St. Michael's

Inspired Care.
Inspiring Science.

Pocket P.E.P.

Clinical management of non-occupational and occupational exposure to blood borne pathogens

Development Team:
Deborah Yoong, PharmD[1]
Kevin Gough, MD, MEd[1, 2, 3]

Reviewers:
Mark Naccarato, BScPharm[1]
Darrell H.S. Tan, MD, PhD[1, 2, 3]

[1] Positive Care Clinic, Toronto, ON
[2] Department of Medicine, St. Michael's Hospital
[3] Faculty of Medicine, University of Toronto

- A Pocket Reference -

March 2019
(next review: March 2020)

STEP 1 TREAT EXPOSURE SITE & REPORT FOR ASSESSMENT

An individual who experiences an occupational or non-occupational exposure to blood borne pathogens needs to have immediate first aid treatment for any wound and a risk assessment for the likelihood of transmission of a pathogen.

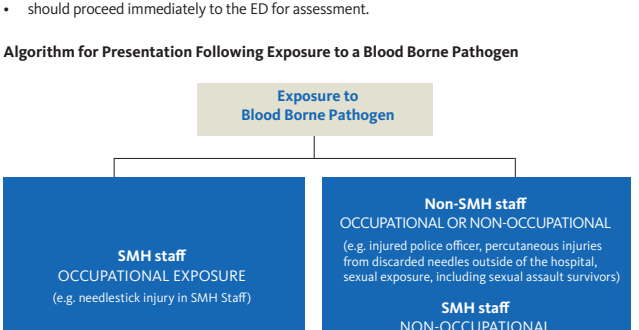
SMH staff with occupational exposures should immediately:

- Remove any contaminated clothing
- Allow wound to bleed freely. Needlestick injuries should not be squeezed.
- Flush thoroughly with water
- If exposed area involves the eyes, nose or mouth, thoroughly flush well with water
- Report the incident to his/her immediate supervisor and complete the Blood Borne Pathogen Exposure Report. If the source patient is known, it is important to record the source patient's full name and hospital number in the exposure report.
- Proceed **immediately** for risk assessment:
  - During Business Hours (Monday to Friday, 0700-1500h):
    - Corporate Health and Safety Services (3 Shuter, Ext 5013)
  - After hours, weekends, holidays:
    - Emergency Department

non-SMH staff with occupational exposures and all non-occupational exposures:

- should proceed immediately to the ED for assessment.

Algorithm for Presentation Following Exposure to a Blood Borne Pathogen



STEP 2 ASSESS THE EXPOSURE RISK

Many factors contribute to the risk of transmission of a blood borne pathogen, including the type of body fluid involved, the type of injury that occurred, the size of the inoculum, and the attributes of the source and exposed patient. All of the following information should be obtained and recorded.

a. Body fluid:

- body fluids considered potentially infectious for hepatitis B, hepatitis C and HIV include blood, serum, plasma, visibly bloody fluids, semen, vaginal secretions, rectal secretions, cerebrospinal, synovial, pleural, peritoneal, pericardial and amniotic fluid
- body fluids NOT considered potentially infectious for a blood borne pathogen include feces, nasal secretions, saliva, sputum, sweat, tears, urine and vomitus, unless they are visibly bloody

b. Type of Injury/Exposure

Occupational exposure:

- percutaneous - skin puncture or laceration by needle or sharp object
- mucosal - splash to mucous membranes (e.g. eyes, nose, mouth)
- cutaneous - contact through nonintact skin (e.g. cuts, dermatitis)

Non-occupational exposure:

- sexual activity (eg. insertive or receptive, anal or vaginal intercourse)
- needle sharing

c. Inoculum size

- volume of infectious fluid involved (e.g. hollow bore vs. solid needle; large volume vs. small volume splash)
- viral titre in the infectious fluid if known (e.g. well controlled disease vs. poorly controlled)

d. Source patient

- unknown for hepatitis B, hepatitis C, or HIV
- positive for hepatitis B, hepatitis C, or HIV
  - stage of disease – risk of HIV transmission is 8-12X higher during the acute stage of HIV (first 6 months)
  - most recent viral load
  - current and past antiretroviral/antiviral use
  - known or suspected drug resistance
- negative with no risk factors
- negative with risk factors (e.g. men who have sex with men, multiple sexual partners, people who inject drugs)

e. Presence of sexually transmitted infections (in cases of sexual exposures)

