. For creatinine clearance 30-60 mL/min, administer clarithromycin 500 mg orally once daily. For creatine clearance &lt;30 mL/min administer clarithromycin 250 mg orally once daily. Monitor for QTc prolongation with co-administration</p> <p><b>Rifabutin:</b> RFB AUC ↑ 3-fold; 25-O-desacetyl metabolite ↑ 47.5-fold – ↓ RFB dose to 150 mg qod. Monitor rifabutin serum concentrations</p>
<b>Cardiac Glycosides</b>	<p><b>Digoxin:</b> Digoxin AUC ↑ 81% with LPV/r co-administration. Monitor digoxin serum concentrations and PR interval with co-administration</p>
<b>Erectile Dysfunction Agents</b>	<p><b>Sildenafil:</b> Sildenafil AUC ↑ 11-fold when co-administered with RTV – Use cautiously, start with reduced dose of 25 mg q48h, and monitor for adverse effects</p> <p><b>Tadalafil:</b> Substantial ↑ in tadalafil AUC and half-life – Start with a 5-mg dose, and do not exceed a single 10-mg dose in 72 hours</p> <p><b>Vardenafil:</b> May substantially ↑ vardenafil AUC – Start with a 2.5-mg dose, and do not exceed a single 2.5-mg dose in 72 hours</p>
<b>Lipid-Lowering Agents</b>	<p><b>Atorvastatin:</b> ATO AUC ↑ 5.88-fold – Use lowest possible starting dose of ATO with careful monitoring. Consider pravastatin</p> <p><b>Rosuvastatin:</b> ROS AUC ↑ 108%. Use lowest possible starting dose 5-10 mg/day</p> <p><b>Pravastatin:</b> Pravastatin AUC ↑ 33%. Use standard dose</p>
<b>Oral Contraceptives</b>	<p><b>Ethinyl estradiol:</b> EE ↓ 42% – Use alternative or additional method of contraception</p>

<b>Pulmonary Hypertension Agents</b>	<b>Bosentan:</b> LPV/r ↑ bosentan AUC 48-fold on day 4 and 5-fold on day 10 (steady-state). Co-administer bosentan at a reduced dose of 62.5 mg only after RTV dosing has reached steady-state (after 10 days of RTV). If patient is taking bosentan, discontinue bosentan for $\geq 36$ hrs prior to initiating RTV and restart bosentan 62.5 mg 10 days after initiating RTV
<p><sup>a</sup> Capsules discontinued in early 2006.</p> <p><sup>b</sup> Lopinavir/ritonavir should not be administered as a once-daily regimen in combination with efavirenz, nevirapine, amprenavir, or nelfinavir.</p> <p><sup>c</sup> Cases of worsening glycemic control in patients with preexisting diabetes, and cases of new-onset diabetes including diabetic ketoacidosis have been reported with the use of all protease inhibitors.</p> <p><sup>d</sup> Discontinuation of PIs may be required to reverse fat redistribution. Patients with hypertriglyceridemia or hypercholesterolemia should be evaluated for risks for cardiovascular events and pancreatitis.</p> <p><sup>e</sup> Can be used with caution as a single dose in a monitored situation for procedural sedation.</p> <p><sup>f</sup> In one small study, an increased dose of LPV/r 800/200 mg was used to offset rifampin-inducing activity of LPV; the standard dose of rifampin was used. 28% of patients discontinued this regimen due to increases in LFTs. The safety of this combination has not been established, and if used, close monitoring, including measuring LPV concentrations, is recommended.</p>	

