Alberta Guidelines for Non-Occupational, Occupational and Mandatory Testing and Disclosure Act Post-Exposure Management and Prophylaxis:

HIV, Hepatitis B, Hepatitis C and Sexually Transmitted Infections

PEP Guidelines

Alberta Government

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TABLE OF CONTENTS

ACRONYM LIST 4

LIST OF TABLES AND FIGURES 5

QUICK REFERENCE GUIDES 6

QUICK REFERENCE HIV PEP Drug Regimens 12
- Adult Regimens 12
- Pediatric and Adolescent Regimens 13
- Pregnancy Regimens* 15

INTRODUCTION 16

Goal 17

Non-occupational PEP 17

Occupational Exposures 18

Mandatory Testing and Disclosure Act 18

GENERAL CONSIDERATIONS FOR PEP 20

Management of the Exposed Site 20

Human Immunodeficiency Virus (HIV) 20
- Rationale for HIV PEP 20
- Clinical Evidence for the Use of PEP 20
- Social and Ethical Considerations 22
- Considerations for HIV PEP 22
- Risk of HIV Transmission/Acquisition 23
- Factors Affecting HIV Transmission 24
- Timing of PEP 26
- Duration of PEP 26
- Recipient's Current HIV Status 26
- Consensual Exposure to HIV 27
- PEP and Behavioral Change 28
- Choice and Number of Antiretroviral Drugs used for PEP 28
  - Children and Adolescents 33
  - Pregnancy and Breastfeeding 34
- Dispensing of HIV PEP 38
- Follow up of Patients Prescribed HIV PEP 38

Hepatitis B Virus (HBV) 39

Hepatitis C Virus (HCV) 40

Sexually Transmitted Infections (STI) 41

TESTING RECOMMENDATIONS 42

Human Immunodeficiency Virus (HIV) 42

Hepatitis B Virus (HBV) 43

Hepatitis C Virus (HCV) 44

Antiretroviral Therapy Follow-up 45

Syphilis 46

Other Sexually Transmitted Infections (STI) 47

PEP RECOMMENDATIONS FOR NON-SEXUAL EXPOSURES (EXCLUDING PERINATAL EXPOSURES) 50
Human Immunodeficiency Virus (HIV) 50
Hepatitis B Virus (HBV) 53
Hepatitis C Virus (HCV) 54
PEP RECOMMENDATIONS FOR SEXUAL EXPOSURES AND SEXUAL ASSAULT/ABUSE 55
Background 55
Human Immunodeficiency Virus (HIV) 56
Hepatitis B Virus (HBV) 60
Hepatitis C Virus (HCV) 61
Syphilis 62
Other Sexually Transmitted Infections (STI) 62
Other Management Issues 65
COUNSELLING 67
REFERENCES 68
APPENDIX A - PROBABILITY OF TRANSMISSION OF HIV, HBV and HCV 77
APPENDIX B - PREVALENCE OF HIV/AIDS 80
APPENDIX C - ANTIRETROVIRAL DRUGS USED FOR ADULT AND ADOLESCENT HIV POST-EXPOSURE PROPHYLAXIS 82
APPENDIX D - ANTIRETROVIRAL DRUGS USED FOR PEDIATRIC HIV POST-EXPOSURE PROPHYLAXIS 87
ACKNOWLEDGEMENTS 93

ACRONYM LIST

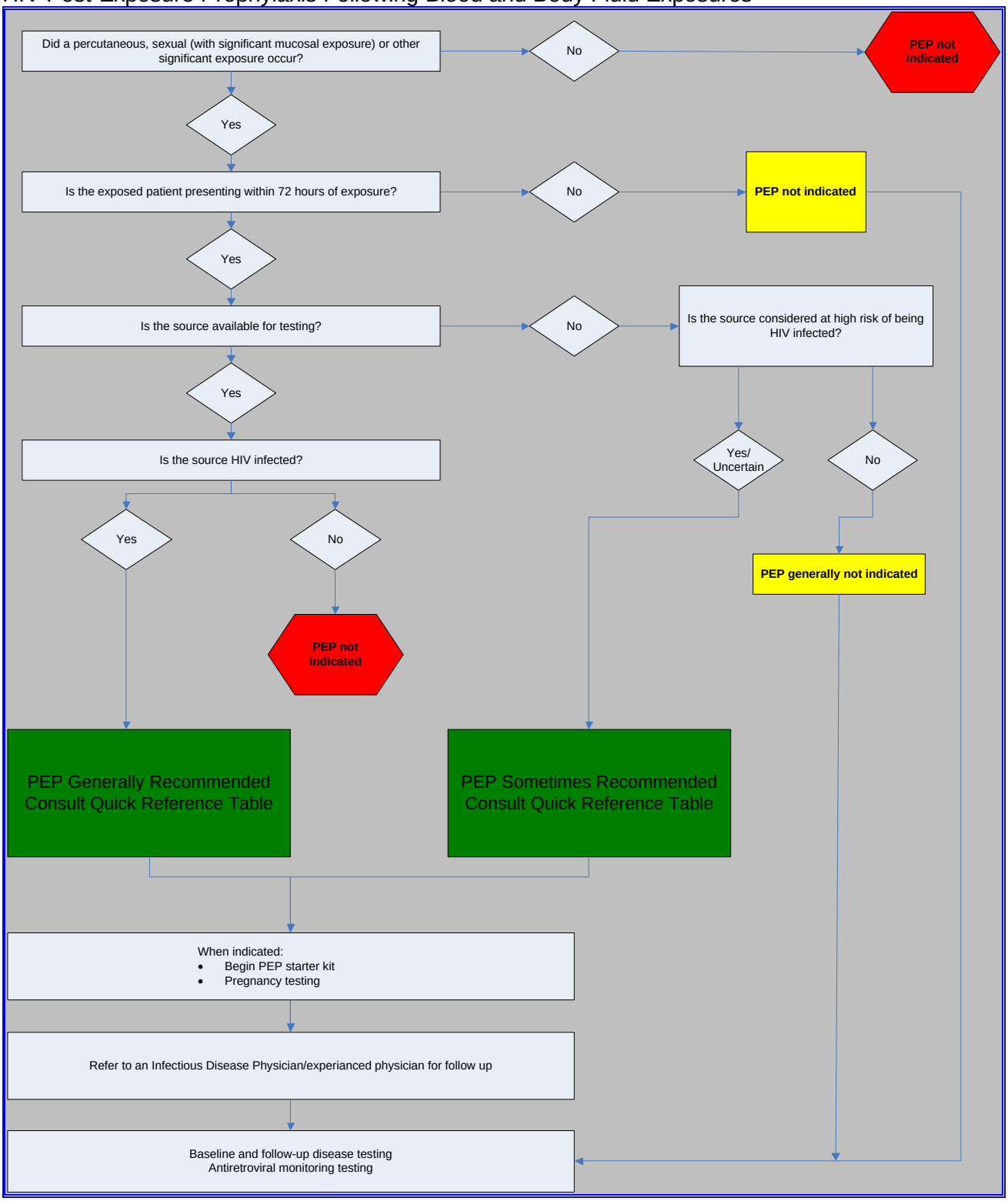
ACTG	AIDS Clinical Trials Group
AIDS	Acquired Immunodeficiency Syndrome
ALT	Alanine Aminotransferase
Anti-HBs	Hepatitis B surface antibody
ART	Antiretroviral therapy
ARV	Antiretroviral
AST	Aspartate Aminotransferase
BBF	Blood and Body Fluid
BBFE	Blood and Body Fluid Exposure
BBP	Blood Borne Pathogen
BID	Bis-in-die (twice per day)
CBCD	Complete Blood Count with Differential
CCR5	Chemokine receptor type 5
CoMOsH	Council of Medical Officers of Health
Cr	Creatinine
CYFEA	Child, Youth and Family Enhancement Act
DFA	Direct Fluorescent Antibody
DNA	Deoxyribonucleic acid
dTap	Diphtheria, tetanus and acellular pertussis
EC	Emergency Contraception
ECP	Emergency Contraceptive Pill
EIA	Enzyme immunoassay
ER	Emergency room
HBeAg	Hepatitis B “e” antigen
HBIG	Hepatitis B Immune Globulin
HBsAg	Hepatitis B surface antigen
HBV	Hepatitis B Virus
HCV	Hepatitis C Virus
HCV-RNA	Hepatitis C Virus-Ribonucleic acid
HIV	Human Immunodeficiency Virus
HSV	Herpes Simplex Virus
IFA	Indirect Fluorescent Antibody
IM	Intramuscular
IU/L	International unit/Litre
IVD	Intravenous drug use
kg	kilogram
mg	milligram
ml/mL	milliliter
MSM	Men who have sex with men
MTDA	Mandatory Testing and Disclosure Act
NAAT	Nucleic Acid Amplification Test
NNRTI	Non-Nucleoside Reverse Transcriptase Inhibitor
nPEP	non-occupational Post-Exposure Prophylaxis
NRTI	Nucleoside Reverse Transcriptase Inhibitor
OCMOH	Office of the Chief Medical Officer of Health
OHS	Occupational Health and Safety
PCR	Polymerase Chain Reaction
PEP	Post-Exposure Prophylaxis
PI	Protease inhibitor
PO	Per os (by mouth)
POC	Point-of-Care
PrEP	Pre-Exposure Prophylaxis
RCT	Randomized Control Trial
RNA	Ribonucleic acid
RPR	Rapid Plasma Reagin
SIV	Simian Immunodeficiency Virus
STI	Sexually Transmitted Infection
TP-PA	Treponema pallidum particle agglutination test
UK	United Kingdom
US/USA	United States/United States of America

LIST OF TABLES AND FIGURES

Figure 1 Risks and Benefits of HIV PEP……..23
Table 1: Risk Matrix for HIV PEP Drug Selection (Refer to Appendix A) 30
Table 2: ADULT Regimens for 28-day Post-exposure Prophylaxis for HIV Infection. 32
Table 3: Recommended Regimens for Pediatric Post-Exposure Prophylaxis 33
Table 4: Recommended Antiretroviral Therapy Regimen for Post-exposure Prophylaxis During Pregnancy or Breastfeeding 37
Table 5: HIV Testing Recommendations for ALL Exposures 42
Table 6: HBV Post-exposure Prophylaxis Testing for ALL Exposures 43
Table 7: HCV Post-exposure Prophylaxis Testing for ALL Exposures 44
Table 8: Antiretroviral Therapy Follow-up Recommendations 45
Table 9: Syphilis Post-exposure Testing 46
Table 10: Other Sexually Transmitted Infections Post-exposure Prophylaxis Testing 47
Table 11: HIV Post-exposure Prophylaxis for Non-Sexual Exposures - Known HIV-Positive 50
Table 12: HIV Post-exposure Prophylaxis for Non-Sexual Exposures – High-Risk Source 51
Table 13: HIV Post-exposure Prophylaxis for Non-Sexual Exposures - Unknown Source 52
Table 14: HBV Post-exposure Prophylaxis for Non-Sexual Exposures 53
Table 15: HIV Post-exposure Prophylaxis for Sexual Exposures - Known HIV-Positive Source for Sexual Exposures 56
Table 16: HIV Post-exposure Prophylaxis for Sexual Exposures – High-Risk Source 58
Table 17: HIV Post-exposure Prophylaxis for Sexual Exposures - Unknown Source 59
Table 18: HBV Post-exposure Prophylaxis for Sexual Exposures 60
Table 19: Syphilis Post-exposure Prophylaxis 62
Table 20: Sexually Transmitted Infections Post-exposure Prophylaxis 63

QUICK REFERENCE GUIDES

HIV Post-Exposure Prophylaxis Following Blood and Body Fluid Exposures



<table>
<tr><th colspan="4">Testing</th></tr>
<tr><td>Source Testing (if possible):</td><td colspan="3">Recipient Testing:</td></tr>
<tr><td></td><td>Source Status</td><td>Specific tests</td><td>Intervals</td></tr>
<tr><td>HIV antibody; Rapid point-of-care testing should be considered for a source when available. Generally, if source tests negative, no further testing is required in the source or recipient. However, if the source is believed to be in the “window period” for HIV, and is at high risk for HIV, additional testing may be performed after consultation with a physician knowledgeable in HIV.

For testing under the Mandatory Testing and Disclosure Act please visit

www.health.alberta.ca/professionals/mandatory-testing.html</td><td>Source HIV negative</td><td>None</td><td>Not applicable</td></tr>
<tr><td></td><td>Source unknown, or known HIV positive</td><td>HIV antibody</td><td>Baseline
4-6 weeks
12 weeks</td></tr>
<tr><td rowspan="4">Hepatitis B surface antigen (HBsAg)</td><td rowspan="4">Source unknown or HBsAg positive

(if recipient is known to be immune to HBV (anti-HBs ≥ 10 IU/L) or HBsAg positive, source and recipient testing may be unnecessary)</td><td>Hepatitis B surface antibody (anti-HBs)

Hepatitis B surface antigen (HBsAg)

(surface antigen testing may be omitted when individuals have already been pre-screened for HBV immunity or infection (e.g., health-care workers)</td><td>Baseline</td></tr>
<tr><td>Hepatitis B surface antibody (anti-HBs)</td><td rowspan="2">6 months [or as indicated in the HBV Post-exposure Prophylaxis Tables 14 or 18 (pg. 53/60)]</td></tr>
<tr><td>Hepatitis B core total antibody (anti-HBc)

Hepatitis B surface antigen (HBsAg)

(to rule out HBV infection, follow up at 6 months for those not immune at time of exposure)</td></tr>
</table>

Hepatitis C antibody; if source tests negative, no further testing routinely required in recipient; if source tests positive, a follow-up HCV-RNA should be performed. *If recipient develops illness consistent with acute seroconversion (e.g., nausea, vomiting, abdominal pain, jaundice) to HCV within 4 to 10 weeks of exposure, further testing may be considered after consultation with an infectious disease specialist or hepatologist*	Source HCV-antibody negative	None	Not applicable
	Source unknown or HCV-antibody positive and/or HCV-RNA positive	HCV antibody	Baseline
		HCV-RNA	6 weeks
Other Sexually Transmitted Infections	As indicated in TESTING RECOMMENDATIONS		

HIV Post-exposure Prophylaxis Recommendations			
Source: / **Type of exposure:**	Known HIV positive	HIV status unknown, however, high risk¶ for HIV	Unknown, or unknown HIV status, or unknown risk factors for HIV
Percutaneous injury: – IDU needle sharing – large bore needle – deep puncture – visible blood (fresh) on device/syringe Note: "Cold needle" exposures (e.g., needle stick injuries from a needle found in the community) rarely require post-exposure prophylaxis	PEP Recommended (see page 50)	PEP Recommended (see page 51)	PEP Not generally recommended but may be considered in exceptional circumstances (see page 52)
Percutaneous injury – solid bore needle – superficial injury OR Mucous membrane exposure to blood or visible blood-stained bodily fluids OR Non-intact skin exposure to blood or visible blood-stained bodily fluid	PEP Recommended (see page 50)	PEP Not generally recommended but may be considered in exceptional circumstances (see page 51)	PEP Not recommended (see page 52)
Mucous membrane exposure to non-blood containing bodily fluids OR Intact skin exposure to blood or visible blood-stained bodily fluid	PEP Not recommended (see page 50)	PEP Not recommended (see page 51)	PEP Not recommended (see page 52)

HIV Post-exposure Prophylaxis Recommendations			
Source: / **Type of exposure:**	Known HIV positive	HIV status unknown, however, high risk¶ for HIV	Unknown, or unknown HIV status, or unknown risk factors for HIV
RECEPTIVE PARTNER with: Anal or vaginal penetration* without condom or condom broke or condom status unknown OR Unknown exposure (e.g., victim under influence of drugs/alcohol)	PEP Recommended (see page 56)	PEP Recommended (see page 58)	PEP Not generally recommended but may be considered in exceptional circumstances (see page 59)
INSERTIVE PARTNER with: Anal or vaginal penetration* without condom or condom broke or condom status unknown	PEP Recommended (see page 56)	PEP Not recommended (unless additional factors that increase the risk are present‡) (see page 58)	PEP Not recommended (see page 59)
RECEPTIVE PARTNER with: Oral penetration* without condom or condom broke or condom status unknown	PEP Recommended (see page 56)	PEP Not recommended (unless additional factors that increase the risk are present‡) (see page 58)	PEP Not recommended (see page 59)
INSERTIVE PARTNER with: Oral penetration* without condom or condom broke or condom status unknown OR No anal, vaginal or oral penetration* OR Anal, vaginal or oral penetration* with intact condom	PEP Not generally recommended (unless additional factors that increase the risk are present‡) (see page 56)	PEP Not recommended (see page 58)	PEP Not recommended (see page 59)

¶ High risk includes: known intravenous drug user; known HCV positive; history of incarceration; shared needles or other drug paraphernalia for drug use in preceding 6 months; multiple sexual partners or sex with sex trade workers in preceding 6 months; presence of symptoms consistent with an acute seroconversion illness with HIV.