- in both the source and exposed patient

Estimated risk of transmission:

Following percutaneous exposure to blood or potentially infectious fluid:

- hepatitis B: 6-30%
- hepatitis C: 3-10%
- HIV: 0.23% (0.1% for mucous membrane exposure)

Table 1. Estimated Per-Act Risk for Acquisition of HIV by Exposure Route

Exposure route	Probability of transmission by an infected source	
	Point estimate	95% confidence interval
Parenteral Exposure		
Blood transfusion	92.5%	89 - 96%
Needle-sharing injection-drug use	0.63%	0.41 - 0.92%
Percutaneous needle stick	0.23%	0 - 0.46%
Sexual Exposure		
Receptive anal intercourse	1.38%	1.02 - 1.86%
Insertive anal intercourse	0.11%	0.04 - 0.28%
Receptive vaginal intercourse	0.08%	0.06 - 0.11%
Insertive vaginal intercourse	0.04%	0.01 - 0.14%
Receptive oral intercourse	extremely low	0 - 0.04%
Insertive oral intercourse	extremely low	0 - 0.04%

The risk of transmission to receptive partner increases with ejaculation, presence of ulcers and sexually transmitted infections in the mucous membrane (oral, genital, rectal), and high viral load in the source (e.g. acute or late-stage disease).

STEP 3 PERFORM BASELINE TESTING

Since serologic testing of the source patient is the most reliable method to assess the risk of exposure, this is strongly recommended. Ascertain if the exposed individual is willing to be tested for antibody to hepatitis B, hepatitis C, and HIV. **If the exposed individual is not willing to be tested, do not test the source patient unless they have a separate indication for testing.**

Source patient (if available):

- The source patient should be informed of the incident, and asked to undergo testing. Informed consent must be obtained (and for source patients admitted within the hospital, this must be documented in the chart by the attending medical staff or alternate medical delegate). If the source patient is a neonate, testing should be done on the mother.
- If the source patient does not consent to testing, an application can be made to the medical officer of health requiring mandatory blood testing to protect victims of crime, emergency service workers, and other persons. The application process can be found at: http://www.health.gov.on.ca/en/common/legislation/bill105/

Tests:

- HIV antibody (HIV Ab) using a fourth generation combination p24 antigen-HIV antibody assay or rapid HIV test as per SMH ED PEP protocol; if suspect acute HIV, consider HIV RNA
- Hepatitis B surface antigen (HBsAg)
- Hepatitis C antibody (HCV Ab); if HCV Ab positive, test for hepatitis C RNA

Source patient (if not available):

- If the source patient is unknown or cannot be tested, consider their likelihood of having a blood borne pathogen based on local epidemiology. e.g. what is the prevalence of infection in this population? Does the source have risk factors for infection?

Exposed individual:

- If the exposed individual is not willing to be tested for HIV, HIV PEP should not be initiated

Tests:

- HIV antibody (HIV Ab) using a fourth generation combination p24 antigen-HIV antibody test or rapid HIV test as per SMH ED PEP protocol; if suspect acute HIV, consider HIV RNA
- Hepatitis B surface antigen (HBsAg)
- Hepatitis B surface antibody (anti-HBs)
- Hepatitis B core antibody (anti-HBc)
  Consider testing only if both anti-HBs and HBsAg are negative and there is the possibility of previous exposure. The presence of isolated anti-HBc can be as high as 10-20% in endemic countries. Isolated anti-HBc can be due to a) acute hepatitis B, b) a decline of anti-HBs to undetectable titers years after clearance of acute hepatitis, c) chronic infection with decline of HBsAg to undetectable titers, or rarely, d) false positive test.
- Hepatitis C antibody (HCV Ab); if positive, test for HCV RNA
- If starting on HIV PEP: complete blood count, serum creatinine, alanine aminotransferase
- Pregnancy test (ß-HCG) if appropriate
- STI testing (for sexual exposures): syphilis serology, gonorrhea and chlamydia culture/nucleic acid amplification test (throat, vaginal, rectal, urine) as indicated. Consider incubation periods to distinguish *prevalent* from *incident* infection: syphilis (2-12 weeks), gonorrhea (2-7 days), chlamydia (2-3 weeks).