## APPENDIX B

**TABLE 1**  
**OCCUPATIONAL EXPOSURE TO HIV: COMPARISON OF NYSDOH AND CDC**  
**RECOMMENDATIONS**

NYSDOH Recommendations	CDC Recommendations
<p><b>Indication for PEP</b></p> <p>Percutaneous or mucocutaneous exposure with blood or visibly bloody fluid or other potentially infectious material.</p>	<p><b>Indication for PEP</b></p> <p>Percutaneous or mucocutaneous exposure with blood or visibly bloody fluid <b>and</b> the source patient is HIV infected or at risk for HIV infection.</p>
<p><b>Prophylaxis Recommendations</b></p> <p>The standard of clinical practice for the treatment of HIV is triple-drug ARV therapy. Whenever the decision to prescribe ARV therapy is made, including PEP, the treatment should meet this standard and not be a potentially less effective regimen. In the event of HIV seroconversion, a potent triple-drug regimen is critical to the success of early management.</p> <p>If the source patient is known to be HIV-positive, the specific antiretroviral treatment history, including viral load and resistance testing data, should be used to determine the PEP regimen in consultation with an HIV Specialist.</p>	<p><b>Prophylaxis Recommendations</b></p> <p>Prophylaxis recommendations must be tailored to the specific characteristics of the exposure and the stage of disease of the source (if available).</p> <p><b>The specific regimen is then determined based on exposure type and stage of HIV disease in the source.*</b></p>
<p><b>Recommended Antiretroviral Regimens†</b></p> <p>Zidovudine 300 mg po bid +  Lamivudine 150 mg po bid } or Combivir 1 po bid  <b>plus</b>  Tenofovir 300 mg po qd</p> <p style="text-align: center;"><b>OR</b></p> <p>Zidovudine 300 mg po bid  <b>plus</b>  Emtricitabine 200 mg po qd + } or Truvada 1 po qd  Tenofovir 300 mg po qd</p>	<p><b>Recommended Antiretroviral Regimens</b></p> <p><u>Basic Regimen:</u></p> <p>Zidovudine (ZDV) 600 mg/day in  2 or 3 divided doses } <b>(or Combivir  1 po bid)</b>  <b>plus</b>  Lamivudine (3TC) 150 mg bid</p> <p><u>Basic Regimen Plus:</u></p> <p>Indinavir (IDV) 800 mg q8h <b>or</b>  Nelfinavir 750 mg q8h or 1250 mg bid <b>or</b>  Efavirenz 600 mg qhs <b>or</b>  Abacavir 300 mg bid</p> <p><b>Duration of PEP: 4 weeks</b></p>
<p><b>HIV Antibody Testing of Healthcare Worker</b></p> <ul style="list-style-type: none"> <li>• Baseline</li> <li>• 1 month post-exposure</li> <li>• 3 months post-exposure</li> <li>• 6 months post-exposure‡</li> </ul>	<p><b>HIV Antibody Testing of Healthcare Worker</b></p> <ul style="list-style-type: none"> <li>• Baseline</li> <li>• 1 month post-exposure</li> <li>• 3 months post-exposure</li> <li>• 6 months post-exposure</li> </ul>
<p><b>Initiation of PEP</b></p> <p>PEP should be promptly initiated ideally within 2 hours and no later than 36 hours after the exposure to optimize effectiveness.</p>	<p><b>Initiation of PEP</b></p> <p>Occupational exposure should be regarded as an urgent medical concern, and PEP should be started as soon as possible after the exposure. For highest risk exposures, PEP may be initiated up to 1 to 2 weeks post-exposure.</p>

\* See CDC. Updated USPHS Guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. *MMWR Recomm Rep* 2001;50(RR-11):1-67.

† See Appendix A for dosing recommendations in patients with renal impairment.

‡ Seroconversion virtually always detected by 6 months.

## **APPENDIX C**

### **INFORMED CONSENT FORM DOH-4054**

For the most recent Informed Consent forms, please visit:  
[www.nyhealth.gov/forms/doh-4054.pdf](http://www.nyhealth.gov/forms/doh-4054.pdf)

## APPENDIX D

### HIV COUNSELING AND EDUCATION FOR HEALTHCARE WORKERS AFTER AN OCCUPATIONAL EXPOSURE

Although the risk of HIV transmission from an occupational exposure is low when compared with hepatitis B virus (HBV) and even hepatitis C virus (HCV), the emotional impact of such an exposure on the worker is often profound. Studies have shown that healthcare workers (HCWs) experience acute psychological distress after an exposure. For some, it may trigger a serious psychological and/or career crisis; exacerbate existing personal problems, such as marital difficulties; create fear of social repercussions; and disrupt sexual relationships and childbearing plans. The need for comprehensive counseling that addresses both psychosocial and disease transmission issues applicable to all bloodborne viruses is evident.