***** Partial or complete insertion of penis (with or without ejaculation) into mouth, vagina or anus.

‡ Factors that increase the risk include:

•An oral mucosa that is not intact (e.g., oral lesions, gingivitis, wounds);
•Known blood exposure — it is important to note that blood exposure can be minimal and therefore not recognized by the exposed person. If the exposed person reports frank blood exposure, PEP would be indicated;
• Presence of genital ulcer disease or other STIs.

HBV Post-exposure Prophylaxis			
Source: / **Type of exposure:**	Known HBV positive	HBV status unknown, however, high risk for HBV*	Unknown, or unknown HBV status, or unknown risk factors for HBV*
All Types of Blood and Body Fluid Exposure (Even if the exposure is not deemed significant, HBV immunization should still be recommended/offered for all non-HBV immune persons. Individuals with one BBFE may be at risk for subsequent exposures)	PEP Recommended* (see page 53/60)	PEP Recommended* (see page 53/60)	PEP Recommended* (see page 53/60)
	*Prophylaxis is recommended in all individuals non-HBV immune. Follow the guidelines on HBV PEP recommendations for HBV immunization and HBIG on pages 39 and 40. Note: It is suggested to assess eligibility of susceptible (non-immune) sources for pre-exposure hepatitis B vaccine.		

HCV Post-exposure Prophylaxis			
Source: / **Type of exposure:**	Known HCV positive	HCV status unknown, however, high risk for HCV	Unknown, or unknown HCV status, or unknown risk factors for HCV
All Types of significant Blood and Body Fluid Exposure	PEP Not available (see page 54/61)	PEP Not available (see page 54/61)	PEP Not available (see page 54/61)

QUICK REFERENCE HIV PEP Drug Regimens

Adult Regimens

	Two-drug regimens (See Appendix C for drug dosages and side effects)	**Three-drug regimens¶** (See Appendix C for drug dosages and side effects)
Preferred	tenofovir – emtricitabine‡ (Truvada®)	tenofovir – emtricitabine‡ (Truvada®) **Plus** dolutegravir (Tivicay®) **or** raltegravir (Isentress®)
Alternate	zidovudine – lamivudine§ (Combivir®)	tenofovir – emtricitabine‡ (Truvada®) **or** zidovudine – lamivudine§ (Combivir®) **Plus** darunavir – ritonavir¶ (Prezista®)

¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ As a fixed dose combination product (Truvada®). Tenofovir-emtricitabine should not be administered with lamivudine-containing products (Gilead Sciences Canada, Inc. Pr-Truvada® PM, 2009). The dose of tenofovir–emtricitabine should be reduced to one tablet every 48 hours in patients with a creatinine clearance of 30 to 49 ml per minute. Tenofovir–emtricitabine is not recommended in patients with a creatinine clearance of less than 30 ml per minute or in patients who are undergoing hemodialysis. Expert consultation should be sought in these cases.
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.

Pediatric and Adolescent Regimens

AGE		Two-drug regimen* (See Appendix D and C for drug dosages and side effects)	Three-drug regimen (See Appendix D and C for drug dosages and side effects)
Children >14 days - <2 years of age ***or*** **For those who cannot chew or swallow pills**	Preferred	zidovudine syrup - lamivudine§ oral solution	zidovudine syrup – lamivudine§ oral solution **Plus** lopinavir - ritonavir¶ oral solution§ (Kaletra® solution)
Children 2 years - <12 years of age	Preferred	zidovudine – lamivudine§ (Combivir® or separate formulation to allow for dosing flexibility)	zidovudine - lamivudine§ (Combivir®) **Plus** raltegravir (Isentress®)
	Alternative		zidovudine - lamivudine§ (Combivir® or separate formulation to allow for dosing flexibility) **Plus** lopinavir - ritonavir¶ (Kaletra®)
Adolescents ≥ 12 years of age	Preferred	tenofovir – emtricitabine‡ (Truvada®)	tenofovir‡ – emtricitabine‡ (Truvada®) **Plus** dolutegravir† (Tivicay®) **or** raltegravir (Isentress®)
	Alternate	zidovudine – lamivudine§ (Combivir®)	tenofovir – emtricitabine‡ (Truvada®) **or** zidovudine–lamivudine§ (Combivir®) **Plus** darunavir – ritonavir¶ (Prezista®)

***** It is important to be aware that children may be at a higher risk of transmission of HIV because child sexual abuse is often associated with multiple episodes of assault and often results in mucosal trauma (CDC, 2010). Three-drug regimens should be considered in all situations of sexual abuse involving children or infants.

¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ As a fixed dose combination product (Truvada®). Truvada® should not be administered with lamivudine-containing products and not recommended as part of a triple NRTI regimen (Gilead Sciences Canada, Inc. Pr-Truvada® PM, 2009; Gilead Sciences, TRUVADA Highlights of Prescribing Information, 2011). Truvada® in Canada has not been evaluated for safety in patients <18 years of age however it has been approved for use in pediatric patients 12 years of age and older in the United States. Safety and effectiveness of Truvada® in pediatric patients less than 12 years of age have not been established. Tenofovir has been shown to decrease bone mineral density in children.
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.
† Raltegravir (Isentress®) should be used if <40kg.

Pregnancy Regimens*

	Two-drug regimens (See Appendix C for drug dosages and side effects)	**Three-drug regimens¶** (See Appendix C for drug dosages and side effects)
Preferred	tenofovir – emtricitabine‡ (Truvada®)	tenofovir – emtricitabine‡ (Truvada®) **Plus** atazanavir – ritonavir† (Reyataz®- Novir®)
Alternate	zidovudine – lamivudine§ (Combivir®)	tenofovir – emtricitabine‡ (Truvada®) **or** zidovudine – lamivudine§ (Combivir®) **Plus** lopinavir - ritonavir† (Kaletra®)
Contraindicated **or** **Not Recommended**	didanosine and stavudine (combined) tipranavir fosamprenavir indinavir (unboosted) in the 2nd or 3rd trimester efavirenz	

***** It is recommended to consult with an infectious disease specialist physician or health professional knowledgeable in HIV when using ARVs during pregnancy, especially prior to 12 weeks gestation.
¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ Tenofovir–emtricitabine is also the preferred NRTI in HBV co-infection.
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.
† Limited data on raltegravir use in pregnancy, but raltegravir may be considered when drug interactions with PI regimens are a concern.

INTRODUCTION

In January 1997, the Council of Medical Officers of Health (CoMOsH) identified the need for a set of province-wide guidelines for post-exposure follow-up and prophylaxis of blood borne pathogens (BBP) in the community setting (non-occupational settings). In response, the "*Alberta Health Standards for Non-Occupational Community Post-Exposure Follow-up and Prophylaxis of Bloodborne Pathogens*" was developed in 1998. Additionally, in 2006, Alberta published guidelines that meet the criteria outlined in the *Mandatory Testing and Disclosure Act,* 2006 Chapter M-3.5 (MTDA). Alberta had not previously published direct guidance for managing blood and body fluid exposures (BBFE) in other occupational settings e.g., healthcare settings.

This document is intended to provide guidance in the development of policies and procedures for reducing the risk of transmitting Hepatitis B (HBV), Hepatitis C (HCV), Human Immunodeficiency Virus (HIV) and other sexually transmitted infections (STI) as a result of BBFE in occupational and community settings (including those through sexual assault), as well as those that meet the criteria under the MTDA. It is recognized that the management protocols and recommendations for occupational settings do not differ from the recommendations in non-occupational situations. As such, it is beneficial to establish a single set of guidelines for the management of BBFE in Alberta. The MTDA was established to provide an additional mechanism to gain information to guide PEP decisions in certain well-defined occupational settings. It is important to note that while the clinical management recommendations do not differ significantly in these three situations, the responsibilities for implementing and funding BBFE are different. It is not the intent of this document to outline or define the process for accessing PEP or to provide information on the utilization of the MTDA. However, a brief description of roles and responsibilities is included.

This guideline has been reviewed and updated by the Alberta Non-occupational Post-Exposure Prophylaxis Review Group to address changing evidence and clinical recommendations. The "*Alberta Guidelines for Non-occupational, Occupational and Mandatory Testing and Disclosure Act Post-Exposure Management and Prophylaxis, February 2015*" replaces all previous protocols for BBFE post-exposure prophylaxis.

The guidance in this document does not indicate an exclusive course of treatment or serve as an absolute standard of medical care. Variations, taking into account individual circumstances, may be appropriate and clinical discretion remains paramount. The medical and psychological assessment and medico-legal aspects of sexual assaults are beyond the scope of this document. In addition, this document does not address PEP for perinatal exposures.

This guidance applies to all residents of Alberta including those living in First Nations communities.

This document will be reviewed and revised by Alberta Health on an ongoing basis as needed.

Goal

The goal of these guidelines is to reduce the risk of transmission of blood borne pathogens to individuals exposed to HBV, HCV, and HIV through accidental exposures as employees, community exposures, or sexual assault/abuse. This is accomplished by:

- standardizing BBFE management in Alberta;
- assessing the risk of transmission in exposed individuals;
- laboratory testing of the exposed individuals and the source individual if possible;
- providing post-exposure prophylaxis or treatment for exposed individuals where indicated;
- counselling exposed individuals to reduce anxiety and the risk of transmission to others; and
- ensuring adequate management and follow-up.

Non-occupational PEP

In Canada, since the early 1990s, antiretroviral medicines have been prescribed for occupational PEP following potential occupational exposure to HIV. This practice has since been extended to non-occupational situations. Despite the absence of national guidelines in Canada, the use of non-occupational post-exposure prophylaxis (nPEP) is widespread. Post-exposure prophylaxis for HIV, HBV, HCV and STI in non-occupational settings in Alberta (including sexual assault/abuse) in both adults and children, is a well-established practice.

However, questions remain about certain aspects of using HIV nPEP: in particular, about the indications for PEP, the most suitable antiretroviral (ARV) medicines to use, and various issues relating to prescribing protocols and clinical management. There is some evidence suggesting that the liberal use of HIV nPEP is not a cost-effective intervention to prevent the transmission of HIV (Guinot, 2009; Herida, 2006; Roland, 2006) while other economic evaluations have indicated that nPEP is cost-effective only for high-risk exposures where there is a high risk of transmission (Pinkerton, 1998; Pinkerton, 2004; Braitstein, 2001). Evidence has suggested that nPEP may be a valuable preventative intervention for an individual, but it can only play a minor role in HIV prevention at the population level when targeting is unrefined (Poynten, 2007). This highlights the need for provincial guidelines to ensure that there is consistency in the use of nPEP and to maintain intervention cost-effectiveness. Ongoing reviews and revisions to keep the guidelines updated are required due to evolving evidence and changing clinical practice guidelines. More analysis of the public health, social, ethical, and economic benefits is outlined in the General Considerations section.

Non-occupational exposures follow the process outlined in the *Alberta Health Non-occupational Post-exposure Prophylaxis Policy, November 2014*. The role of public health professionals is predominantly to follow-up on significant exposures that occur in **community** settings. Public health professionals provide the primary assessment and evaluation for the PEP protocol in these situations. Significant exposures that occur in **occupational** settings are not generally considered the responsibility of public health. However, in certain situations the provision of assessment and management of individuals exposed in occupational settings may be facilitated by public health professionals on a case-by-case basis and where no other expertise exists to provide this service.

Occupational Exposures

This document provides the management guidelines for occupational BBFE. Where an occupational BBFE occurs, the assessment and follow-up should follow these guidelines.

In Alberta, Occupational Health and Safety (OHS) legislation ensures that worker exposure to Blood Borne Pathogens (BBP) or other biohazardous material is avoided or minimized as much as possible. The Alberta OHS Code, Part 35, Health Care and Industries with Biological Hazards, includes the requirement for post-exposure management of potential exposures to blood borne pathogens. Under section *530 Post-exposure management* of the OHS code, **"**An **employer** must establish policies and procedures for the post-exposure management of workers exposed to biohazardous material." Employers are **required** to have policies and procedures describing employer and worker responsibilities in the event a worker is exposed to "biohazardous material". This means "a pathogenic organism, including a blood borne pathogen, that, because of its known or reasonably believed ability to cause disease in humans, would be classified as Risk Group 2, 3, or 4 as defined by the Public Health Agency of Canada, or any material contaminated with such an organism" (as per the definition listed in the OHS Code, Part 1, Definitions). As required by section 8 of the OHS Regulation, these policies and procedures *must* be in writing and available to workers. The workers must be made aware of the procedure to be followed if they have a BBFE. The employer must ensure worker BBFE is controlled as low as reasonably practicable. Employers are to ensure that where a BBFE may occur in the workplace, the BBFE is treated as potentially infectious, protective work practices are established and workers are trained in such practices.

In case of an exposure, the employer is responsible to make sure that first aid and medical attention are made available to the affected worker(s), and that workers are made aware of the requirement to report and seek attention for such exposures. An employer is responsible to provide and pay for these services (through insurance in most cases) as they are not provided through the publicly funded health system.

Mandatory Testing and Disclosure Act

The *Mandatory Testing and Disclosure Act* (MTDA) provides a mechanism for certain individuals exposed to the risk of communicable disease infection through contact with another individual (the source) to compel them to provide a bodily substance for testing. An order for testing may be issued if the Court is satisfied that the information that may be obtained under the proposed testing order cannot reasonably be obtained in any other manner.

The MTDA in no way affects the routine clinical management of a patient exposed to a bodily substance of another individual (source). Management of an individual with a BBFE that meets the criteria under the MTDA should be managed in accordance with these guidelines. The provision and potential benefit of PEP is strongly influenced by timing of initiation whereas earlier initiation greatly enhances potential effectiveness. Assessment and initiation (offering) of PEP should be completed in accordance with these guidelines and information gained from a MTDA submission should only serve to inform withdrawal of

PEP as required. A decision to provide PEP should not be delayed until information is obtained from a MTDA submission.

The MTDA and the assessment and reporting processes only apply in specific emergency situations as outlined in the legislation and at the patient's request. It is important that the patient be treated and the Physician Report completed by a physician knowledgeable in assessing and managing BBFE. The assessment and reporting processes as outlined in this document are important for all applications under the MTDA. More information and guidance to physicians regarding assessment and management of a patient who wishes to make an application under the MTDA is available at www.health.alberta.ca/professionals/mandatory-testing.html

GENERAL CONSIDERATIONS FOR PEP

Management of the Exposed Site

Body sites exposed to potentially infectious fluid should be cleansed immediately. Wound and skin exposure sites should be washed with soap and water. Alcohol, hydrogen peroxide, bleach or other chemical cleansers/antiseptics/disinfectants should be avoided. No attempt to “milk” the wound should be made. Squeezing the wound may promote hyperemia and inflammation at the wound site, potentially increasing exposure if HIV is present in the contaminating fluid. Allow injury/wound site to bleed freely, and then cover lightly. Exposed mucous membranes (including the eyes) should be flushed with water or normal saline.

Human Immunodeficiency Virus (HIV)

Rationale for HIV PEP

The most effective methods for preventing HIV infection are those that prevent exposure to HIV in the first place. However there is a continuing need to provide antiretroviral therapy (ART) for individuals who have been potentially exposed to HIV. The use of HIV PEP within the context of these guidelines is supported by a number of factors including demonstrated clinical usefulness, social, legal, and ethical arguments.