Results of Baseline Testing and Action to be taken for Exposed patient

Baseline test result	Exposed	Source	Action
HBsAg	Positive	positive, negative, unknown	Provide medical referral for hepatitis B management
	Negative	positive, unknown*	**See Step 4a**
		negative	Vaccinate for hepatitis B if not immune (see table 2)
HCV Ab and HCV RNA	Positive	positive, negative, unknown	Provide medical referral for hepatitis C management
	Negative	positive, unknown	**See Step 4b**
		negative	No further testing required
HIV Ab	Positive	positive, negative, unknown	Provide medical referral for HIV management
	Negative	positive, unknown*	**See Step 4c**
		Negative	No further testing required and PEP can be discontinued in the exposed unless there is strong suspicion of recent HIV infection in the source*

*initiation of post-exposure prophylaxis for hepatitis B or HIV exposure should not be delayed pending source test results

STEP 4a PEP MANAGEMENT - HBV EXPOSURE

Management of potential hepatitis B exposure is dependent on the vaccination and antibody status of the exposed individual, in addition to the serologic status of the source (Table 2).

For the **exposed individual who is IMMUNE** (e.g. has anti-HBs > 10mIU/mL after completing the 3-dose hepatitis vaccination or natural immunity from previous exposure):

- no further action is required.

For the **exposed individual who is NOT IMMUNE** (never been vaccinated, anti-HBs < 10mIU/mL after one or two complete series of the hepatitis B vaccine, or has not completed their vaccination series):

- hepatitis B prophylaxis and vaccination may be required.

For the **exposed individual whose antibody status is UNKNOWN**:

- immediately draw blood for anti-HBs (and label as "needlestick injury") prior to giving hepatitis B immune globulin or vaccine. Proceed as if non-immune. Initiation of post-exposure prophylaxis should not be delayed pending test result

The **management** of an individual who is **not immune or unknown** may include the following:

a. Hepatitis B immune Globulin (HBIG)

- When indicated, HBIG should be given as soon as possible, preferably within 24 hours after the exposure. Efficacy decreases substantially when it is given >48 hours post-exposure, and effectiveness when administered after 7 days is unknown.
- Dosage is 0.06 mL/kg body weight, total dose to be divided into two separate intramuscular administration sites. Dose should be repeated in one month in a known non-responder (e.g. anti-HBs < 10 mIU/mL after two complete hepatitis B vaccination series).

b. Hepatitis B vaccine series

- A 3-dose series is indicated in the individual who has not been immunized. Doses should be administered at a site separate from HBIG if co-administered.
- A second 3-dose series of the hepatitis B vaccination is indicated in an individual who is non-immune (anti-Hbs<10mIU/mL) after the first course.
- Completion of the vaccination is indicated in individuals who started the vaccination series, but did not complete all three doses.

Pregnant or lactating women can receive the hepatitis B vaccine and the hepatitis B immune globulin

Counseling and Follow-up:

In addition to receiving general counseling, the non-immune individual should be:

- counseled on the signs and symptoms of hepatitis that may occur within 6 weeks to 6 months after exposure (e.g. fatigue, loss of appetite, abdominal discomfort, jaundice, change in colour of urine and stool, rash, sore joints)

Follow-up Tests:

- Hepatitis B surface antigen (at 6 months) for possible seroconversion in the non-immune patient
- Hepatitis B surface antibody (1-2 months after completion of the vaccine series); if HBIG was given at the same time, testing should occur at least 6 month after the HBIG dose

Table 2 - Management of hepatitis B exposure

Vaccination Status of Exposed	HBV Status of Source	
	HBsAg Negative	HBsAg Positive or Unknown ‡
Unvaccinated		
Anti-HBs ≥ 10mIU/mL	No further action required	No further action required
Anti-HBs < 10mIU/mL	Initiate vaccine series	HBIG x 1* Initiate vaccine series
Vaccinated		
Anti-HBs ≥ 10mIU/mL	No further action required	No further action required
Anti-HBs < 10mIU/mL	**Completed 2 vaccine series** • No further action required **Completed 1 vaccine series** • initiate second vaccine series	**Completed 2 vaccine series** • HBIG x 2, separated by 1 month* **Completed 1 vaccine series** • HBIG x 1* • initiate second vaccine series
Anti-HBs level unknown	Measure Anti-HBs level in exposed, and if: **Anti-HBs ≥ 10mIU/mL** • No further action required **Anti-HBs < 10mIU/mL** a. Completed 2 vaccine series • No further action required b. Completed 1 vaccine series • Initiate second vaccine series	Measure Anti-HBs level in exposed¶, and if: **Anti-HBs ≥ 10mIU/mL** • No further action required **Anti-HBs < 10mIU/mL** a. Completed 2 vaccine series • HBIG x 2, separated by 1 month* b. Completed 1 vaccine series • HBIG x 1* • initiate second vaccine series
Incompletely vaccinated		
Received less than 3 doses	Complete vaccine series If anti-HBs < 10 mIU/mL after first series, a second vaccine series should be completed	HBIG x 1* Complete vaccine series (at regular schedule) If anti-HBs < 10 mIU/mL after first series, a second vaccine series should be completed