This section provides guidance on issues that may present during each phase of post-exposure management. Although it is intended for situations in which the HIV exposure is known, the principles apply to a number of circumstances (e.g., the HCW is waiting for the patient's test results or the patient has refused testing), each of which creates its own anxiety for HCWs.

The term "counselor" will be used to denote any individual who is providing psychological support for an exposed HCW. Regardless of title, counselors should be well versed in issues of HIV infection, available support services, and the general concerns of exposed and infected individuals.

Several subjects should be covered in post-exposure counseling, including assessment of transmission risk from the exposure, information about medical follow-up and laboratory testing, and education to prevent secondary transmission. The counselor must assess the emotional status and ability of the HCW to be actively involved in the decision-making process and must gauge accordingly and tailor to each situation the scope and timing of information provided.

#### Initial Counseling Session

The initial counseling session should occur as soon as possible after the exposure and seek to accomplish the following tasks:

- **Establish a trusting environment.** This is among the most important aspects of post-exposure counseling; the HCW needs the counselor's full attention. One should communicate support, concern, confidence, competence, and confidentiality. The worker may need to hear that his/her job is not in jeopardy and that the purpose of counseling is not punitive in nature.
- **Assess the HCW's emotional status.** Acknowledge feelings the HCW may be experiencing and allow for their expression. Each person's coping strategies are unique; reactions may include hysteria, anger, fear, disbelief, silent acceptance, etc.
- **Describe the post-exposure protocol.** Indicate what services are provided by the employer, who will be involved in the process, what support services are available and how they can be accessed, and what is expected from the HCW. If there are needs

- **Review the relative risk of transmission represented by the specific exposure.** Scientifically accurate information about the known risk of seroconversion following an occupational exposure to HIV should be accessible to the counselor and employee. Discussion should include the significance of the exposure and whether similar events have led to infection. Counselors should periodically update their knowledge of relevant epidemiological data to ensure that current information is provided.
- **Obtain informed consent for HIV testing as required by New York State law (Article 27-F).**
- **Describe confidential HIV testing.** The most important reason for immediate post-exposure testing is to establish a baseline record of the HCW's HIV status at the time of exposure. In the rare event of seroconversion, subsequent claims for Workers' Compensation or avenues of legal recourse will rely on the establishment of this fact. For this reason, anonymous testing programs, which use no personal identifiers, are not recommended for individuals who desire documentation of testing. If there is reluctance to receive confidential testing through the institution's resources, the counselor may suggest that the worker see his/her personal healthcare provider or visit an alternative site that offers confidential testing.
- **Explain HIV testing.** Describe the testing process and interpretation of various test results within the context of post-exposure management. If test methods other than ELISA and Western blot are used (e.g., PCR), these also should be described.

Most individuals who become infected will develop antibodies within 1 month after exposure. For this reason, HIV antibody testing after an occupational exposure is performed serially (i.e., baseline, 1, 3, and 6 months). Repeatedly negative/nonreactive test results are more likely to represent the true serostatus of the individual, assuming there have been no other exposures in the interim.

- **Discuss the significance of personal risk behavior** and, if present, the possibility that a positive/reactive test result will be obtained on baseline testing.
- **Educate the HCW on prevention of HIV transmission during the post-exposure period.** Professional judgement should determine the scope and timing of this discussion, taking into consideration the event-specific risks. Exposed HCWs should be advised to:
  - use condoms or sexual abstinence to prevent sexual transmission and avoid pregnancy;
  - stop breastfeeding, if applicable;
  - defer from donating blood, plasma, organs, tissue, or sperm.

Post-exposure precautions should be maintained until HIV infection in the source and/or HCW has been ruled out. If a woman is pregnant, she should consult with her physician about the risk of infection to her fetus.

The clinical record should document that education to prevent transmission was provided.