Clinical Evidence for the Use of PEP

The evidence that suggests that using HIV post-exposure prophylaxis with ART can prevent HIV acquisition comes from expert opinion on the physiopathologic processes of HIV infection, the successful efforts to prevent mother-to-child (vertical) HIV transmission, animal studies and a case control study of PEP (following needlestick injury in health care settings). No Randomized Control Trials (RCT) exist in the context of non-occupational exposures. Although data on the efficacy of HIV PEP is fairly limited, it has established PEP as a widespread standard of care and it is unlikely that an RCT of PEP could now ever be conducted to support PEP (Mayer, 2001). Despite a lack of RCTs, there is enough evidence to support the use of PEP for high-risk exposures (WHO, 2007). Although there is no direct evidence of its efficacy in non-occupational settings, indirect evidence – that is, the results of animal studies and studies involving occupational exposure and mother-to-child transmission – nevertheless supports its biological plausibility.

Pathogenesis of Early HIV Infection

Information about the initial physiopathologic events after HIV exposure suggests that it can take several days for infection to become established in lymphoid and other tissues. During this time, interventions to interrupt viral replication present an opportunity to prevent an exposure from becoming an established infection (Pinto, 1997; Saag, 1997). Pathogenesis studies have indicated that for the first 1 to 3 days following mucosal SIV exposure in primates, virus remains concentrated at the site of infection and regional lymph nodes (Spira, 1996). During acute HIV infection, the viral doubling time is approximately 10 hours

and about 19 newly infected cells will develop from each HIV-infected cell. Therefore, within 48 hours of infection there will be more than 1.3 million HIV-infected cells (Little, 1999; Havens, 2003). These infected cells establish a pool of latently infected cells which serve to perpetuate HIV infection. The earlier that PEP can be initiated the less infected cells will exist and a higher likelihood of successful protection is possible.

Studies of the Efficacy of Antiretrovirals in Preventing Mother-to-Child (Vertical) Transmission of HIV

The PACTG 076 trial of zidovudine administration to HIV-infected women during pregnancy and labor and to their infants post-partum was the first to assess the use of ARVs for reducing mother-to-child transmission of HIV. It demonstrated a reduced perinatal transmission from 25.5% to 8.3% (almost 70%) among those receiving treatment as compared to those receiving placebo (Connor, 1994; Conner 1995). Subsequent clinical trials and observational studies were associated with declines in transmission to less than 2% (Cooper, 2002; Mandelbrot, 2001; Dorenbaum, 2002). Antiretroviral treatment during the perinatal period lowers the risk of HIV transmission from mother to child (Siegfried, 2011). The rationale for the neonatal component of the prophylaxis is based on PEP efficacy data (Coll, 2002) and its importance has been confirmed in an observational study where the mothers did not receive the pregnancy or intra-partum components (Wade, 1998). A number of trials have demonstrated effectiveness of ARVs in preventing vertical transmission including: the DITRAME trial which demonstrated that zidovudine prophylaxis was 38% effective (18% vs. 27.5% placebo) (Dabis, 2001), and the PETRA trial which demonstrated up to a 63% reduction (5.7% vs. 15.3% placebo) (Lallemant, 2002). In a trial conducted in Thailand, zidovudine prophylaxis from 36 weeks of gestation until delivery reduced perinatal transmission from 18.9% to 9.4%, an approximate 50% reduction (CDC, 1996; CDC, 1998). Another study of nevirapine use in pregnant women in Uganda supports the efficacy of the neonatal component in preventing vertical transmission (Guay, 1999).

Studies of Antiretrovirals in Animal Models

Many primate studies have provided evidence to support the use of HIV reverse transcriptase inhibitors for PEP. Single agent PEP has been effective in preventing retroviral infection following both intravenous and mucosal simian immunodeficiency virus (SIV) and HIV-2 exposures (Martin, 1993; Tsai, 1995; Bottiger 1997; Black, 1997; Grob, 1997; Tsai, 1998; Van Rompay, 1998; Van Rompay, 2000; Otten, 2000).

The data from animal studies suggest that decreased PEP efficacy is associated with:

- higher inoculum size;
- longer interval between exposure and treatment;
- shorter duration of treatment;
- lower doses of PEP agents.

Studies of HIV PEP in Occupational Settings

A retrospective case-control study using data from health care workers in France, Italy, the United Kingdom and the United States showed that zidovudine decreased the risk for HIV

infection by 81% (95% CI 48%-94%) from 0.3% to approximately 0.06% (3 in 1000 to 3 in 5,000) after percutaneous exposure to HIV-infected blood (CDC, 1996; CDC, 1998; CDC, 1995; Cardo, 1997). Despite the limitations of the study, this remains the most convincing data to support the use of HIV PEP.

Social and Ethical Considerations

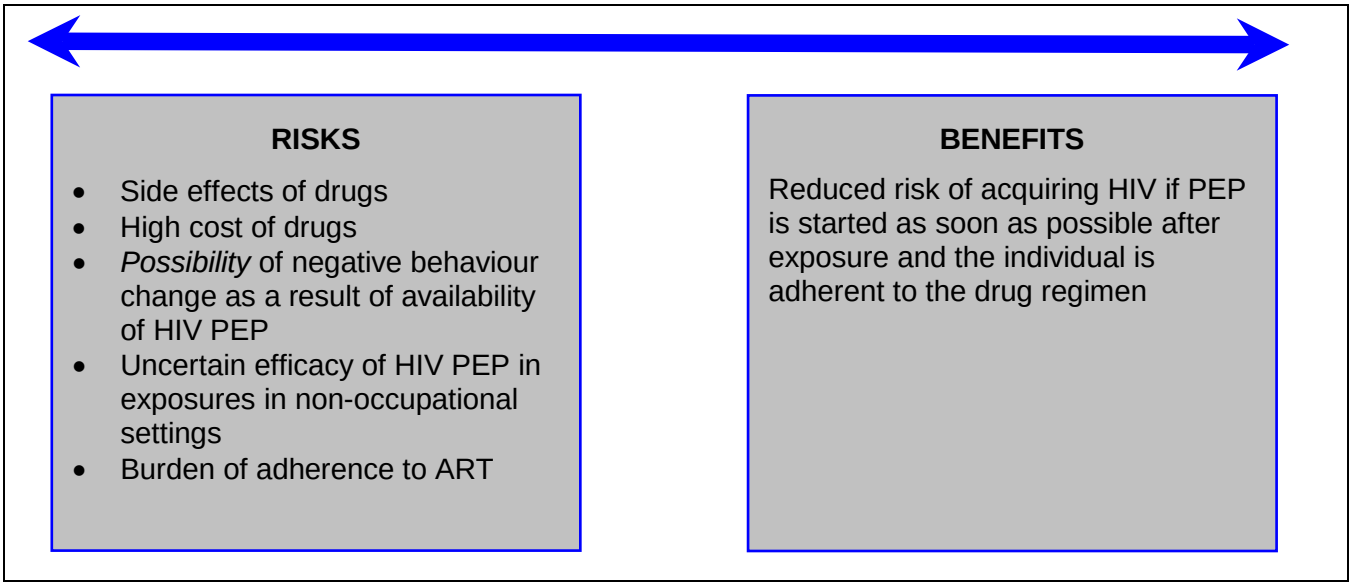
There are a number of social and ethical considerations for the provision of PEP as a standard of care in Alberta. Considerations are based on both factual information and evaluative judgments where factual information was unavailable. Some of the considerations in the development of this document include (WHO, 2007):

- PEP can preserve life and health;
- timely PEP is currently the only way of reducing the risk of acquiring HIV infection in an individual who has been exposed to the virus;
- Alberta's guidelines are founded on the principle of equity;
- Alberta's guidelines are based on clinical considerations of risk while recognizing considerations for the psychological impact of PEP;
- Alberta's guidelines reduce financial or administrative barriers to PEP;
- Alberta's guidelines are built on the principles of informed choice;
- PEP has been established as a standard of care in Alberta and there is no evidence to support a change to this standard of care. Withdrawing this standard of care is not appropriate;
- Alberta has a duty to offer PEP, when indicated, to people who have been sexually assaulted.

Considerations for HIV PEP

Decisions to provide PEP to individuals after significant BBFE to prevent the establishment of HIV infection must balance the potential benefits and risks as summarized in Figure 1 Risks and Benefits of HIV PEP. As such, widespread use of PEP outside of this guideline is not generally recommended; using HIV drugs carries real risks, low cost effectiveness, the potential to promote negative behaviour (lifestyle choices), and uncertainty in the clinical evidence. Changes in the availability of ARVs with better tolerability and safety is changing the risk profile associated with providing PEP; however, the provision of PEP, even with the advent of better PEP regimens, still has associated risks. A decision to provide PEP must be based on a balance where the true benefits justify the toxicity and cost. Thus, PEP should only be provided where there is an identifiable and reasonable risk of transmission/acquisition and where PEP has the potential of limiting this risk.

Figure 1 Risks and Benefits of HIV PEP



There are a number of factors that are considered to determine a recommendation for PEP. The evaluation includes:

- nature and risk of exposure;
- HIV status of source and risk factors for HIV in source;
- patient's current HIV status;
- timing of therapy initiation;
- likelihood of full adherence with PEP; and
- lifestyle choices (in the case of non-occupational exposures).

Risk of HIV Transmission/Acquisition

Methods that prevent HIV exposure remain the most effective means of preventing HIV infection. In the analysis of acquisition risk to the individual, the most significant considerations are based on the nature/risk of exposure and the risk of HIV status. Antiretroviral drugs should only be used for these indications after careful consideration of the potential risks and benefits with a full awareness of the current gaps in knowledge.

HIV transmission risk for a single-exposure event is directly related to both the risk that the source is infected and the risk of transmission from the exposure (nature of exposure).

RISK OF HIV TRANSMISSION =

RISK THAT THE SOURCE IS INFECTED and INFECTIOUS

X

RISK CARRIED BY NATURE OF EXPOSURE

Factors Affecting HIV Transmission

The estimated risk of a single exposure to HIV is summarized in Appendix A, Table 1 and 2.

The risk that the source is infected with HIV is estimated based on the type of population group the individual belongs to (assuming HIV status unknown). This is summarized in Appendix B, Tables 1 to 3. It should be noted, however, that HIV prevalence may have a wide geographical variation within the province in any given risk group.

Other **associated factors** may increase the likelihood of transmission:

- high plasma viral load in the source (Lee, 1996). A very low or undetectable viral load significantly decreases, but does not completely eliminate, transmission risk (see below);
- a deep percutaneous injury with a large hollow-bore needle, direct injection into a vein or artery with a needle/syringe containing HIV-positive blood (Cardo, 1997);
- viral subtype (Yang, 2003; Renjufi, 2004);
- in sexual assault/abuse settings:
    - the presence of a sexually transmitted infection in either the source or the recipient (Mastro, 1994). Approximately 5% of sexually abused children acquire an STI from their victimization (Red Book, 2009; AAP, 2005);
    - the presence of oral or mucosal disease of the mouth in either the source or recipient (Rothenberg,1998);
    - degree of trauma associated with the sexual act;
    - children may be at a higher risk of transmission of HIV because child sexual abuse is often associated with multiple episodes of assault and often results in mucosal trauma (CDC, 2010).

The risk of transmission by a source of unknown HIV status is considerably less than by a known positive source.

The risk of transmission from a source individual with an undetectable serum viral load is thought to be very low, but it is not eliminated. In January 2008, the Swiss Federal AIDS Commission stated that HIV-infected people on effective antiretroviral therapy and without other sexually transmitted infections were sexually noninfectious. However, HIV transmission from exposure to a source person who had an undetectable viral load has been described in cases of both sexual and mother-to-child transmissions (Tubiana, 2010; Sturmer, 2008). The risk of transmission is significantly reduced when the source has an undetectable serum viral load; this consideration must factor into a HIV PEP risk assessment, but it does not eliminate the need to complete a risk assessment. Plasma viral load reflects only the free virus in peripheral blood and does not measure the persistence or quantity of HIV latently infected cells. Latently infected cells persist in individuals on effective treatment and with undetectable plasma serum levels (Furtado, 1999; Ibanez, 1999). Transmission has been identified from adequately treated source patients with that transmission possibly being related to these latently infected cells.

Subsequent systematic reviews and meta-analysis indicate that heterosexual transmission was reduced, but not eliminated when using ART (Loutfy et al, 2013; Anglemyer, 2011; Attia, 2009) with an estimate of a 92% reduction by Attia. The HIV Prevention Trials Network Study 052 has demonstrated a similar 96% reduction in transmission among serodiscordant couples when ART is initiated earlier (Cohen et al, 2011). However limitations of these studies include the applicability to anal sex (mostly reported vaginal sex) and some reported condom use by participants. The 2014 interim analysis results of a large serodiscordant observational study, the PARTNER study, has demonstrated a significant risk reduction for sexual transmission (including MSM partners and unprotected anal sex) when the HIV-infected partner had demonstrated undetectable HIV viral loads (Roger el al, 2014). In the PARTNER study, an undetectable viral load was defined as being <200 copies/ml. The final results of the study, which will provide greater certainty in the mathematical transmission risk reduction, are expected in 2017. A study ending in 2015, the OPPOSITES ATTRACT study, is exploring to what extent anti-HIV treatment reduces the risk of passing on HIV to an HIV-negative partner in gay men and will provide further insight into the transmission risk reduction from low serum viral loads. The evidence to date indicates that sexual HIV transmission in serodiscordant couples is significantly reduced with low or undetectable plasma viral loads.

When the source individual is HIV infected but has a low serum viral load, the risk of transmission is reduced sufficiently to affect decisions for PEP. An exposure to a source individual with demonstrated virologic suppression, defined as:

1. low serum viral load (<200 copies/ml) for 3 consecutive tests with the most recent being within 3-4 months (extended to 6 months for adherent patients whose viral load has been suppressed for more than 2 years and whose clinical immunological status is stable); **and**
2. has had no changes in adherence to current regimen (e.g., interrupted dosing); **and**
3. is not infected with other STIs

should be assessed based on the risk profile of a “high-risk source” instead of a “known HIV-positive” source. This approach utilizes an estimated reduction in risk of approximately one order of magnitude (~90% risk reduction) which results in risk calculations very similar to those in the “high-risk source” category. Although the current evidence of transmission risk has indicated the potential for a substantially higher reduction for sexual exposures, the uncertainty in the current mathematical estimates makes it difficult to support a further reduction in the resulting transmission risk calculations at this time. Further, the applicability of the risk reductions based on studies of sexual exposures to parenteral exposures also remains uncertain.

When an individual has a low serum viral load, PEP decisions based on the “high-risk source” category is an appropriate although conservative approach. Evidence of the impacts of serum viral load and transmission risk will continue to be reviewed and PEP recommendations will be updated accordingly as uncertainty continues to be reduced.

Although HIV transmission through human bites is thought to be extremely low and epidemiologically insignificant (Tsoukas, 1988; Richman,1993), it remains biologically possible (Deshpande, 2011). When bite wounds result in blood exposure, HIV PEP should be

considered for the person(s) who was(were) exposed to blood; this could be the person bitten, the biter, or both (New York State Department of Health AIDS Institute, 2013).

Timing of PEP

PEP should be started **AS SOON AS POSSIBLE**. **Ideally PEP should be started within 1 to 4 hours of the exposure, and no longer than 72 hours, as efficacy declines rapidly with time.** PEP should **not be provided** if over 72 hours have elapsed since exposure (Martin, 1993). Although an absolute elapsed time after which PEP should not be administered cannot be stated with certainty, it is extremely unlikely that PEP started after 72 hours will be effective.

The optimal interval from time of exposure to initiation of PEP is not known, but efficacy declines with time. The more time that elapses after exposure, the less potential benefit PEP will have. Based on biological plausibility, animal (simian) models and expert opinion, PEP is now considered unlikely to be effective more than 36 hours post exposure. Animal models of PEP have shown that effective ARV treatment is most likely to prevent infection when initiated within 24 hours of experimental simian immunodeficiency virus (SIV) exposure (Tsai, 1995; Otten, 2000). Some of the currently recommended PEP drugs (NRTIs) require an intracellular activation step that delays the onset of antiviral activity. Pathogenesis studies have indicated that for the first 1 to 3 days following mucosal SIV exposure in primates, virus remains concentrated at the site of infection and regional lymph nodes (Spira, 1996). During acute HIV infection, the viral doubling time is approximately 10 hours and about 19 newly infected cells will develop from each HIV-infected cell. Therefore, within 48 hours of infection there will be more than 1.3 million HIV-infected cells (Little, 1999; Havens, 2003). These infected cells establish a pool of latently infected cells which serve to perpetuate HIV infection. The earlier that PEP can be initiated the less infected cells will exist and a higher likelihood of successful protection is possible. Seventy-two (72) hours remains Alberta's standard until stronger evidence to support a decrease is available.