* Follow-up testing should be done at 6 months to assess for hepatitis B seroconversion

‡ If test results on the source patient reveal the source is not infected, the only required action is to ensure that the exposed individual complete the course of hepatitis B vaccination series and antibody testing.

¶ Do not delay management to wait for results of anti-HBs

STEP 4b PEP MANAGEMENT - HCV EXPOSURE

There is no prophylactic treatment currently available for a person exposed to hepatitis C. Data do not support the use of immune globulin (IG) or antiviral agents, and thus these agents cannot be recommended.

Counselling and Follow-up:

In addition to receiving general counselling, the individual should be:

- counseled on the signs and symptoms of hepatitis that may occur within 6 weeks to 6 months after exposure (eg. fatigue, loss of appetite, abdominal discomfort, jaundice, change in colour of urine and stool, rash, sore joints)

Follow-up Tests:

- HCV antibody at 3 and 6 months if source known or unknown to be HCV positive

STEP 4c PEP MANAGEMENT - HIV EXPOSURE

Management of a potential HIV exposure is dependent on the risk for HIV transmission which varies with 1) the likelihood the source has transmissible HIV and 2) the nature of the exposure.

In the occupational setting:

PEP is indicated in the following exposures if the source is known to be HIV-positive with a detectable viral load or unknown status with significant HIV risk factors (e.g. men who have sex with men, people who inject drugs):

- Percutaneous exposure to potentially infectious body fluid (e.g. needlestick injury including hollow-bore or solid needle)
- Mucous membrane exposure to potentially infectious body fluid (e.g. blood splash to eye)

In the non-occupational setting:

Exposure type	Characteristic of source				
	HIV Positive			HIV status unknown	
	Viremic or unknown viral load levels	unconfirmed VL<40	confirmed VL<40 and no STIs at time of exposure	From high risk population (eg. MSM, PWID)	From low risk population
Needle sharing	Initiate PEP	Initiate PEP	Consider PEP	Initiate PEP	Consider PEP
Anal intercourse (receptive or insertive)	Initiate PEP	Consider PEP	PEP not required	Initiate PEP	Consider PEP
Vaginal intercourse (receptive or insertive)	Initiate PEP	Consider PEP	PEP not required	Initiate PEP	PEP not required
Human bite	Consider PEP	Consider PEP	PEP not required	Consider PEP	PEP not required
Oral contact (oral-penile/ oral-vaginal/ oral-anal; receiving or giving)	PEP not required	PEP not required	PEP not required	PEP not required	PEP not required

Risk of transmission to receptive partner increases with ejaculation, the presence of ulcers, and STIs in the mucous membrane
MSM = men who have sex with men, PWID = people who inject drugs, STIs = sexually transmitted infections, VL = viral load

PEP is NOT needed:

- exposure to stool, urine, tears, saliva, nasal secretions, vomitus, sweat, unless bloody.
- oral-to-oral contact without mucosal damage
- contact with intact skin
- if source was taking PrEP

HIV Post Exposure Prophylaxis Drug Regimens

Treatment should be initiated within hours of exposure, ideally within 72 hours; however, the interval after which there is no benefit from PEP is undefined

There are no human prospective randomized trials to establish the optimal number of HIV medications for PEP and no data showing superiority of any single 3-drug regimen to prevent HIV infection. If available, the source patient should be interviewed for his/her history of antiretroviral medication use to help avoid prescribing medications to which the virus may be resistant.