- **Discuss whether and with whom to share information about the exposure.** A supportive environment is important to help with any emotional crisis that might follow. However, prudence in choosing with whom information about an HIV exposure is shared can avoid unanticipated repercussions. The worker also needs to consider the impact of this information on family, friends, and co-workers. Remind the worker of his/her continued obligation to protect the identity/confidentiality of the source individual.
- **Establish a follow-up plan.** It is good practice to see the employee again soon after the exposure (i.e., within 24-48 hours), to assess his/her coping abilities and answer any questions that may have arisen in the interim. At that time, the need for additional counseling can be determined. Give the HCW a telephone number or contact person to use in the event of a crisis.
- **Explain that HIV test results should be given in person.** Schedule a return appointment, reserving enough time in the event a positive/reactive result is received. Give special attention to the scheduling process and the location of counseling sites in order to respond with sensitivity to the issues of confidentiality and privacy. Acknowledge that waiting for HIV test results is an anxiety-provoking situation, and offer referral for support services.

Prior to the follow-up session, the counselor should review the range of needs that may be identified and should have on hand a list of resources for referral.

### **Ongoing Counseling**

It may be necessary to establish ongoing counseling for the worker and possibly his/her spouse or sexual partner. In some cases, co-workers who witnessed the event, or who inadvertently contributed to the exposure, may need counseling support as well. The services the institution is able to offer and the circumstances that necessitate referral to another provider should be clearly defined.

## APPENDIX E

### POST-TEST COUNSELING FOLLOWING OCCUPATIONAL EXPOSURE

This section guides counselors in giving HIV test results based on the stage of post-exposure follow-up and HIV antibody test result.

#### I. General Concepts

- Give the test results immediately. A preliminary greeting, while appropriate, should not prolong the HCW's anxiety. Each HCW comes with his/her own expectation of what he/she will be told, which may not be consistent with the result. This expectation will be influenced by several factors including the stage of follow-up, level of risk represented by the exposure, and any personal risk factors.
- Allow time to react to the information provided. Depending on the test result, many emotions may surface. The HCW's expectations, anxiety level, relief, joy, disbelief, sadness, anger, or the absence of emotion may be seen.
- Explain the significance of the result. This will vary depending on what the result is and at what stage in the post-exposure series the test was performed. Counselors should give accurate information without creating false expectations.
- Evaluate the HCW's understanding of the information and offer clarification as indicated; provide literature and/or written instruction as needed.
- Review risk reduction recommendations, and schedule the next appointment, as indicated.

#### II. Interpretation of Test Results

##### A. Negative Test Result

**Baseline test:** At the time of exposure, the HCW shows no evidence of HIV infection. This, however, does not indicate that infection has not occurred, especially if testing was performed within a few days of the exposure. Antibodies are usually produced within 1 to 3 months after infection but may take longer (in rare instances).

**Follow-up test:** The significance is determined by when it was performed during the follow-up series and the magnitude of the exposure. If the test is the first in the follow-up series (i.e., 6 weeks post-exposure), it is an encouraging sign, but the possibility of transmission cannot be ruled out.

At the 3-month stage, it is reasonable to tell the HCW that a negative result is a good indication that transmission has not occurred. However, a negative test at 6 months will provide greater reliability.

## B. Indeterminate Test Result

Conveying an “indeterminate” result is problematic because of its uncertainty and because such a result is often difficult for HCWs to understand and accept.

**General interpretation:** An “indeterminate” HIV test result may be reported when the ELISA and Western blot test results do not conform to standards for reactive or non-reactive classification. In explaining the significance of this result, the counselor should first determine the laboratory-specific criteria used and the recommended explanation. Among the factors that the employee should be told can result in such an outcome are:

- an unrelated health condition, infection with HIV-2 or unusual HIV-1 subtypes, or some other unknown cause.
- less commonly, the HCW is in the window period of HIV seroconversion, especially if this test followed a negative baseline HIV antibody test.

**Submission of another blood sample:** Another blood sample submission should be encouraged. The testing laboratory should provide instructions for specimen resubmission and any additional clinical information that should be obtained.

In rare circumstances, an indeterminate result may be reported in subsequent HIV tests. If this should occur, the HCW should be referred by the counselor for clinical evaluation.

## C. Positive Test Result

This test result indicates that the HCW is infected with HIV and able to transmit it to others. It does not mean the HCW has AIDS or will develop AIDS in the near future.