Alberta recognizes the publication of recent guidelines that include provisions for initiating PEP up to one week after exposure in some circumstances (Kuhar et al, 2013). After careful review and consideration of these guidelines, Alberta believes the timeframe for effective initiation of PEP should remain at 72 hours.

Duration of PEP

The recommended duration of PEP based on animal data (Tsai, 1998) and efficacy in occupational studies (Cardo, 1997) is **28 days** (Fisher, 2006).

Recipient's Current HIV Status

It is recommended that HIV testing be completed for all individuals before initiation of PEP. A lack of testing should **not** prohibit the timely initiation of PEP therapy where a high risk of transmission has occurred.

PEP should not be provided to individuals who are already known to be HIV positive. Recipients who are already known to be HIV positive or are found to be newly HIV positive should not receive HIV PEP since the use of ARVs in these individuals would not prevent already established HIV infection. In the absence of knowledge of HIV status, exposing an individual to sub-optimal ART creates a danger that may compromise future therapy, a risk of loss of important drugs or drug classes and a risk of transmission of drug-resistant HIV. Cessation of a 28-day course of ART in an undiagnosed HIV-infected individual could also potentially trigger increased cardiovascular risk, concomitant with a viral load rebound (Weber, 2010).

HIV-positive individuals should be managed in accordance with Alberta Health's Public Health Notifiable Disease Management Guidelines available here www.health.alberta.ca/professionals/notifiable-diseases-guide.html. The use of ARVs for patient management in known HIV-positive individuals should be done in conjunction with an HIV specialist.

Consensual Exposure to HIV

HIV Post-Exposure Prophylaxis should be provided (where indicated within this guideline) to persons exposed to HIV as part of their personal lives (e.g., consensual adult sex or sharing drug injection equipment). PEP is recommended in situations where there is a significant exposure from a known HIV-positive source or from a high-risk but unknown HIV status source. Examples of situations that may prompt a request for PEP include: condom slippage, breakage, or lapse in use; unsafe needle sharing; accidental exposure in serodiscordant partners.

The use of HIV PEP for repeated consensual risk-taking behaviour such as injection drug use and unprotected sexual exposures must be carefully considered and a more effective strategy may include risk counselling and other primary prevention strategies. The potential toxicity of repeated courses of PEP outweighs the benefit of PEP for use in patients who plan to continue to engage in high-risk behaviours and who rely on PEP as the sole intervention for HIV prevention (New York State Dept of Health, AIDS Institute, 2010). In the case of repeating behaviour, such individuals should also be the focus of intensified education and prevention interventions which are more effective at reducing the overall risk of acquiring HIV.

PEP is not 100% effective and HIV post-exposure prophylaxis should always be considered a second line of intervention (WHO, 2007). Effective risk-reduction counselling and primary prevention strategies will have a greater impact on the overall risk of acquiring HIV infection than that provided by PEP for repeated consensual exposures. The benefit of providing PEP is based on reducing the risk of acquisition of HIV after a single exposure where the benefits of using ART outweigh the risks.

In situations of repeated risk behaviour or repeat presentation for PEP where other interventions are more effective at reducing the overall risk of acquiring HIV, an assessment should be completed to determine the best management strategy to prevent the individual from becoming HIV positive. In the case of repeated high-risk behaviours despite behavioral intervention, a decision to provide PEP should consider potential

medication toxicity, adherence, and potential resistance. Intent to change behaviour should be assessed, and an individualized risk-reduction plan should be developed. Where exposure events are part of an ongoing pattern of behaviour, these individuals should be referred to Alberta's STI clinics and/or HIV clinics for lifestyle management counselling.

Other jurisdictions have recommended consideration for pre-exposure prophylaxis (PrEP) after completion of the 28-day PEP regimen for persons who present with repeated high-risk behavior or for repeat courses of PEP (New York State Department of Health AIDS Institute, 2013). Alberta continues to review the evidence and the policy implications with pre-exposure prophylaxis.

PEP and Behavioral Change

Although concern has been raised that HIV PEP may result in increased risk-taking behaviour in some populations, and HIV risk-taking behaviour may not be constant over time (Mayer, 2010), most studies of PEP after sexual exposure have not demonstrated increases in risk-taking behaviour after PEP (Schechter, 2004; Guest, 2008; Roland, 2005; Martin, 2004). Some studies included effective counselling where PEP provided an entry for intensified risk-reduction interventions (Schechter, 2004; Guest, 2008; Roland, 2005; Martin, 2004). Providing PEP may even reduce further risk-taking, as individuals experience a sample of life on ARVs (Martin, 2004). Some uncertainty remains with a few studies suggesting an increased risk behaviour among some groups [e.g., younger men with a history of intravenous drug use (IVD)] (Drug and Therapeutics Bulletin, 2011; Poynten, 2009).

Choice and Number of Antiretroviral Drugs used for PEP

HIV PEP has failed in at least 21 instances where the source was known to be HIV-infected, with 16 of the cases using zidovudine as single agent PEP, 2 cases using a combination of zidovudine and didanosine, and 3 cases using ≥ 3 drugs in combination (Jochisem, 1997; Ippolito, 1998; Pratt, 1995; Lot, 1995; Weisburd, 1996; Perdue, 1999; Lot, 1999; Beltrami, 2000). Reasons proposed for the failures include delayed treatment, large inoculum, and lower than recommended doses of drug used for shorter than recommended durations. In addition, antiretroviral resistance was considered to be a factor in the failure of PEP because 13 of the source cases had received antiretroviral therapy prior to the exposure.

The optimal components of a PEP regimen remain uncertain. Based on the ability of highly active antiretroviral therapy to reduce viral load and limit the development of antiviral resistance, the use of combination regimens has been advocated for PEP (Puro, 2000; Puro, 2001). The goal of preventing transmission, however, differs from that of treatment (Bassett, 2004). After a needlestick, the intent is to prevent small amounts of virus from establishing infection, a rare event even in the absence of prophylaxis (CDC, 2001).

Drug selection for PEP must consider a number of factors including availability, evidence of effectiveness, cost of the regimen, tolerability and side effects, pill burden, adherence and operational ease of use. Selection of the preferred or alternative PEP regimen should try to minimize the risks of adverse events, be effective at preventing acquisition of HIV,

minimize pill burden and have a tolerability that will maximize adherence while minimizing costs.

There is no direct evidence to support the greater or lesser efficacy of three-drug regimens versus two-drug regimens. Mathematical modeling suggests that the optimal regimen (balancing side effects, efficacy and cost) is a dual nucleoside regimen unless the background rate of viral resistance is greater than 15%, in which case a three-drug regimen would be favored (Bassett, 2004). In Canada, the overall rate of resistance to either one or more therapies exhibited in newly diagnosed treatment-naive individuals was 9.8% (1999-2008). The majority of drug-resistant specimens were resistant to the nucleotide/nucleoside reverse transcriptase inhibitor (NRTI) (38.2%) and the non-nucleoside reverse transcriptase inhibitor (NNRTI) (32.4%) drug classes, while approximately 10.2% exhibited multi-drug resistance (≥ 2 drugs) (PHAC, 2012). The argument for two drugs is increased tolerability and completion rates, whereas the argument for three is more drugs provide extra protection against drug-selected or spontaneous mutations. There is still no clear evidence that two- versus three-drug regimens have superior tolerability, completion rates or cost-effectiveness. Two-drug regimens may have fewer side effects than three-drug regimens, but the higher incidence of side effects did not appear to influence the discontinuation of drug regimens in health care workers in some reports (Puro, 2000; Puro, 2001; Wang, 2000; National, 2003). Other investigators, however, have reported that three-drug regimens carry an unacceptable risk of severe side effects as compared to two-drug regimens (Laporte, 2002; Wang, 2000; Jochimsen, 1999). In addition, non-adherence to treatment regimens in PEP recipients is seen more frequently than in patients receiving ART for known HIV.

More recently, new ARVs that are much better tolerated (e.g., integrase inhibitors) have become available and therefore the safety and tolerability of three-drug regimens is improving. With these newer drugs, three-drug regimens are increasingly being included in new guidelines as the only preferred regimen and the use of a two-drug regimen is only recommended if there is a risk of discontinuing a regimen where tolerability is a concern. (New York State Department of Health AIDS Institute, 2013; Kuhar et al, 2013). The use of only a three-drug regimen also has some perceived advantages over a risk-based regimen including simplifying regimens and reducing the need for multiple starter kits. However, there is still no clear evidence indicating a benefit from three-drug regimens over two-drug regimens and the use of even these newer ARVs poses a real, if reduced, risk. The routine use of three-drug regimens at this time, especially during pregnancy, seems unnecessary and Alberta will continue to use a risk stratified recommendation for the selection of PEP regimens. Early evidence of PEP efficacy found a significant (81%) reduction in risk was achieved with zidovudine monotherapy suggesting that treatment with any active antiretroviral agent is beneficial in reducing risk from exposures. The time between the exposure and initiation of therapy and the adherence may have a much greater impact on effectiveness of PEP than selection of two- versus three-drug regimens. Alberta will monitor the evidence and current practices in other jurisdictions to review this decision.

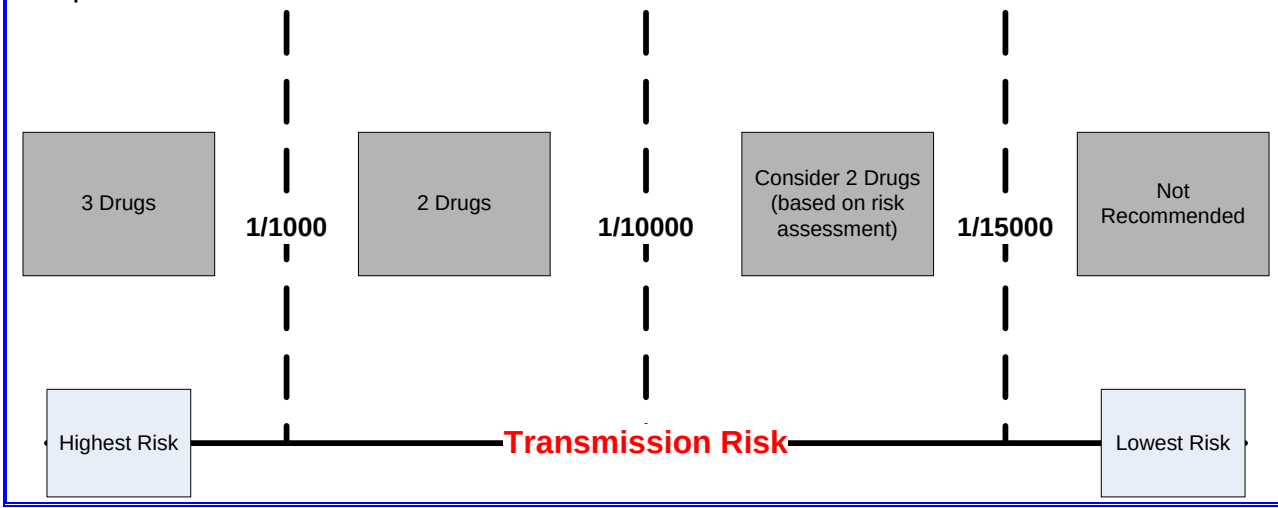
Two- or three-drug regimens chosen for PEP should be based on the level of HIV transmission risk represented by exposure (CDC, 2001; Australian Government 2007) and the current resistance prevalence data. Except in specific circumstances, a two-drug regimen

is preferred over a three-drug regimen (Roland, 2007). These guidelines recommend a three-drug regimen only in the highest risk exposures or if there is significant prevalence of viral resistance in the community. This provides an appropriate balance between protection and tolerability, adherence and cost effectiveness. The risk matrix used to create these recommendations is outlined in Table 1 (adapted from Australian Government, 2007).

Table 1: Risk Matrix for HIV PEP Drug Selection (Refer to Appendix A)

Recommendation	Transmission Risk
Recommend 3 drugs	1. Transmission risk > 1/1,000 or 2. Viral resistance background rate is >15% (if known) or 3. Consider if recipient may already be HIV positive but testing is unavailable
Recommend 2 drugs	1/1,000 > transmission risk > 1/10,000
Consider 2 drugs	1/10,000 > transmission risk > 1/15,000
Not recommended	Transmission risk < 1/15,000

Graphic



NRTIs are the cornerstone of two-drug regimens, largely for historical reasons. Until recently the recommended NRTI combination has been zidovudine-lamivudine. Zidovudine is the only antiretroviral agent for which PEP efficacy data are available (CDC, 1995; Cardo, 1997). Rapid changes to optimal therapy for established HIV and new classes of drugs have resulted in changes to the preferred regimen for PEP. A 28-day course of tenofovir-emtricitabine is now the preferred regimen (Landovitz, 2009) in adults. This is due to substantially less toxicity and improved adherence, as compared with previous combinations (Gallant, 2006; Mayer, 2008). When the source is known to be HIV-infected, information including previous ART, current level of viral suppression, or

genotypic/phenotypic resistance profile should be used (when available) to individualize the PEP regimen in consultation with an experienced HIV provider (Roland, 2001). Initiation of the first dose and continuation of PEP should not be delayed while awaiting this information.

Traditionally a protease inhibitor (PI), often boosted with low-dose ritonavir, was commonly used as the third drug in PEP regimens (Landovitz, 2009). Lopinavir-ritonavir had been the preferred protease inhibitor for a three-drug regimen due to effectiveness, availability and cost. Alternative regimens are now available that can be used to reduce pill burden, decrease adverse events (specifically GI intolerance, nausea, vomiting and diarrhea and lipid elevations), and have demonstrated noninferiority (treatment) to lopinavir-ritonavir (Molina, 2008; Ortiz, 2008).

Experience with the use of integrase inhibitors for PEP has greatly increased in recent years. Studies of the combination use of raltegravir (an integrase inhibitor) and tenofovir-emtricitabine have demonstrated that individuals reported fewer side effects, better completion rates and less drug-drug interactions compared to historical controls using a protease inhibitor in combination with two NRTIs for PEP (Mayer, 2009, McAllister, 2014). Data suggests that raltegravir may penetrate the genital tract well and prevent HIV entry into CD4 cells or integration with host DNA, thus having hypothetical advantages for PEP (Clavel, 2010). Virologic evidence also supports the use of raltegrevir as effective for PEP (Marsden, 2012). Two additional integrase inhibitors have been recently approved in Canada: evlitegravir-cobicistat and dolutegravir. Neither raltegravir nor dolutegravir is metabolized through the cytochrome p450 enzyme system and therefore both have the advantage of reducing the potential for drug–drug interactions (US Department of Health and Human Services, 2011; Merck Frosst Canada Ltd, October 2010; Barber, 2010, ViiV Healthcare ULC, 2014). Based on considerations of drug-drug interactions, cost, tolerability and adherence, pill burden and dosing, if a third drug is added to the PEP regimen, dolutegravir **or** raltegravir would be preferred over protease inhibitors. The PI Darunavir-ritonavir is the recommended third drug alternative. Atazanavir-ritonavir was considered as an alternative PI but it must be used with caution and appropriate dosing separation when combined with antacids and H2 blockers, and therefore is not included in these guidelines (US Department of Health and Human Services, 2011;,Bristol-Meyer Squibb Canada, Reyata PM, 2011). Alberta's recommended regimens for post-exposure prophylaxis in ADULTS are outlined in Table 2.

NNRTIs such as efavirenz-based treatment regimens demonstrated excellent potency, durability (successful treatment for 12 months or longer), and superior virologic response when compared to lopinavir plus ritonavir for the treatment of HIV. To date, in almost all studies efavirenz has been either noninferior or superior to every comparator with which it has been studied (with the exception of dolutegravir with abacavir/lamivudine) (Riddler, 2008; ACTG 5142, 2008). However, efavirenz commonly causes neuropsychiatric side effects during the first few days or weeks of therapy, and therefore has limited attractiveness in short-term PEP use (US Department of Health and Human Services, 2011; Bristol-Meyer Squibb Canada, Pr-Sustiva PM, 2010). Nevirapine, another NNRTI is not recommended for use in PEP regimens due to the high rate of serious adverse events associated with its use for PEP (CDC, 2001; MMWR, 2001; Patel, 2004).