The recommended HIV PEP regimen is:

Truvada® (tenofovir DF 300mg/emtricitabine 200mg) **1 tablet po once daily x 28 days** Dose based on adequate renal function (CrCl ≥ 50ml/min) Side effects include nausea, headache, diarrhea, fatigue, renal failure (rare)	+	***dolutegravir 50mg** **1 tablet po once daily x 28 days** Side effects include headache, diarrhea, nausea, fatigue, insomnia

* Based on an interim analysis of an ongoing study which has reported an increased risk of neural tube defects among infants of women who became pregnant while taking dolutegravir, until more information is available, dolutegravir should be avoided in

- Non-pregnant women of childbearing potential who are sexually active or have been sexually assaulted and who are not using an effective birth control method AND
- Women in early pregnancy

If a dolutegravir-free regimen is required in these situations, consider using Truvada + darunavir + ritonavir OR Truvada + raltegravir as listed below

Alternate antiretrovirals may be required if the source virus is known or suspected to be resistant to the above HIV PEP regimen, or based on availability, convenience or drug interactions. Other regimens that could be considered include the following:

- Truvada® 1 tablet daily + raltegravir 400mg twice daily x 28 days
- Truvada® 1 tablet daily + darunavir 800mg daily + ritonavir 100mg daily x 28 days
- Truvada® 1 tablet daily + Prezcobix® (darunavir/cobicistat 800/150mg) 1 tablet daily x 28 days
- Stribild® 1 tablet daily with food x 28 days
- Genvoya® 1 tablet daily with food x 28 days (expert opinion)

If the source patient's HIV serology is subsequently found to be negative and has no symptoms of acute infection, post-exposure prophylaxis can be discontinued and no further follow up for HIV testing is necessary.

The likelihood of the source person being in the "window period" of HIV infection in the absence of symptoms of acute retroviral syndrome is low. The maximum window period with the 4th generation tests is as low as 42 days.

Consider **consulting the Infectious Disease or HIV service** for selection of optimal PEP regimen in the following scenarios:

- source patient is known or suspected to harbour drug resistant HIV
- exposed individual is known or suspected to be pregnant
- exposed individual is breast-feeding
- exposed individual with renal or liver disease which may require antiretroviral dosing adjustment
- exposed individual on multiple medications that may increase risk of drug interactions
- delayed evaluation (greater than 72 hours since exposure)

Initiation of PEP should not be delayed pending this consultation. Modifications can be made later.

Cautions and Contraindications for Using Truvada® and dolutegravir

Truvada® - Emtricitabine and tenofovir are primarily excreted by the kidneys by a combination of glomerular filtration and active tubular secretion; thus, coadministration of Truvada® with drugs that reduce renal function or compete for active tubular secretion may increase serum concentrations of emtricitabine, tenofovir, or other renally eliminated drugs. Some examples include, but are not limited to NSAIDs, acyclovir, valacyclovir, and valganciclovir. Patients should use other nephrotoxic drugs with caution while taking Truvada.

Cautions, Contraindications and Drug Interactions with Truvada®

Contraindicated	Use with Caution
• Patients with severe renal insufficiency (creatinine clearance of <30mL/min, including patients requiring hemodialysis)	• Patients with renal insufficiency (dose adjustment required) Creatinine Clearance: ≥ 50mL/min: 1 tablet daily 30 – 49 mL/min: 1 tablet every 48 hours

dolutegravir - dolutegravir is metabolized by UGT1A1 with some contribution from CYP3A. Dolutegravir is also a substrate of UGT1A3, UGT1A9, Pgp, and BCRP in vitro; therefore, drugs that induce those enzymes and transporters, may decrease dolutegravir plasma concentration and reduce the therapeutic effect of dolutegravir. Dolutegravir inhibits the renal organic cation transporter (OCT2) and may increase plasma concentrations of drugs that depend on OCT2 for elimination (eg. dofetilide, metformin).

Cautions, Contraindications and Drug Interactions with dolutegravir

The chart below lists some of the major drug interactions identified; other drug interactions may exist.