**Baseline test:** If the specimen was obtained at the time of the exposure or within 2 weeks of the incident (the earliest point when antibodies can be detected), the infection is not a result of that specific event. If the baseline test was obtained after this period, it cannot be known from this test alone whether infection was present at the time of exposure or whether transmission from the recent occupational exposure occurred.

**Follow-up test:** A positive HIV antibody test in the post-exposure follow-up period is supportive evidence that occupational transmission has occurred, assuming there has been no interim exposure to infection, occupational or non-occupational.

## III. Counseling the Occupationally HIV-Infected HCW

Occupational HIV seroconversion, although rare, has a sobering impact on all involved: the affected employee; his/her family, friends and significant others; the counselor who has to give the test result; and the institution. There are many issues that will need to be addressed, and counseling the occupationally HIV-infected HCW is the first step in what will become a lengthy process for the HCW and the institution. The following describes in more detail the type of interaction that may take place:

**Communicate the result in a straightforward manner, and allow the employee time to react. Do not anticipate a specific response; be prepared to support whatever reaction occurs.**

**Explain the significance of the result.** The HCW is HIV infected, most likely as a result of the reported incident.

**Offer the opportunity to have a second test** to verify the positive/reactive result.

**Address immediate concerns,** including fear and the implications for one's own personal health and mortality; concern about the reaction of family members and sexual partners; anxiety about job implications, especially if the HCW performs invasive procedures; and concerns that confidentiality might be breached.

**Discuss the health implications.** Having HIV infection does not mean the HCW has AIDS; however, it is important that the HCW establish a relationship with a physician experienced in HIV care who can monitor the HCW's health status and recommend the appropriate drug regimen.

**Discuss implications for secondary transmission.** The HCW needs to understand that he/she is capable of transmitting the virus and will need information to prevent the spread through sexual contact. Recommendations for infection control, appropriate to the HCW's job responsibilities and nature of patient interactions, should be reinforced. Based on the HCW's job or professional responsibilities, a lengthier discussion and referral to an expert panel may be indicated.

**Develop a plan of action.** The next several hours and days are a critical time emotionally for the HCW. In preparing a plan of action, some of the issues that should be explored include:

**Crisis intervention:**

- What are the worker's plans for the next 24 hours? How will he/she get home that day?
- Does the worker clearly understand the meaning of the test result?
- Does the HCW have a support system in place? Is a referral for psychosocial services or to a community-based support organization appropriate? (The counselor should provide referrals for emergency and ongoing psychological support services to all individuals undergoing HIV testing.)
- Does the HCW need assistance in disclosing results of the test to his/her partner(s)? What reaction is expected? (Remind the worker to carefully consider decisions to disclose HIV-related information to co-workers or others.)

**Referral to medical care:**

- Is the need for early medical evaluation clearly understood?
- Does the worker understand the importance of continuous adherence to HAART?

- Is the worker currently under the care of a physician? If so, does he/she anticipate any difficulty in divulging the results of the HIV test to the physician? If the worker does not have a physician or if he or she would like a referral to another provider, is the counselor able to assist? If not, where can referral information be obtained?
- What medical services are available through the employer?
- Will the HCW have to bear any financial burden?

### **Plan for referrals and follow-up:**

Write out a summary of the action plan that was developed with the HCW. Include referrals made for medical and psychosocial intervention. In some cases, it may be appropriate to delay discussion of certain issues until the follow-up visit when a more comprehensive dialogue can take place. In such instances, the follow-up should occur within a few days of giving the positive/reactive test result.

During the initial session, or in subsequent appointments, a review of the modes of HIV transmission as well as risk-reduction strategies and basic infection control guidelines for the home and workplace should be discussed with the worker. The conversation should proceed in an interactive manner, allowing the employee to ask specific questions and allowing the counselor to clarify any misperceptions.

### **Written information:**

Much of the information provided in the post-test counseling session may not be clearly understood by the affected worker. For this reason, printed material that highlights the recommendations and instructions given should be made available to the HCW for future reference. A list of referrals for medical and psychosocial support services should be included in the information package.