Similarly, using chemokine receptor type 5 (CCR5) antagonists such as maraviroc prevents HIV entry into human CD4 T-lymphocytes, and has been shown to achieve very high concentrations in the genital tract and rectum, characteristics which may be attractive for PEP (Brown, 2010). Maraviroc is metabolized through the cytochrome p450 pathway and therefore has increased potential for drug–drug interactions. There are case reports of the use of maraviroc for PEP when an individual has been exposed to drug-resistant HIV (Mechai, 2008) and studies are ongoing (or planned) to evaluate the tolerability of raltegravir or maraviroc as part of PEP regimens. At the present time, there is insufficient evidence to recommend the use of CCR5 antagonists as preferred agents for HIV PEP. The recommendations for regimens using CCR5 antagonists or newer antiretroviral drug classes such as the fusion inhibitors will be reviewed on an ongoing basis.

Table 2: ADULT Regimens for 28-day Post-exposure Prophylaxis for HIV Infection

	Two-drug regimens (See Appendix C for drug dosages and side effects)	**Three-drug regimens¶** (See Appendix C for drug dosages and side effects)
Preferred	tenofovir – emtricitabine‡ (Truvada®)	tenofovir – emtricitabine‡ (Truvada®) **Plus** dolutegravir (Tivicay®) **or** raltegravir (Isentress®)
Alternate	zidovudine – lamivudine§ (Combivir®)	tenofovir – emtricitabine‡ (Truvada®) **or** zidovudine – lamivudine§ (Combivir®) **Plus** darunavir – ritonavir¶ (Prezista®-Norvir®)

¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ As a fixed dose combination product (Truvada®). Tenofovir-emtricitabine should not be administered with lamivudine-containing products (Gilead Sciences Canada, Inc. Pr-Truvada® PM, 2009). The dose of tenofovir–emtricitabine should be reduced to one tablet every 48 hours in patients with a creatinine clearance of 30 to 49 ml per minute. Tenofovir–emtricitabine is not recommended in patients with a creatinine clearance of less than 30 ml per minute or in patients who are undergoing hemodialysis. Expert consultation should be sought in these cases.
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.

Triple NRTI drug regimens have been recommended as PEP regimens in other jurisdictions (New York State Dept of Health AIDS Institute, 2010; New York State Dept of Health, 2010; Sturt, 2011; Winston 2005). This drug regimen option is not recommended in these guidelines.

Children and Adolescents

Recommendations for ART regimens in children and adolescents differ from adults. The recommendation from New York State indicates a three-drug regimen, however it is reasonable to consider a two-drug regimen (New York State Dept of Health, 2010; Jacin B, 2010). It is important to be aware that children may be at a higher risk of transmission of HIV because child sexual abuse is often associated with multiple episodes of assault and often results in mucosal trauma (CDC, 2010). **Three-drug regimens should be considered in all situations of sexual abuse involving children or infants**. Both two- and three-drug regimens are outlined as this guideline reflects both sexual and parenteral exposures and the selection should be based on the criteria outlined in previous sections. Recommended regimens are outlined in Table 3. Alternative agents may be used in the setting of drug intolerance, toxicity, or known HIV resistance. 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 voluntarily available, the regimen should be individualized to more effectively suppress viral replication (New York State Dept of Health, 2010). However, initiation of the first dose and continuation of PEP should not be delayed while awaiting this information. If indicated, the regimen can be changed when information becomes available.

Recommendations for testing children and adolescents remain the same as for adults.

Table 3: Recommended Regimens for Pediatric Post-Exposure Prophylaxis

AGE		Two-drug regimen* (See Appendix D and C for drug dosages and side effects)	Three-drug regimen (See Appendix D and C for drug dosages and side effects)
Children >14 days - <2 years of age ***or*** **For those who cannot chew or swallow pills**	Preferred	zidovudine syrup - lamivudine§ oral solution	zidovudine syrup – lamivudine§ oral solution **Plus** lopinavir - ritonavir¶ oral solution§ (Kaletra® solution)
Children 2 years - <12 years of age	Preferred	zidovudine – lamivudine§ (Combivir® or separate formulation to allow for dosing flexibility)	zidovudine - lamivudine§ (Combivir®) **Plus** raltegravir (Isentress®)

	Alternative		zidovudine - lamivudine§ (Combivir® or separate formulation to allow for dosing flexibility) **Plus** lopinavir - ritonavir¶ (Kaletra®)
Adolescents ≥ 12 years of age	Preferred	tenofovir – emtricitabine‡ (Truvada®)	tenofovir‡ – emtricitabine ‡ (Truvada®) **Plus** dolutegravir† (Tivicay®) **or** raltegravir (Isentress®)
	Alternate	zidovudine – lamivudine§ (Combivir®)	tenofovir – emtricitabine‡ (Truvada®) **or** zidovudine–lamivudine§ (Combivir®) **Plus** darunavir – ritonavir¶ (Prezista®)

***** It is important to be aware that children may be at a higher risk of transmission of HIV because child sexual abuse is often associated with multiple episodes of assault and often results in mucosal trauma (CDC, 2010). Three-drug regimens should be considered in all situations of sexual abuse involving children or infants.
¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡As a fixed dose combination product (Truvada®). Truvada® should not be administered with lamivudine-containing products and not recommended as part of a triple NRTI regimen (Gilead Sciences Canada, Inc. Pr-Truvada® PM, 2009; Gilead Sciences, TRUVADA Highlights of Prescribing Information, 2011). Truvada® in Canada has not been evaluated for safety in patients <18 years of age however it has been approved for use in pediatric patients 12 years of age and older in the United States. Safety and effectiveness of Truvada® in pediatric patients less than 12 years of age have not been established. Tenofovir has been shown to decrease bone mineral density in children.
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.
†Raltegravir (Isentress®) should be used if <40kg.

Pregnancy and Breastfeeding

Pregnancy

All women of childbearing age should have a baseline pregnancy test completed when initiating PEP. However PEP **MUST NOT** be delayed pending the results. It is recommended to begin the appropriate ADULT regimen starter kit when PEP is indicated unless pregnancy is known or suspected. Regimens should be altered if pregnancy is subsequently identified with little risk from the short-term use (i.e., days) of an adult regimen starter kit. Due to the complexities associated with appropriate counselling about the risks and benefits of PEP and the selection of antiretroviral drugs in pregnant women, expert consultation should be sought in cases in which antiretroviral medications are

prescribed to pregnant women for PEP (US Public Health Service Guideline, 2013). Antivirals can be used safely and effectively during pregnancy (Sturt, 2011), but clinical trial data regarding ART in pregnancy is still limited. PEP is indicated at any time during pregnancy when a significant exposure has occurred. It is important to remember that each antiretroviral agent comes with inherent risks and benefits, especially during the first trimester (Sturt, 2011). **It is strongly recommended to consult with an infectious disease specialist physician or health professional knowledgeable in HIV when using ARVs during pregnancy, especially prior to 12 weeks gestation.**

A relationship between preterm birth and PI ARV therapy has been described in the literature in Europe and Africa (Sibiude, 2012; Rundin, 2011; Powis, 2011; Grosh-Woerner, 2008; Townsend, 2010; Townsend, 2007; Thorne, 2004; Lorenzi, 1998). Conversely, evidence from the US does not find any relationship (Patel, 2010; Kourtis, 2007; Tuomala, 2002). There is currently insufficient evidence to support a change in recommendation for the use of ARV for PEP in pregnancy for high-risk exposures: this potential association highlights the need for prudent and only necessary use of ARV during pregnancy. This document will be updated as evidence evolves.

Dual nucleoside regimens are not recommended for perinatal transmission (Sturt, 2011) because these duel NRTI regimens do not provide clear benefits in terms of transmission prevention (perinatal) as compared with zidovudine and nevirapine. However, nevirapine is not recommended for PEP and dual nucleoside regimens remain favored for PEP for BBFE. Selection of ART for PEP should consider clinical effectiveness and potential fetal toxicities. For example, a study on the use of nelfinavir during pregnancy suggested that the recommended dose of 1250 mg twice daily was inadequate (Read, 2008). Efavirenz should not be used as part of a PEP regimen in females of childbearing age because of reported fetal toxicities, especially during the first trimester (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2010; De Santis, 2002). Because fetal hepatotoxicity and lactic acidosis were reported with didanosine and stavudine, combining these nucleoside analogues in pregnancy is also contraindicated (Sturt, 2011). Tipranavir and fosamprenavir are not recommended during pregnancy based on limited efficacy and safety data (Sturt, 2011). Darunavir has been added to US Department of Health and Human Services Guidelines as alternate PI for HIV treatment during pregnancy and is expected that it can be safely used during pregnancy (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2014). 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 (New York State Dept of Health AIDS Institute, 2010).

International guidelines recommend tenofovir-emtricitabine as possible components of a first-line treatment regimen for pregnant HIV-1 infected women who meet treatment criteria. The US treatment guideline and the UK pregnancy treatment guideline now include tenofovir-emtricitabine as a preferred drug regimen in treatment-naïve pregnant individuals (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2014; British HIV Association, 2014). Evidence continues to support the safety and efficacy of tenofovir-emtricitabine during pregnancy (Wang, 2013; Ransom 2013; Celen, 2013). According to the Canadian product monograph, tenofovir-emtricitabine is recommended for use in pregnant women only when the potential benefits outweigh the potential risk to the

fetus according to the product monograph (Gilead Sciences Canada, Inc. Pr-Truvada PM, 2009). Tenofovir-emtricitabine is now a preferred backbone for PEP during pregnancy; but tenofovir-emtricitabine is considered "off-label" during pregnancy. Zidovudine–lamivudine is the alternative regimen.

There is limited data on raltegravir use in pregnancy, but it is considered an alternative regimen for treatment when PIs are a concern according to the US treatment guidelines (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2014). At this time there is insufficient safety data to promote the widespread use of raltegravir for PEP during pregnancy considering the availability of alternatives and the differing risk profile of PEP compared to vertical transmission or for an HIV-infected mother's health. US guidelines previously recommended lopinavir-ritonavir as a preferred PI for treatment in pregnancy due to extensive experience in clinical trials (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2010; US Dept of Health and Human Services, 2011). However, the increasing experience with atazanavir-ritonavir has resulted in a stronger safety profile for use during pregnancy. Atazanavir-ritonavir has the advantages of reduced pill burden, decreased adverse events (specifically GI intolerance, nausea, vomiting and diarrhea and lipid elevations), and has demonstrated non-inferiority (treatment) to lopinavir-ritonavir (Molina, 2008; Ortiz, 2008). Atazanavir-ritonavir is recommended as the third drug to be used for three-drug regimens during pregnancy.

Other more complex regimens are suggested in the literature to be effective and safe, but to maintain simplicity these will not be considered in the guidelines. Table 4 outlines the ART regimens during pregnancy.

Consideration may be given to continuing ART through to delivery (longer than 28 days) if PEP is started after 30 weeks gestation and the risk of transmission is high (Alberta Post Exposure Prophylaxis Guideline Review Expert Group, April, 2012). This will serve to protect the fetus from perinatal transmission in case of PEP failure. Decisions on the continuation of ART longer than 28 days and during labour and delivery must be done in consultation with a physician knowledgeable in ART.

Table 4: Recommended Antiretroviral Therapy Regimen for Post-exposure Prophylaxis During Pregnancy or Breastfeeding*

	Two-drug regimens (See Appendix C for drug dosages and side effects)	**Three-drug regimens¶** (See Appendix C for drug dosages and side effects)
Preferred	tenofovir – emtricitabine‡ (Truvada®)	tenofovir – emtricitabine‡ (Truvada®) **Plus** atazanavir – ritonavir† (Reyataz® - Norvir®)
Alternate	zidovudine – lamivudine§ (Combivir®)	tenofovir – emtricitabine‡ (Truvada®) **or** zidovudine – lamivudine§ (Combivir®) **Plus** lopinavir – ritonavir† (Kaletra®)
Contraindicated **or** **Not Recommended**	didanosine and stavudine (combined) tipranavir fosamprenavir indinavir (unboosted) in the 2nd or 3rd trimester efavirenz	

***** It is recommended to consult with an infectious disease specialist physician or health professional knowledgeable in HIV when using ARVs during pregnancy, especially prior to 12 weeks gestation.
¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ Tenofovir–emtricitabine is also the preferred NRTI in HBV co-infection
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.
† Limited data on raltegravir use in pregnancy, but raltegravir may be considered when drug interactions with PI regimens are a concern.

Breastfeeding

The recommendation to initiate PEP in the breastfeeding patient presents several concerns. Both HIV and ARV drugs may be found in breast milk that can pose a small risk to a breastfeeding infant. The benefits of breastfeeding outweigh the potential risks of HIV transmission to an infant or risk from ARV presence in breast milk during the PEP period (New York State Dept of Health AIDS Institute, 2010). Clinicians should discuss the risks and benefits with the patient and the infant's pediatrician should be informed of any potential exposure to HIV or ART medications. To minimize the risk to infants and fetus, the PEP recommendations for breastfeeding follow those for pregnancy in Table 4.

Recommendations for laboratory testing remain the same for both pregnancy and/or breastfeeding.

Dispensing of HIV PEP

Starter kits for HIV PEP (sufficient for a number of days) should be available for use within minutes or hours of potential exposure to HIV in locations where individuals with BBFE may present. An adequate number of starter kits should be provided (e.g., 3 days) and continued until follow up with a physician knowledgeable in ART is possible and a prescription can be filled.

Generally, at the first follow-up visit, HIV PEP should be dispensed for a maximum of one week at a time unless unusual circumstances exist (e.g., patient living in remote community, etc). One week dispensing will allow for ongoing adverse event monitoring, clinical care and decreased wastage.

Follow up of Patients Prescribed HIV PEP

Ideally, a physician experienced in prescribing ARVs should follow patients continuing on HIV PEP. All patients prescribed a PI should ideally be followed by, or in conjunction with, a medical specialist knowledgeable in HIV ART.

Initial PEP will most often be started in ER departments with dispensing of starter kits to the patient until a physician who will provide ongoing care can assess the patient. Follow-up testing should be done in accordance with the TESTING RECOMMENDATIONS section. Arrangements for follow-up care will vary by region.

Hepatitis B Virus (HBV)

For percutaneous and mucosal exposures to blood, several factors should be considered when making a decision to provide prophylaxis, including how infectious the source is (if known) and the hepatitis B immunization status and vaccine response in the recipient. Provincial immunization programs should result in an ever-declining number of persons at risk of acquiring HBV. The risk of transmission is summarized in Appendix A, Table 2.

HBV is known to be transmitted 8.6 times more efficiently than HIV (Kingsley, 1990) and is thought to be as high as 50-100 times more infectious that HIV.
Similar to STI, several factors increase the risk of sexual transmission of HBV including:

- type of sexual act (anal intercourse > vaginal intercourse > oral-anal); oral-genital and/or oral-oral contact do not appear to influence the risk of becoming infected with HBV (Schreeder, 1982);
- the presence of proctitis;
- high HBV DNA levels or HBeAg positivity in the source.

Although HIV transmission through bites is thought to be extremely low and epidemiologically insignificant, HBV transmission is possible. Both the individual being bitten and the one engaging in biting are at risk of HBV exposure and should be assessed (Seem, 2013).

The effectiveness of PEP for HBV including hepatitis B immune globulin (HBIG) and/or hepatitis B vaccine in various post-exposure settings has been evaluated by prospective studies. Initiation of the HBV vaccine series within 12 to 24 hours of an exposure has been demonstrated to be 70-90% effective in preventing HBV infection. The combination of vaccine and HBIG achieves a similar level of efficacy (Weinbaum, 2003). Among known non-responders to vaccination, one dose of HBIG is 70-90% effective in preventing HBV when administered within 7 days of percutaneous HBV exposure (Weinbaum, 2003) and multiple doses are shown to be 75-95% effective (Beasley, 1983). Occupational use of multiple doses of HBIG within 7 days of exposure have shown to be 75% effective at preventing HBV (Seem, 2013; Fabrega, 2013; Nery, 2003; Wachs, 1995; Castells, 2002; Loss, 2001). The maximum effective interval for prophylaxis is likely within 14 days for sexual exposure (Szmuness, 1980; Redeker, 1975; Papaevangelou, 1988; Roumeliotou-Karayannis, 1986; Perrillo, 1984). For perinatal exposure to HBV, HBIG and hepatitis B vaccine administered to the infant commencing at birth is 85-95% effective in preventing HBV infection (Beasley, 1983; Stevens, 1985). The relative benefit of HBIG and HBV vaccine in occupational settings remains unknown (Seem, 2013).