Contraindicated		Use with caution – dose adjustment may be required	
Patients with severe hepatic impairment (Child Pugh class C)		Increased dolutegravir dosing may be required in setting of severe renal impairment and possible integrase resistance	
Antiarrhythmics	dofetilide	Antacids, laxatives, or mineral supplements containing polyvalent cations	aluminum (Maalox™), calcium (Tums™), magnesium (Maalox™), iron (dolutegravir should be administered 2 hours before or 6 hours after medications containing polyvalent cations)
		Anticonvulsants	carbamazepine, oxcarbazepine, phenytoin, phenobarbital
		Antibiotics	rifampin
		Antiretrovirals	efavirenz, etravirine, nevirapine, tipranavir, fosamprenavir
		Herbal products	St. John's Wort (hypericum perforatum)
		Oral hypoglycemics	metformin

Counseling and Follow-up:

In addition to receiving general counseling, the exposed individual should be:

- counseled on the signs and symptoms of HIV infection that may occur within 2-4 weeks after exposure (e.g. "flu-like" symptoms, weight loss, skin rash, fever, lymphadenopathy, fatigue)
- counseled on the benefits and side effects of antiretroviral PEP, including the importance of adherence to prevent PEP failure
- counseled on the importance of safer sex practices pending negative serology in follow-up

Follow up HIV-associated Tests:

2 week: Serum creatinine and ALT if abnormal at baseline
12 week: HIV Ab using a fourth generation combination p24 antigen-HIV antibody test; consider repeat at 6 months if hepatitis C virus acquired from exposure
A confirmatory assay should be done to confirm a diagnosis of HIV infection if a test result is positive

GENERAL COUNSELLING AND SUMMARY OF ALL TESTS

General Counseling Following a Significant Exposure

The individual should receive counseling regarding the risk of transmission following exposure to blood or potentially infectious fluid (see Risk of Transmission)

To minimize secondary transmission during the first 12 weeks post-exposure, the individual should be counseled to:

- not donate blood, semen, tissues, or organs
- prevent sexual transmission (e.g. barrier protection)
- avoid needle-sharing
- not share razors or toothbrushes

If the source is known or suspected to be positive for HIV, the exposed individual should be counseled to avoid pregnancy and breast-feeding.

If hepatitis B, hepatitis C, or HIV seroconversion occurs after a documented exposure and the exposure occurred in an occupational setting, this must be reported to the Joint Health & Safety Committee, Workplace Safety and Insurance Board (WSIB) and the Medical Officer of Health. A referral should be made for medical evaluation and consideration of antiviral therapy.

Testing in the Source (if available)	Baseline
HIV (HIV antibody using fourth generation antigen-antibody test OR rapid HIV test per SMH ED protocol)	x[a]
Hepatitis B (surface antigen)	x
Hepatitis C (hepatitis C antibody)	x[e]

Testing in the Exposed	Baseline	Week 2	Week 12	other
HIV (HIV antibody using fourth generation antigen-antibody test OR rapid HIV test per SMH ED protocol)	x[a]		x[a]	x[b]
Hepatitis A (hepatitis A antibody)	x			
Hepatitis B • Surface antigen • Surface antibody • Core antibody (if required)	x x x			x[c] x[d]
Hepatitis C (hepatitis C antibody)	x[e]		x[e]	x[ef]
Gonorrhea and chlamydia screen (urine NAAT, throat and rectal swabs for culture depending on type of sexual exposure)	x		x	
Syphilis serology	x		x	
Complete blood count	x			
ALT	x	x[g]		
Serum creatinine	x	x[g]		
ß-hcg (if applicable)	x			

[a] Consider HIV RNA testing if there are signs/symptoms of acute HIV

[b] Consider repeating HIV serology at 6 months after exposure if hepatitis C infection was acquired from the exposure

[c] Repeat at 6 months if hepatitis B non-immune at time of exposure to exclude hepatitis B transmission

[d] Hepatitis B surface antibody should be repeated 1-2 months after completion of the vaccine series; if HBIG was given at the same time, testing should occur at least 6 month after the HBIG dose

[e] If HCV antibody is positive, follow-up with HCV RNA testing

[f] Consider repeating at 6 months. Anti-HCV can be detected in 80% of patients within 15 weeks after exposure, in >90% within 5 months, and in >97% within 6 months (ref: MMWR 2001;50(RR05;1-43))

[g] Recommended if abnormal at baseline

If testing in the source reveals the source is HIV negative, hepatitis B negative, or hepatitis C negative, follow-up testing for corresponding tests are not necessary in the exposed.

References: See full document at
http://www.stmichaelshospital.com/programs/hiv/index.php

Form No. 72090 Dev. 06/2011 Rev. 03/2017