## APPENDIX F

### POST-EXPOSURE MANAGEMENT: EMPLOYER ISSUES AND RESPONSIBILITIES

Organizations that employ health professionals or other persons who are at risk for occupational exposure to blood, body fluids, or other potentially infectious materials are generally required to establish policies and procedures that guide the management of such exposures. Private employers subject to OSHA must conform to the OSHA Bloodborne Pathogen Standard (OSHA Bloodborne Pathogen Standard 29 CFR, Part 1910.1030, and Compliance Directive CPL 2-2.44D, 11/05/99, Enforcement Procedures for the Occupational Exposure to Bloodborne Pathogens), and public employers are subject to PESH regulations. OSHA and PESH standards with regard to occupational exposure to bloodborne pathogens are identical. These regulations require that a management plan be in place.

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

#### Definition of Persons Covered:

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

#### Access to Occupational Health Services:

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

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

- Post-exposure evaluation and follow-up post-exposure vaccinations.
- A full course of post-exposure prophylaxis medications, at no cost to the employee.

- Care provided under the supervision of a licensed physician or other licensed healthcare professional.
- The performance of laboratory tests by an accredited laboratory.
- Supportive counseling.

**Federal law requires covered employers to ensure that all medical evaluations and procedures, vaccines, and post-exposure prophylaxis are made available to the employee within a reasonable time and place and are made available at no cost to the employee** (OSHA, 29 CFR, Part 1910.1030, CPL 2-2.44D, 11/05/99, Enforcement Procedures for the Occupational Exposure to Bloodborne Pathogens).

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

- PEP will be made available within 1 to 2 hours of exposure, ideally within 1 hour.
- A “starter kit” or 3-day supply of the PEP will be made available to the employee.
- A mechanism is in place to provide the balance of the PEP medications needed to complete the 4-week regimen to the employee at no cost.

#### **Access to Source Patient HIV-Related Information:**

If already part of the health care team, the exposed employee may have access to the medical record and know the HIV status of the source patient, as well as information about drug resistance. Alternatively, the patient may have signed an informed consent form (see Appendix C) authorizing disclosure of this information to the exposed worker or to undergo consented HIV testing with disclosure of the test results to the exposed worker. When neither of these situations apply, New York regulations (10 NYCRR part 63.8m) now authorize disclosure of existing HIV-related information to persons who have been exposed in the workplace when significant risk exposure has occurred.

#### **Consented Testing of the Source Patient for HIV:**

- The source individual's blood should be tested as soon as feasible after consent is obtained to determine HIV infectivity. Informed consent from the source patient should be obtained utilizing the form DOH-4054 (Rev. 6/00) “Informed Consent to Perform a Confidential HIV Test and Authorization for Release of HIV-Related Information for Purposes of Providing Post-Exposure Care to a Healthcare Worker Exposed to a Patient's Blood or Body Fluids” (see Appendix C). If consent is not obtained for HIV testing, the employer should document that consent cannot be obtained.

- When the source individual is already known to be infected with HBV, HCV, or HIV, testing for the source individual's known HBV, HCV, or HIV status need not be repeated. Testing for other bloodborne pathogens should still occur.
- With a signed release, results of the source individual's HIV testing should be made available to the exposed employee.
- Information related to drug regimens, and, if available, resistance information should be made available to the exposed employee to determine the best regimen for the employee.

The employer is responsible for establishing and implementing policies to protect the confidentiality of both the exposed employee and the exposure source (PH Law 27-F & 21 Title 111).

### **Disclosure of HIV-Related Information Under 10 NYCRR part 63.8 (m):**

**As of June 1, 2000, health regulations 10 NYCRR part 63.8 (m) permit disclosure of HIV-related information regarding the source individual to exposed individuals and their physicians.** The process for accessing this information is straightforward and should be incorporated into the facility's occupational exposure protocol. The procedure should be clearly delineated, should identify the designated medical officer responsible for implementing the procedure, and should emphasize the importance of a timely response. Detailed information regarding the regulations follows.