Both HBIG and the first dose of HBV vaccine should ideally be administered **within 24 hours of exposure** (New York State Dept of Health AIDS Institute, 2010) and generally within 48 hours of exposure (CIG, 2006). HBIG should not be given more than 14 days after exposure in the case of sexual exposure or sexual assault (New York State Dept of Health AIDS Institute, 2010; CIG, 2006). Even if the exposure is not deemed significant, HBV vaccination should still be recommended for all non-HBV-immune persons as it is expected that a majority of individuals who will present for PEP will meet the indications for provincially funded HBV immunization.

Pregnant women can safely receive both the HBV vaccination and HBIG.

There are currently no antiviral agents recommended for HBV post-exposure prophylaxis.

Hepatitis C Virus (HCV)

While HCV is transmitted more efficiently by the parenteral route than HIV, it is transmitted by sexual contact much less efficiently than either HBV or HIV. Transmission probabilities for HCV are summarized in Appendix A, Table 3.

Persons in long-term monogamous partnerships are at lower risk of acquisition (0-0.6% per year) as compared to persons with multiple partners or those at risk for sexually transmitted diseases (0.4-1.8% per year) (Terreault, 2002). This difference may reflect differences in sexual risk behaviours or differences in exposure to non-sexual sources of HCV, such as injection drug use or razor/toothbrush sharing. HIV co-infection appears to increase the rate of HCV transmission, while individuals without detectable HCV RNA appear to be at extremely low or near zero risk of transmitting HCV (Terreault, 2002; Rooney, 1998).

There is **currently no effective or recommended PEP** against HCV. In the absence of PEP against HCV, recommendations are to identify infection early and, if present, refer for evaluation for treatment options.

Data suggests that early treatment of acute HCV infection with interferon is highly effective in curing HCV, perhaps as high as 95% (Szmuness, 1980). The first study reporting treatment benefit of acute HCV was reported in 2001 (Jaeckel, 2001). In patients treated with interferon monotherapy for an average of 89 days from time of infection [defined as diagnosis of acute HCV infection, positive HCV RNA, and increased serum Alanine Aminotransferase (ALT)] 98% had undetectable levels of HCV RNA in serum and normal levels of serum ALT at 24 weeks after infection. Subsequently, other reports show benefits of early treatment with either interferon or pegylated interferon with or without ribavirin (Gerlach, 2003; Krycka, 2003; Kamal, 2004; Nomura, 2004). New drugs such as telaprevir (Incivek®), boceprevir (Victrelis®), and sofosbuvir (Sovaldi®) taken in combinations with pegylated interferon and/or ribavirin are effective in the treatment of HCV infection in adult patients. Although these new antiviral treatment regimens are highly efficacious and more tolerable than interferon-based therapy, there are no data on the efficacy or cost-effectiveness of antiviral therapy for pre-exposure or post-exposure prophylaxis of HCV infection.

Approximately 40-50% of symptomatic patients (e.g., jaundice, nausea, vomiting, right upper quadrant discomfort, influenza-like symptoms) will clear the virus spontaneously by 3 months after infection (Gerlach, 2003); treatment for individuals newly infected with HCV should wait until 3 to 4 months following presentation to see if persistent HCV RNA positivity is demonstrated (Sherman, 2004). Asymptomatic persons are less likely to clear infection spontaneously, so earlier treatment may be considered in these individuals due to the lower rate of spontaneous viral clearance and high rates of successful treatment with early administration (Jaeckel, 2001; Sherman, 2004).

Sexually Transmitted Infections (STI)

Uninfected persons may or may not acquire sexually transmitted infections when exposed to an infected sex partner. Many factors increase the probability of transmission, including:

- the general transmissibility of the pathogen (syphilis > gonorrhea > chlamydia);
- high concentration of the pathogen in semen or other genital fluids;
- presence of another STI in either the infected or susceptible person;
- type of sexual act (anal intercourse > vaginal intercourse > oral);
- absence of male circumcision;
- cervical ectopy;
- no condom use during sexual act;
- no use of microbicides; and
- trauma associated with the sexual act.

PEP for STI prophylaxis should be considered in sexual assault/abuse cases. Gonorrhea, chlamydia and trichomoniasis are the most frequent infections identified in women who have a history of sexual assault (PHAC 2010). The peak age incidence of sexual assault victims is similar to that of many STI and, as such, the presence of an STI does not necessarily indicate acquisition as a result of the assault. Although no direct data exist to support the use of STI prophylaxis, nonetheless it is recommended by many national guidelines including Canada and the United States (CDC, 2010; PHAC 2010).

TESTING RECOMMENDATIONS

Human Immunodeficiency Virus (HIV)

Table 5: HIV Testing Recommendations for ALL Exposures

HIV Post-exposure Testing		
Source (if possible):	**Recipient:**	
HIV antibody Generally, if source tests negative, no further testing is required in the source or recipient. However, if the source is believed to be in the "window period" for HIV, and is at high risk* for HIV, additional testing may be performed after consultation with an infectious disease specialist. Rapid point-of-care testing should be considered for the source when available.	**Intervals**	**Specific tests**
	Baseline 4-6 weeks¶ 12 weeks‡	HIV antibody *If recipient develops illness consistent with acute seroconversion to HIV (e.g., fever, headache, rash, lymphadenopathy) within 4 to 6 weeks of exposure, further testing may be considered after consultation with an infectious disease specialist* *HIV RNA may be considered in consultation with an infectious disease specialist if the situation requires prompt diagnosis.*

* High-risk includes: known intravenous drug user; known HCV-positive; history of incarceration; shared needles or other drug paraphernalia for drug use in preceding 6 months; multiple sexual partners or sex with sex trade workers in preceding 6 months; presence of symptoms consistent with an acute seroconversion illness with HIV.

¶ The second HIV antibody test is recommended between weeks 4 and 6. The current testing protocols employed by Provincial Laboratory for Public Health (ProvLab) allows for detection of HIV antigen and antibody at less than 4 weeks i.e., reducing the "window period", however testing should occur after completion of the 28 day antiretroviral regimen. To ease the burden of testing, HIV antibody may be delayed until week 6 to coincide with the HCV-RNA test.

‡ There is no longer a requirement for a 6-month (24 week) test (Branson, 2012). However, a 6-month follow-up test should be considered if:

1) PEP has been extended significantly past 28 days;
2) recipient patient is HCV infected/co-infected; or
3) there is a strong indication of potential exposure to HIV-2.

Hepatitis B Virus (HBV)

Table 6: HBV Post-exposure Prophylaxis Testing for ALL Exposures

HBV Post-exposure Testing		
Source (if possible):	**Recipient*:**	
	Interval	**Specific tests**
Hepatitis B surface antigen (HBsAg)	Baseline **if recipient is known to be immune to HBV (anti-HBs ≥ 10 IU/L) or HBsAg positive, source and recipient testing may be unnecessary.*	Hepatitis B surface antibody (anti-HBs) Hepatitis B surface antigen (HBsAg) (surface antigen testing may be omitted when individuals have already been pre-screened for HBV immunity or infection (e.g., health-care workers)
	Follow-up: 1-6 months (as indicated in the HBV Post-exposure Prophylaxis table page 53 and 60)	Hepatitis B surface antibody (anti-HBs)
	Follow-up: 6 months	Hepatitis B core total antibody (anti-HBc) Hepatitis B surface antigen (HBsAg) (to rule out HBV aquired infection)

Hepatitis C Virus (HCV)

Table 7: HCV Post-exposure Prophylaxis Testing for ALL Exposures

<table>
<tr><th colspan="4">HCV Post-exposure Testing</th></tr>
<tr><th rowspan="2">Source (if possible):</th><th colspan="3">Recipient:</th></tr>
<tr><th>Source</th><th>Intervals</th><th>Specific tests*</th></tr>
<tr><td rowspan="3">Hepatitis C antibody

If source tests anti-HCV positive, a follow-up HCV-RNA should be performed on the sourceΨ

If source tests negative, no further testing routinely required in recipient</td><td>Source HCV-antibody negative</td><td>None</td><td>None</td></tr>
<tr><td rowspan="2">Source unknown
or
Source HCV-antibody positive and/or HCV-RNA positive</td><td>Baseline</td><td>HCV antibodyΨ</td></tr>
<tr><td>6 weeks</td><td>HCV-RNA†</td></tr>
</table>

* If recipient develops illness consistent with acute seroconversion (e.g., nausea, vomiting, abdominal pain, jaundice) to HCV within 4 to 6 weeks of exposure, further testing (most often HCV-RNA) may be considered after consultation with an infectious disease specialist or hepatologist.

† HCV-RNA testing is recommended as it can identify acute infection within 2 weeks of exposure where the HCV serological window period is approximately 5–10 weeks and it is estimated that 30% of acute infections may be missed if anti-HCV is the only marker of infection used during this time period (Alberta Public Health Notifiable Disease Management Guidelines, Hepatitis C, 2011). If HCV-RNA is used solely to confirm active infection, a repeat HCV-RNA test is recommended (Alberta Public Health Notifiable Disease Management Guidelines, Hepatitis C, 2011).

Ψ A positive antibody should be confirmed by a second manufacturer's EIA, immunoblot or nucleic acid (e.g., PCR) for HCV-RNA (Alberta Public Health Notifiable Disease Management Guidelines, Hepatitis C, 2011).

Antiretroviral Therapy Follow-up

Table 8: Antiretroviral Therapy Follow-up Recommendations

Follow-up Testing Recommendations if PEP is initiated		
	Timeline	**Testing**
Nucleoside Reverse Transcriptase Inhibitor only (two-drug regimen)	Baseline visit	– Complete Blood Count with Differential (CBCD), Creatinine (Cr), Pregnancy (females of childbearing age) – Review possible side effects of medications – Review need for 100% adherence with medications and need to complete full course – Psychological supports
	Two week follow-up	– Cr (if signs/symptoms of renal issues are identified), CBCD (only if receiving zidovudine) – Assess adherence with medications – Review and assess side effects – Psychological supports
	One month follow-up	– Cr (if signs/symptoms of renal issues are identified), CBCD (only if receiving zidovudine) – Assess adherence with medications – Review and assess side effects – Psychological supports
Nucleoside Reverse Transcriptase Inhibitor plus raltegravir, dolutegravir or Protease Inhibitor (three-drug regimen)	Baseline visit	– CBCD, Cr, ALT (only if receiving a PI), Pregnancy – Review past medical history and concurrent medications for potential drug interactions e.g., with PIs (See Appendix C) – Review possible side effects of medications – Review need for 100% adherence with medications and need to complete full course – Psychological supports

Follow-up Testing Recommendations if PEP is initiated		
	Timeline	**Testing**
	Two week follow-up	– CBCD (only if receiving zidovudine), Cr, ALT (only if receiving a PI) – Assess adherence with medications – Review and assess side effects – Psychological supports
	One month follow-up	– CBCD (only if receiving zidovudine), Cr, ALT (only if receiving a PI) – Assess adherence with medications – Review and assess side effects – Psychological supports

Syphilis

Table 9: Syphilis Post-exposure Testing

Syphilis Post-exposure Testing (if no syphilis PEP provided)		
Source (if possible):	**Recipient:**	
	Interval	**Specific tests**
It is assumed that the source will not be available for timely testing in most instances. Approximately 5% of sexually abused children acquire an STI from their victimization (American Academy of Pediatrics, 2009)	Baseline	Syphilis serology should be performed. A screening test for syphilis should be performed (e.g., EIA or rapid plasma regain (RPR))
	2-4 weeks 12 weeks	Syphilis serology should be repeated at 2-4 and 12 weeks after exposure

Other Sexually Transmitted Infections (STI)

Table 10: Other Sexually Transmitted Infections Post-exposure Prophylaxis Testing

Other STI Post-exposure Testing (ADULTS)	
Source: It is assumed that the source will not be available for testing in most instances	
Recipient: post-pubertal† adolescents or adults	
STI	**Recommended specimen type**
Gonorrhea	– Gram stain (for gram negative intracellular diplococci) if available. – Culture from all penetrated (partially or fully) orifice(s) and urethra in males and females. In addition, a nucleic acid amplification test (NAAT) [if available] should be collected from all penetrated (partially or fully) orifice(s) and urine (males and females). – NAAT are generally more sensitive than culture but may not be acceptable for medico-legal purposes unless confirmed by a second set of primers or in some cases a second test sent to another laboratory for testing. Either NAAT or culture may be used to guide clinical management decisions. – Culture tests collected < 48 hours after exposure may be falsely negative, they should be repeated 1 to 2 weeks after exposure if prophylaxis is not offered; post-exposure NAAT can be taken at the time of presentation.
Chlamydia	– NAAT [if available] from all penetrated (partially or fully) orifice(s) and urine (males and females). – NAAT are more sensitive than culture and should be performed whenever possible. – Cultures have been the preferred method for medico-legal purposes, but NAAT may be acceptable if the positive results are confirmed by a second set of NAAT primers or in some cases a second test sent to another laboratory for testing. – As of March 28, 2014 the Alberta Provincial Laboratory for Public Health will no longer undertake Chlamydia trachomatis cell culture on submitted specimens due to a cessation of the production of reagents by commercial suppliers.
Trichomonas	– If available, wet mount and/or culture for *T. vaginalis*.

† Clinician determination at the time of exposure.

Other STI Post-exposure Testing (CHILDREN)	
Source: It is assumed that the source will not be available for testing in most instances. Approximately 5% of sexually abused children acquire an STI from their victimization (American Academy of Pediatrics, 2009). All testing should be done in consultation with a pediatric referral centre and/or a physician knowledgeable in STIs.	
Recipient: pre-pubertal† or peri-pubertal† children	
Specimen* type by gender	**Condition or organism to be detected**
Urine (**Strongly Preferred**): males and females – First void urine (10-20 mL) or after not voiding for 2 hours	– NAAT for gonorrhea and chlamydia. This test is generally more sensitive than genital culture and may be acceptable for medico-legal purposes if confirmed by a second set of NAAT primers or in some cases, a second test sent to another laboratory for testing. – Post-exposure NAAT can be taken at the time of presentation.
Vagina [vestibule or discharge (if present)] and urethra: females – 1 urethral swab, pre-moistened with sterile water to minimize discomfort – vaginal wash technique preferred to multiple vaginal swabs if NAAT used for *C. trachomatis* and *N. gonorrhoeae*	– Gram stain for abnormal bacterial flora, bacterial vaginosis, candida, and gonorrhea. – NAAT, are more sensitive than culture for *C. trachomatis* and *N. gonorrhoeae.* – Cultures have been the preferred method for medico-legal purposes, but NAAT may be acceptable if the positive results are confirmed by a second set of NAAT primers or in some cases, a second test sent to another laboratory for testing. – As of March 28, 2014 the Alberta Provincial Laboratory for Public Health will no longer undertake Chlamydia trachomatis cell culture on submitted specimens due to a cessation of the production of reagents by commercial suppliers.
Urethra: males – 1 urethral swab, pre-moistened in sterile water to minimize discomfort	– Gram stain for urethritis, gonorrhea. – NAAT, are more sensitive than culture for *C. trachomatis* and *N. gonorrhoeae.* – Cultures have been the preferred method for medico-legal purposes, but NAAT may be acceptable if the positive results are confirmed by a second set of NAAT primers or, in some cases, a second test sent to another laboratory for testing.

Other STI Post-exposure Testing (CHILDREN)	
Source: It is assumed that the source will not be available for testing in most instances. Approximately 5% of sexually abused children acquire an STI from their victimization (American Academy of Pediatrics, 2009). All testing should be done in consultation with a pediatric referral centre and/or a physician knowledgeable in STIs.	
Recipient: pre-pubertal† or peri-pubertal† children	
Specimen* type by gender	**Condition or organism to be detected**
	– If available, culture tests and NAAT should be performed. – If available, wet mount and/or culture for *T. vaginalis.* – Since culture tests collected <48 hours after exposure may be falsely negative, they should be repeated 1 to 2 weeks after exposure if prophylaxis is not offered; post-exposure NAAT can be taken at the time of presentation.
Pharynx: males and females – 1 swab	– *N. gonorrhoeae* culture. – NAAT (if available) for *N. gonorrhoeae* and *C. trachomatis*; organisms can be detected in oropharynx from perinatal transmission for up to 6 months following birth.
Rectum: males and females – 1-2 swabs	– *N. gonorrhoeae* and *C. trachomatis* culture. – NAAT (if available) for *N. gonorrhoeae* and *C. trachomatis.* – Herpes Simplex Virus (HSV) culture (if inflammation present) or PCR (if available).
Genital ulcers: males and females – 1 swab	– HSV culture or PCR (if available). – Swabs for syphilis PCR should be collected.