**Note: These regulations do not authorize unconsented testing of the source patient.**

Briefly, when an exposure incident occurs, the medical officer at the facility (occupational exposure designee) should:

- Assess the exposure for risk of transmission or potential risk of transmission.
- Obtain consent and test the exposed individual for HIV. The exposed individual must be either HIV negative or of unknown HIV status.
- Ensure that a copy of the exposure incident report and the request for disclosure of the source patient's HIV status is placed in the medical record of the exposed person.

The medical officer may seek permission of the source patient to review the information contained in his/her medical chart. If the source patient is unavailable, unable to consent, or refuses, then permission to access the information may be obtained if the criteria in the regulations (as delineated below) have been met.

The regulations permit release of HIV-related information without consent of the source patient in the following circumstances:

- The incident must involve exposure to blood or other potentially infectious body fluid.
- The exposed individual must have contact with potentially infectious body substances to mucous membranes, non-intact skin, or to the vascular system. Examples of such contact may include needlesticks, puncture wound injuries, and direct saturation or permeation of non-intact skin by potentially infectious substances.

- The regulations apply to staff, employees, or volunteers in the performance of employment or professional duties in:
  - A medical or dental office.
  - A facility regulated, authorized, or supervised by the Department of Health, Office of Mental Health, Office of Mental Retardation and Developmental Disabilities, Office of Children and Family Services, Office of Alcoholism and Substance Abuse Services, or the Department of Correctional Services.
  - Emergency response employee (paid or volunteer, including an emergency medical technician, a firefighter, a law enforcement officer or local correctional officer, or medical staff).
  
- An incident report documenting the details of the exposure is on record with supervisory staff.
- A request for disclosure of the HIV status of the source is made by the exposed person or by that person's provider, as soon as possible after the alleged exposure if the initiation or continuation of post-exposure prophylactic treatment is being considered. The request is placed in the medical record of the exposed person.
- The medical provider for the exposed person or the medical officer designated by the facility reviews, investigates, and evaluates the incident and certifies that the information is necessary for an immediate decision regarding initiation or continuation of PEP for the exposed person provided that the exposed person's status is either HIV negative or unknown, and the person has consented to an HIV test.
- In the event that the exposed person's baseline test results indicate that he/she is already infected with HIV prior to the receipt of the information regarding the source's HIV status, no disclosure of the source's HIV status will be made.
- If the provider of the source patient or the medical officer (e.g., occupational health physician or infectious disease physician) designated by the facility determines through reasonable exercise of professional judgment that a risk of transmission has occurred or is likely to have occurred, he/she may release the HIV status of the source, if known. The release of information is limited to the exposed individual and his/her medical provider.

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

### **Workers' Compensation Program:**

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

The following is provided as background information but does not substitute for communicating directly with an organization's Workers' Compensation provider as situations arise.

- **Filing an injury or illness claim**

When an HCW has an occupational exposure, the employer or the healthcare provider who initially treats an injured worker customarily submits the first report to the Workers' Compensation Board and to the insurance carrier. However, an injured worker also may file a claim on his/her own behalf.

Workers who wish to file on their own behalf are required to report the injury to their employer, immediately if possible, but minimally within 30 days. If an immediate claim for benefits is not made, the employee has 2 years from the date of the accident to file with Workers' Compensation. If the employee does not report the accident within 2 years, Workers' Compensation will not consider the claim. Because options for other legal action may be affected by filing a claim with Workers' Compensation, an injured employee may benefit from discussion with an attorney before filing.

- **Documentation of claim**

In order to document a claim of occupationally acquired HIV infection, the employee who sustains an exposure that may cause transmission of HIV should have a confidential baseline HIV antibody test and the recommended series of follow-up testing. It is the responsibility of the claimant to provide evidence that proves the work-related cause of HIV infection. Documentation of a negative HIV test with seroconversion occurring after the injury or exposure is probative evidence of HIV infection resulting from occupational exposure. For this reason, anonymous testing programs, which prohibit the release of person-identified HIV antibody test results, are not recommended in the context of an occupational exposure.

- **Benefits covered in an injury claim**

Workers' Compensation covers only approved medical care. Consequently, in the event of an occupational exposure, all testing and medically recommended treatment generally would be covered. Although provisional guidelines for PEP have been published, it is not clear whether all Workers' Compensation providers will cover antiretroviral drugs for PEP.