* In an acute assault, collection of specimens for forensic evidence should follow established sexual assault protocols. At a minimum, specimens should be collected for chlamydia and gonorrhea.
† Clinician determination at the time of exposure.

PEP RECOMMENDATIONS FOR NON-SEXUAL EXPOSURES (EXCLUDING PERINATAL EXPOSURES)

The management of potential percutaneous or mucosal exposure to HIV, HBV and HCV should be based on the antibody and/or immunization (in the case of hepatitis B) status of the injured person (the recipient) and the infectious status, if known, of the source. Whenever possible, in significant exposures deemed to require further follow up, every attempt should be made to test the source.

Human Immunodeficiency Virus (HIV)

Table 11: HIV Post-exposure Prophylaxis for Non-Sexual Exposures - Known HIV-Positive Source

<table>
<tr><th colspan="3">HIV Post-exposure Prophylaxis</th></tr>
<tr><td colspan="3">Source: Known HIV positive*</td></tr>
<tr><td>Type of exposure</td><td colspan="2">HIV PEP</td></tr>
<tr><td rowspan="2">Percutaneous injury (any)
OR
Mucous membrane exposure to blood or visible blood-stained bodily fluids
OR
Non-intact skin exposure to blood or visible blood-stained bodily fluid</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: Three-drug regimen
See Tables 2 or 4 for recommended regimens</td><td>Pediatrics/Adolescents: Three-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td>Mucous membrane exposure to non-blood containing bodily fluids
OR
Intact skin exposure to blood or visible blood-stained bodily fluid</td><td colspan="2">Not recommended</td></tr>
</table>

***** Includes individuals self-reporting HIV status in the absence of confirmatory testing.
† The transmission risk associated with a percutaneous exposure from a known HIV-positive source is reduced but not eliminated when the source has demonstrated virologic suppression. The risk of transmission is reduced sufficiently to affect the decision for PEP and/or the number of drugs associated with PEP. An exposure to a source individual with **demonstrated** virologic suppression, defined as low or undetectable serum viral load (<200 copies/ml) for 3 consecutive tests with the most recent being within 3-4

months (extended to 6 months for adherent patients whose viral load has been suppressed for more than 2 years and whose clinical immunological status is stable), has no changes in adherence to current regimen (e.g., interrupted dosing), and does not have other sexually transmitted infections should be assessed based on the risk profile outlined in Table 12 for "high-risk sources". An infectious disease/HIV specialist/medical specialist expert in HIV PEP may be consulted within 24 to 48 hours for advice on the continuing regimen with a view to altering the prophylactic regimen based on the source's treatment history for HIV, CD4 lymphocyte count and plasma HIV RNA level.

Table 12: HIV Post-exposure Prophylaxis for Non-Sexual Exposures – High-Risk Source

<table>
<tr><th colspan="3">HIV Post-exposure Prophylaxis
(See Appendix C for drug dosages and side effects)</th></tr>
<tr><th colspan="3">Source: HIV status unknown, however, high risk* for HIV</th></tr>
<tr><th>Type of exposure</th><th colspan="2">HIV PEP</th></tr>
<tr><td rowspan="2">Percutaneous injury
– IDU needle sharing
– large bore needle
– deep puncture
– visible blood (fresh) on device/syringe
Note: "Cold needle" exposures (e.g., injuries from a needle found in the community) almost never require post-exposure prophylaxis</td><td colspan="2">Recommended</td></tr>
<tr><td>Adults: Two-drug regimen

See Tables 2 or 4 for recommended drug regimens</td><td>Pediatrics/Adolescents: Two-drug regimen

See Table 3 for preferred pediatric regimens</td></tr>
<tr><td>Percutaneous injury
– solid bore needle
– superficial injury
OR
Mucous membrane exposure to blood or visible blood-stained bodily fluids
OR
Non-intact skin exposure to blood or visible blood-stained bodily fluid</td><td colspan="2">Not generally recommended; but a two-drug regimen may be considered in exceptional circumstances (e.g., deep injury, extensive mucosal/non-intact skin exposure to blood)</td></tr>
<tr><td>Mucous membrane exposure to non-blood containing bodily fluids</td><td colspan="2">Not recommended</td></tr>
</table>

OR Intact skin exposure to blood or visible blood-stained bodily fluid	

* High risk includes: known intravenous drug user; known HCV positive; history of incarceration; shared needles or other drug paraphernalia for drug use in preceding 6 months; multiple sexual partners or sex with sex trade workers in preceding 6 months; presence of symptoms consistent with an acute seroconversion illness with HIV.

Table 13: HIV Post-exposure Prophylaxis for Non-Sexual Exposures - Unknown Source

HIV Post-exposure Prophylaxis (See Appendix C for drug dosages and side effects)	
Source: unknown, or unknown HIV status, or unknown risk factors for HIV	
Type of exposure	**HIV PEP**
Percutaneous injury with hollow bore needle, including “cold” needle (i.e., discarded or “found” needle) OR Mucous membrane exposure to blood or visible blood-stained bodily fluids OR Non-intact skin exposure to blood or visible blood-stained bodily fluid	**Not generally recommended; but may be considered in exceptional circumstances** (e.g., fresh blood on device or in syringe, deep puncture/injury, extensive mucosal/non-intact skin exposure to blood)
Percutaneous injury – solid bore needle – superficial injury OR Mucous membrane exposure to non-blood containing bodily fluids OR Intact skin exposure to blood or visible blood-stained bodily fluid	**Not recommended**

Hepatitis B Virus (HBV)

Table 14: HBV Post-exposure Prophylaxis for Non-Sexual Exposures

HBV Post-exposure Prophylaxis (Adapted from: *Canadian Immunization Guide*, 7th edition, 2006; Alberta Immunization Policy)			
RECIPIENT± Immunization & baseline antibody response (anti-HBs) status		**SOURCE** HBsAg Positive, high risk*, unknown or not available for testing	**SOURCE** HBsAg negative or low risk
Unimmunized		HBIG§ and initiate vaccine series‡ anti-HBs 1-6 months after series complete and at least 6 months after HBIG§	Initiate vaccine series‡ anti-HBs 1-6 months after series complete
Previously immunized with complete series	Responder**	No treatment	No treatment
	Response <10 IU/L and testing >6 months after last dose	HBIG§ and 1 dose of vaccine anti-HBs 6 months after if still <10 IU/L complete the second series then anti-HBs 1 month after	One dose of vaccine anti-HBs 1 month after if still <10 IU/L complete the second series then anti-HBs 1 month after
	Response <10 IU/L and testing 1-6 months after last dose	HBIG§ and complete second course of vaccine series‡ anti-HBs 1-6 months after series complete and at least 6 months after HBIG§	Complete second course of vaccine series‡ anti-HBs 1-6 months after series complete
	Non-responder† after 2 series of 3 doses of vaccine	HBIG§ x 2 administered 1 month apart	No treatment
Previously immunized with incomplete series	Received 1 dose of vaccine	HBIG§ and complete vaccine series‡ anti-HBs 1-6 months after series complete and at least 6 months after HBIG§	Complete vaccine series‡ anti-HBs 1-6 months after series complete
	Received 2 doses of vaccine	Give 3rd dose of vaccine If baseline anti-HBs is adequate, no further treatment is required If baseline anti-HBs inadequate†, administer HBIG§ Test anti-HBs 6 months after HBIG§. If inadequate, complete second course of vaccine series	Give 3rd dose of vaccine‡ anti-HBs 1-6 months after series complete

± Persons who have previously been infected with HBV are immune to re-infection and do not require post-exposure prophylaxis. However, in immunocompromised people, should protection be achieved and then wane, subsequent HBV exposure in these individuals can result in acute disease or carrier state. Therefore, in this population, boosters may be necessary for those who have responded initially.
* A known source is high risk if the person comes from a highly endemic region for HBV, has sexual relations with multiple partners, has a partner infected with HBV or at high risk of being so, is in close family contact with an infected person, uses injection drugs, or received blood or blood products prior to 1970. Wherever possible, the source should be tested. In the case of an unknown source, background circumstances may provide some indication of the degree of risk, e.g., syringe found in the street, attendance at an STI clinic, detoxification or well baby clinic.
§ Hepatitis B immune globulin; dose is 0.06 mL/kg intramuscularly. Dose should be administered as soon as possible after exposure ideally within 24 hours and within 7 days of exposure.
‡ Hepatitis B vaccine (see *Alberta Immunization Policy* for details).
** A responder is a person with demonstrated past or current adequate levels of serum antibody to hepatitis B (i.e., anti-HBs ≥ 10 IU/L). In some circumstances persons with documented past anti-HBs >10 IU/L but are currently anti-HBs <10 IU/L may still benefit from re-immunization e.g., immunocompromised, significant time period since immunization or very high risk exposure.
† A non-responder is a person with inadequate response to vaccination (i.e., anti-HBs <10 IU/L) after 2 complete HBV vaccine series.

Hepatitis C Virus (HCV)

HCV Post-exposure Prophylaxis

Currently, prophylaxis of HCV is neither available nor recommended although early identification of infection following exposure should be accompanied by referral to an infectious disease or gastroenterology/hepatology specialist for further assessment. This referral should be carried out on a semi-urgent basis with assessment occurring within 1 to 3 months of new diagnosis.

PEP RECOMMENDATIONS FOR SEXUAL EXPOSURES AND SEXUAL ASSAULT/ABUSE

Background

The following recommendations pertain primarily to the clinical management of the patient who had a sexual exposure or is the victim of sexual assault/abuse. The forensic requirements of sexual assault are beyond the scope of this document. In conjunction with local sexual assault teams, careful attention should be paid to the documentation of course events (history) and observed injuries and reference made to other existing guidelines.

For the purpose of this guideline, pre-pubertal refers to ages < 11 years of age, peri-pubertal refers to individuals aged 11-13, and post-pubertal to ≥ 14 years (PHAC, Canadian STI Guidelines, 2010).

General Comments Regarding Post-Exposure Prophylaxis

The management of potential sexual exposures to HIV, HBV and HCV should be based on the antibody and/or immunization (in the case of HBV) status of the injured person (the recipient) and the infectious status, if known, of the source. In significant exposures deemed to require further follow up, every attempt should be made to test the source.

Human Immunodeficiency Virus (HIV)

Table 15: HIV Post-exposure Prophylaxis for Sexual Exposures - Known HIV-Positive Source for Sexual Exposures

<table>
<tr><th colspan="4">HIV Post-exposure Prophylaxis
(See Appendix C for drug dosages and side effects)</th></tr>
<tr><td colspan="4">Source: Known HIV-positive *</td></tr>
<tr><td colspan="2">Type of exposure</td><td colspan="2">HIV PEP</td></tr>
<tr><td rowspan="4">Anal penetrationΨ without condom or condom broke or condom status unknown
OR
Unknown exposure (e.g., victim under influence of drugs/alcohol)</td><td rowspan="2">RECEPTIVE PARTNER</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: Three-drug regimen
See Tables 2 or 4 for recommended regimens</td><td>Pediatrics/Adolescents: Three-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td rowspan="2">INSERTIVE PARTNER</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: Two-drug regimen
See Tables 2 or 4 for recommended regimens</td><td>Adolescents: Two-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td rowspan="4">Vaginal penetrationΨ without condom or condom broke or condom status unknown</td><td rowspan="2">RECEPTIVE PARTNER</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: Three-drug regimen</td><td>Pediatrics/Adolescents: Three-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td rowspan="2">INSERTIVE PARTNER</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: Two-drug regimen
See Tables 2 or 4 for recommended regimens</td><td>Adolescents: Two-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
</table>

<table>
<tr><td rowspan="2">Oral penetrationΨ without condom or condom broke or condom status unknown</td><td>RECEPTIVE PARTNER</td><td colspan="2">Recommended†</td></tr>
<tr><td></td><td>Adults: Two-drug regimen
See Tables 2 or 4 for recommended regimens</td><td>Pediatrics: Three-drug regimen¶
Adolescents: Two-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td>No anal, vaginal or oral penetrationΨ
OR
Anal, vaginal or oral penetration* with intact condom</td><td>INSERTIVE PARTNER</td><td colspan="2">Not generally recommended (unless additional factors that increase the risk are present‡)</td></tr>
<tr><td></td><td></td><td colspan="2">Not recommended</td></tr>
</table>

† The transmission risk associated with a sexual exposure from a known HIV-positive source is reduced but not eliminated when the source has low or undetectable serum viral load. The risk of transmission is reduced sufficiently to affect the decision for PEP and the number of drugs associated with PEP. An exposure to a source individual with **demonstrated** virologic suppression, defined as low or undetectable serum viral load (<200 copies/ml) for 3 consecutive tests with the most recent being within 3-4 months (extended to 6 months for adherent patients whose viral load has been suppressed for more than 2 years and whose clinical immunological status is stable), has no changes in adherence to current regimen (e.g., interrupted dosing) and does not have other sexually transmitted infections should be assessed based on the risk profile outlined in Table 16 for "high-risk source". An infectious disease/HIV specialist/medical specialist expert in HIV PEP may be consulted within 24 to 48 hours for advice on the continuing regimen with a view to altering the prophylactic regimen based on the source's treatment history for HIV, CD4 lymphocyte count and plasma HIV RNA level.

* Includes individuals self-reporting HIV status in the absence of confirmatory testing.

Ψ Partial or complete insertion of penis (with or without ejaculation) into mouth, vagina or anus.

¶ Due to the nature of the exposure, three-drug regimens should be used for all sexual assaults involving young children.

‡ Factors that increase the risk include:

- •Source person is known to be HIV-infected with high viral load;
- •An oral mucosa that is not intact (e.g., oral lesions, gingivitis, wounds);
- •Known blood exposure — it is important to note that blood exposure can be minimal and therefore not recognized by the exposed person. If the exposed person reports frank blood exposure, PEP would be indicated;
- • Presence of genital ulcer disease or other STIs.

Table 16: HIV Post-exposure Prophylaxis for Sexual Exposures – High-Risk Source

<table>
<tr><th colspan="4">HIV Post-exposure Prophylaxis
(See Appendix C for drug dosages and side effects)</th></tr>
<tr><th colspan="4">Source: HIV status unknown, however, high risk* for HIV</th></tr>
<tr><th colspan="2">Type of exposure</th><th colspan="2">HIV PEP</th></tr>
<tr><td rowspan="2">Anal penetrationΨ without condom or condom broke or condom status unknown
OR
Unknown exposure (e.g., victim under influence of drugs/alcohol)</td><td>RECEPTIVE PARTNER</td><td colspan="2">Recommended</td></tr>
<tr><td>Adults: Three-drug regimen
See Tables 2 or 4 for recommended drug regimens</td><td>Pediatrics: Three-drug regimen¶
Adolescents: Three-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td></td><td>INSERTIVE PARTNER</td><td colspan="2">Not recommended (unless additional factors that increase the risk are present‡)</td></tr>
<tr><td rowspan="3">Vaginal penetrationΨ without condom or condom broke or condom status unknown</td><td rowspan="2">RECEPTIVE PARTNER</td><td colspan="2">Recommended</td></tr>
<tr><td>Adults: Two-drug regimen
See Tables 2 or 4 for recommended drug regimens</td><td>Pediatrics: Three-drug regimen¶
Adolescents: Two-drug regimen
See Table 3 for preferred pediatric regimens</td></tr>
<tr><td>INSERTIVE PARTNER</td><td colspan="2">Not recommended (unless additional factors that increase the risk are present‡)</td></tr>
<tr><td colspan="2">Oral penetrationΨ without condom or condom broke or condom status unknown</td><td colspan="2">Not recommended (unless additional factors that increase the risk are present‡)</td></tr>
<tr><td colspan="2">Anal or vaginal or oral penetration with intact condom
OR
No anal, vaginal or oral penetration</td><td colspan="2">Not recommended</td></tr>
</table>

***** High risk includes: known intravenous drug user; known HCV positive; history of incarceration; shared needles or other drug paraphernalia for drug use in preceding 6 months; multiple sexual partners or sex with sex trade workers in preceding 6 months; presence of symptoms consistent with an acute seroconversion illness with HIV.
Ψ Partial or complete insertion of penis (with or without ejaculation) into mouth, vagina or anus.
¶ Due to the nature of the exposure, three-drug regimens should be used for all sexual assaults involving young children.
‡ Factors that increase the risk include:

- •An oral mucosa that is not intact (e.g., oral lesions, gingivitis, wounds);
- •Known blood exposure — it is important to note that blood exposure can be minimal and therefore not recognized by the exposed person. If the exposed person reports frank blood exposure, PEP would be indicated;
- • Presence of genital ulcer disease or other STIs.