### **Impact on Employees Who Become HIV Positive Following Occupational Exposure:**

- **Determination of benefits:** Each claim is reviewed on a case-by-case basis. Benefits are not automatically approved subsequent to filing of a claim. Insurance carriers who represent the employer organization determine whether to accept or dispute the claim made by the worker. Claims of occupationally acquired HIV infection can be expected to prompt a thorough investigation to rule out the possibility that another risk behavior was the cause of HIV infection.
- **Scope of benefits:** Workers' Compensation does not provide cash awards for pain or suffering. At this time, the maximum weekly wage replacement benefit for total disability, regardless of the cause, is \$400. Benefits are based on the worker's income and will not increase unless proposed benefit maximums become law. In some cases, unions may have negotiated for supplemental payments from the employer.

- **Confidentiality of information:** The Workers' Compensation system has historically allowed insurance carriers access to injury reports. However, access to an employee's Workers' Compensation file is strictly limited unless otherwise authorized by the claimant. The employer should disclose what circumstances necessitate filing a "C-2" form, what information is provided to the Workers' Compensation Board and to the insurance carrier, and who has access to that information. The employer also should discuss who within the organization may have access to the information as a result of filing a claim.

If an employee has any questions or concerns about filing a claim with Workers' Compensation, he/she should seek the advice of an attorney. Additional information for employees and employers on Workers' Compensation is available through the board that oversees this program. The appropriate district office of the Workers' Compensation Board should be contacted as necessary for guidance and informational material.

## APPENDIX G

### REPORTING RESULTS OF TESTING FOR ANTIBODY TO HEPATITIS C VIRUS

APPENDIX G RECOMMENDATIONS FOR REPORTING RESULTS OF TESTING FOR ANTIBODY TO HEPATITIS C VIRUS (ANTI-HCV) BY TYPE OF REFLEX SUPPLEMENTAL TESTING PERFORMED			
Anti-HCV screening test results	Supplemental test results	Interpretation	Comments
Screening-test-negative*	Not applicable	Anti-HCV-negative	Not infected with HCV, unless recent infection is suspected or other evidence exists to indicate HCV infection
Screening-test-positive* with high signal-to-cut-off (s/co) ratio	Not done	Anti-HCV-positive	Probably indicates past or present HCV infection; supplemental serologic testing not performed. Samples with high s/co ratios usually ( $\geq 95\%$ ) confirm positive, but $< 5$ of every 100 might represent false-positives; more specific testing can be requested, if indicated
Screening-test-positive	Recombinant immunoblot assay (RIBA <sup>®</sup> )-positive	Anti-HCV-positive	Indicates past or present HCV infection
Screening-test-positive	RIBA-negative	Anti-HCV-negative	Not infected with HCV, unless recent infection is suspected or other evidence exists to indicate HCV infection
Screening-test-positive	RIBA-indeterminate	Anti-HCV-indeterminate	HCV antibody and infection status cannot be determined; another sample should be collected for repeat anti-HCV testing ( $> 1$ month) or for HCV RNA testing
Screening-test-positive	Nucleic acid test (NAT)-positive	Anti-HCV-positive, HCV RNA-positive	Indicates active HCV infection
Screening-test-positive	NAT-negative, RIBA-positive	Anti-HCV-negative, HCV RNA-positive	The presence of anti-HCV indicates past or present HCV infection; a single negative HCV RNA result does not rule out active infection
Screening-test-positive	NAT-negative, RIBA-negative	Anti-HCV-negative, HCV RNA-negative	Not infected with HCV
Screening-test-positive	NAT-negative, RIBA-indeterminate	Anti-HCV-indeterminate, HCV RNA-negative	Screening test anti-HCV result probably a false-positive, which indicates no HCV infection

From Centers for Disease Control and Prevention. Guidelines for Laboratory Testing and Result Reporting of Antibody to Hepatitis C Virus. *MMWR Recomm Rep* 2003;52(RR03):1-16.

\*Screening immunoassay test results interpreted as negative or positive on the basis of criteria provided by the manufacturer.