Table 17: HIV Post-exposure Prophylaxis for Sexual Exposures - Unknown Source

HIV Post-exposure Prophylaxis (See Appendix C for drug dosages and side effects)	
Source: Unknown, or unknown HIV status, or unknown risk factors for HIV	
Type of exposure	**HIV PEP**
Anal, vaginal or oral penetration* without condom or condom broke or condom status unknown **Partial or complete insertion of penis (with or without ejaculation) into mouth, vagina or anus* OR Unknown exposure (e.g., victim under influence of drugs/alcohol)	**Not generally recommended; but may be considered in exceptional circumstances** (e.g., significant injuries, multiple assailants, male victim of male sexual assault, etc.)
No anal, vaginal or oral penetration OR Anal, vaginal or oral penetration with intact condom	**Not recommended**

Hepatitis B Virus (HBV)

HBV Post-exposure Prophylaxis

Prophylaxis for hepatitis B should be considered in all cases of sexual exposures and sexual assault/abuse, where the sexual acts have included anal or vaginal penetration or oral-anal contact without protection (i.e., a condom or dental dam) or protection status is unknown. Oral-genital and oral-oral contact do not appear to be significant modes of transmission.

Table 18: HBV Post-exposure Prophylaxis for Sexual Exposures

HBV Post-exposure Prophylaxis (Adapted from: *Canadian Immunization Guide*, 7th edition, 2006; Alberta Immunization Policy)			
RECIPIENT± Immunization & baseline antibody response (anti-HBs) status		**SOURCE** HBsAg Positive, high risk*, unknown or not available for testing	**SOURCE** HBsAg negative or low risk
Unimmunized		HBIG§ and initiate vaccine series‡ anti-HBs 1-6 months after series complete and at least 6 months after HBIG§	Initiate vaccine series‡ anti-HBs 1-6 months after series complete
Previously immunized with complete series	Responder**	No treatment	No treatment
	Response <10 IU/L and testing >6 months after last dose	HBIG§ and 1 dose of vaccine anti-HBs 6 months after if still <10 IU/L complete the second series then anti-HBs 1 month after	One dose of vaccine anti-HBs 1 month after if still <10 IU/L complete the second series then anti-HBs 1 month after
	Response <10 IU/L and testing 1-6 months after last dose	HBIG§ and complete second course of vaccine series‡ anti-HBs 1-6 months after series complete and at least 6 months after HBIG§	Complete second course of vaccine series‡ anti-HBs 1-6 months after series complete
	Non-responder† after 2 series of 3 doses of vaccine	HBIG§ x 2 administered 1 month apart	No treatment
Previously immunized with incomplete series	Received 1 dose of vaccine	HBIG§ and complete vaccine series‡ anti-HBs 1-6 months after series complete and at least 6 months after HBIG§	Complete vaccine series‡ anti-HBs 1-6 months after series complete

HBV Post-exposure Prophylaxis (Adapted from: *Canadian Immunization Guide*, 7th edition, 2006; Alberta Immunization Policy)			
RECIPIENT± Immunization & baseline antibody response (anti-HBs) status		**SOURCE** HBsAg Positive, high risk*, unknown or not available for testing	**SOURCE** HBsAg negative or low risk
	Received 2 doses of vaccine	Give 3rd dose of vaccine If baseline anti-HBs is adequate, no further treatment is required If baseline anti-HBs inadequate†, administer HBIG§ Test anti-HBs 6 months after HBIG§. If inadequate, complete second course of vaccine series	Give 3rd dose of vaccine‡ anti-HBs 1-6 months after series complete

± Persons who have previously been infected with HBV are immune to re-infection and do not require post-exposure prophylaxis. However, in immunocompromised people, should protection be achieved and then wane, subsequent HBV exposure in these individuals can result in acute disease or carrier state. Therefore, in this population, boosters may be necessary for those who have responded initially.

* A known source is high risk if the person comes from a highly endemic region for HBV, has sexual relations with multiple partners, has a partner infected with HBV or at high risk of being so, is in close family contact with an infected person, uses injection drugs, or received blood or blood products prior to 1970. Wherever possible, the source should be tested. In the case of an unknown source, background circumstances may provide some indication of the degree of risk, e.g., syringe found in the street, attendance at an STI clinic, detoxification or well baby clinic.

** A responder is a person with demonstrated past or current adequate levels of serum antibody to hepatitis B (i.e., anti-HBs ≥ 10 IU/L). In some circumstances persons with documented past anti-HBs >10 IU/L but are currently anti-HBs <10 IU/L may still benefit from re-immunization e.g., immunocompromised, significant time period since immunization or very high risk exposure.

§ Hepatitis B immune globulin; dose is 0.06 mL/kg intramuscularly. Dose should be administered as soon as possible after exposure ideally within 24 hours and not more than 14 days of exposure.

‡ Hepatitis B vaccine *(*see *Alberta Immunization Policy* for details*).*

† A non-responder is a person with inadequate response to vaccination (i.e., anti-HBs <10 IU/L) after 2 complete HBV vaccine series.

Hepatitis C Virus (HCV)

HCV Post-exposure Prophylaxis

Currently, prophylaxis of HCV is neither available nor recommended although early identification of infection following exposure should be accompanied by referral to an infectious disease or gastroenterology/hepatology specialist for further assessment. This referral should be carried out on a semi-urgent basis with assessment occurring within 1 to 3 months of new diagnosis.

Syphilis

Syphilis Post-exposure Prophylaxis

Table 19: Syphilis Post-exposure Prophylaxis

Syphilis Post-exposure Prophylaxis
An individual should be referred to STI services for management if post-exposure prophylaxis is required. Offer prophylaxis if: • it is likely that the patient will not return for follow up; • it is known that the assailant is infected or at high risk for syphilis; • requested by the patient/parent/guardian; • the patient has signs or symptoms of syphilis; or • in addition, it may be appropriate to offer prophylaxis in situations where vaginal, oral or anal penetration has occurred because most sexual assault victims do not return for follow up visits. Prophylaxis should be as **recommended for treatment** of syphilis in the *Alberta Treatment Guidelines for Sexually Transmitted Infections (STI) in Adolescents and Adults, 2012* as updated from time to time. The efficacy of antibiotic prophylaxis has not been studied in sexual assault. Prophylaxis with azithromycin (given for prophylaxis against chlamydia) is no longer considered to be effective against incubating syphilis in light of recent emergence of syphilis azithromycin resistance. If recipient subsequently has reactive syphilis serology, consultation with an STI specialist or STI Services is recommended to determine if other prohylaxis, e.g., benzathine penicillin G-long acting, is required.

Other Sexually Transmitted Infections (STI)

Considerations for Other STI Post-exposure Prophylaxis

Other STI should be considered during the assessment and follow-up for sexual assault/abuse. Post-exposure prophylaxis for STIs should utilize a test and treat approach. Offer prophylaxis to the patient on initial visit only if:

- it is likely that the patient will not return for follow up; in addition, it may be appropriate to offer prophylaxis in situations where vaginal, oral or anal penetration has occurred because some sexual assault victims do not return for follow up visits;
- it is known that the assailant is infected or at high risk for an STI;
- requested by the patient/parent/guardian; or
- the patient has signs or symptoms of an STI (syndromic management).

The efficacy of antibiotic prophylaxis has not been studied in sexual assault. Guidelines for the treatment and prophylaxis should be done as recommended in the *Alberta Treatment Guidelines for Sexually Transmitted Infections (STI) in Adolescents and Adults, 2012* as

updated from time to time. The recommendations current as of publication are outlined in Table 20.

Table 20: Sexually Transmitted Infections Post-exposure Prophylaxis

STI Post-exposure Prophylaxis	
STI	**PEP**
Gonorrhea	**Adults (Heterosexual/Pregnant Women)** **Preferred:** cefixime 800mg po as a single dose PLUS azithromycin 1gm po as a single dose **Alternate:** spectinomycin 2gm IM as a single dose PLUS co-treatment for chlamydia with azithromycin 1gm po as a single dose OR azithromycin 2 gm po as a single dose **MSM (Men who have Sex with Men) and Pharyngeal Infections** **Preferred:** ceftriaxone 250 mg IM as a single dose PLUS azithromycin 1gm po as a single dose **Alternate:** cefixime 800mg po as a single dose PLUS co-treatment for chlamydia with azithromycin 1gm po as a single dose OR azithromycin 2 gm po as a single dose **Children** Cefixime 16mg/kg to a maximum of 800 mg po single dose (Barbara Romanowski MD, FRCPC, January 2012 personal correspondence)
Chlamydia (normally done as co-treatment with Gonorrhea PEP)	**Non-pregnant adults** azithromycin 1 gm po single dose (not duplicated if azithromycin regimen is included for gonorrhea post-exposure prophylaxis) ***or*** doxycycline 100 mg po BID x 7 days **Pregnant adults** amoxicillin 500 mg po TID x 7 days *or* azithromycin* 1 gm po single dose **Discuss unknown long-term effects of azithromycin to fetus while emphasizing benefits of treatment of chlamydia and the fact that use of azithromycin to date has not been associated with any harm to fetus.*

STI Post-exposure Prophylaxis	
STI	**PEP**
	Children < 45 kg: azithromycin 15 mg/kg (max 1 gm) po single dose ≥ 45 kg: azithromycin 1 gm po single dose
Trichomoniasis	**Treat only if positive test for trichomonas** ≥ 45 kg: metronidazole 2 gm po single dose < 45 kg: metronidazole 30 mg/kg/day divided q 6 to q 12 hourly x 7 days (Dosing for pediatric Giardiasis, sanofi-aventis Canada Inc., 2011)

Other Management Issues

Sexual Abuse in Children

- In all cases where a person under 18 years of age is suspected or confirmed to have an STI, an assessment should be carried out by the clinician to determine if additional reporting is required.

    - **To Child and Family Services**
      The clinician should determine whether there are reasonable and probable grounds to believe that they are in contact with "a child in need of intervention" [as per Section 1(2) of the *Child, Youth and Family Enhancement Act* (2)] and shall report to a director pursuant to Section 4 of the CYFEA (2).

      Reporting is done by contacting the local Child and Family Services office or calling the CHILD ABUSE HOTLINE: 1-800-387-5437 (KIDS). For local office contact information see: www.child.alberta.ca/home/782.cfm

    - **To Law Enforcement Agency**
      Consent is a key factor in determining whether any form of sexual activity is a criminal offence. Children under 12 years of age do not have the legal capacity to consent to any form of sexual activity. The law identifies the exception for minors under age 16 years as having the ability to consent, in "close in age" or "peer group" situations. The law recognizes that the age of consent for sexual activity is 16 years of age.

      Reporting is done by contacting your local City Police Detachment or RCMP Detachment http://www.rcmp-grc.gc.ca/ab/det-eng.htm.

      For additional information see: Frequently Asked Questions:
      - Age of Consent to Sexual Activity www.justice.gc.ca/eng/dept-min/clp/faq.html (3)
      - The Canadian Criminal Code at: laws.justice.gc.ca/en/C-46/40863.html (4)

- It is recommended that all pre-pubertal and peri-pubertal children be managed in consultation with a referral centre in either:

    - **Edmonton:**
      Child and Adolescent Protection Centre,
      Stollery Children's Hospital, 1C4.24 Mackenzie Health Sciences Centre
      8440-112 Street
      Edmonton, Alberta T6G 2B7
      Tel: 780-407-1240

      OR

    - **Calgary:**
      Child Abuse Service
      Child Development Centre
      Suite 200, 3820-24 Ave NW
      Calgary, Alberta T2N 1N4
      Tel: 403-955-5959

Tetanus Prophylaxis

Immunizing agents (vaccine and/or tetanus immune globulin) are recommended for post-exposure prevention of tetanus in the context of wound management (e.g., dirty wounds/abrasions sustained outdoors). It is important to ascertain the number of doses of tetanus toxoid previously given and the interval since the last dose. See the current *Canadian Immunization Guide* (www.phac-aspc.gc.ca/publicat/cig-gci/index.html) and *Alberta Immunization Policy* for detailed recommendations. For adolescents and adults who have not already received a pertussis booster vaccine dose, the combined preparation of diphtheria, tetanus and acellular pertussis (dTap) is preferred.

Pregnancy

In adults and children who have reached menarche, if pregnancy is a possible result of the assault, emergency contraception (EC) should be considered. Pregnancy and breastfeeding are not contraindications for the use of emergency contraceptive pills. There is no evidence for teratogenicity (Glazier A, 1997; Bracken MB, 1990). Hormonal EC should be started as soon as possible after the assault. The emergency contraceptive pill should be the preferred method of EC (Dunn, 2003). Plan B is considered more effective and better tolerated than the Yupze method (WHO, 1998; Society of Obstetricians and Gynaecologists of Canada, 2003)

There has been some evidence that hormonal EC can be effective up to 5 days after the coital event (PHAC, 2009; Von Hertzen, 2002; Ellertson, 2003; Rodrigues, 2001). Women who have had unprotected intercourse and wish to prevent pregnancy should be offered hormonal EC up to 5 days after intercourse (Society of Obstetricians and Gynaecologists of Canada, 2003). Evidence has shown that a single dose of 1.5 mg of levonorgestrel is as effective as 2 doses of 0.75 mg of levonorgestrel taken 12 hours apart with no significant increase in adverse effects (Society of Obstetricians and Gynaecologists of Canada, 2003):

- Plan B: levonorgestrel 1.5 mg orally as a single dose; *or*
- Levonorgestrel 0.75 mg po BID + 2 doses [Gravol® (dimenhydrinate) 50 mg given 30 minutes before the second dose of levonorgestrel may prevent vomiting of medication].

COUNSELLING

The following recommendations are intended as a guide and are not intended to replace expert consultation where appropriate or individualized case management depending on specific circumstances.

Refer to other existing guidelines e.g., Alberta Notifiable Disease Guidelines for detailed recommendations on disease specific counselling.

Prevention of Further Transmission

Advise potentially exposed individual of the need to practice safer sex (i.e., use condoms) or abstain from sexual intercourse until infection has been ruled out (typically until 12 week serology for HIV can be performed) and to abstain from other practices that can lead to HIV, HBV and HCV transmission e.g., sharing needles for intravenous drug use.

Also advise potentially exposed individual not to donate blood, tissues, organs or semen until infection has been ruled out.

REFERENCES

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APPENDIX A - PROBABILITY OF TRANSMISSION OF HIV, HBV and HCV

Appendix A Table 1: Probability of HIV Transmission by Exposure Type	
Exposure (positive source)	**Probability of transmission per episode**
Blood transfusions (single unit of whole blood)	90% (Donegan, 1990)
Intravenous needle or syringe exposure	0.67% (Kaplan, 1992) [1/150]
Injection drug use – needle sharing	0.67% (Kaplan, 1995) [1/150]
Needlestick	0.3% (95% CI = 0.2 to 0.5%) (Bell, 1997; Cardo, 1997) [1/333] *There have been no reported instances of transmission of HIV from improperly discarded needles outside of the health care setting in either the USA or UK (MG Fowler, CDC, June 15, 2002 cited in Havens, 2003; Robertson, 2001). Another study found no seroconversions in 274 community needlestick injuries in pediatrics indicating that the risk of transmission in these events are very low* (Papenburg, 2008).
Receptive anal intercourse	1 to 30% (CDC, 2005; Powers, 2008; Boily, 2009) [1/100 – 1/3]
Insertive anal intercourse	0.1 to 10% (CDC, 2005; Powers, 2008; Boily, 2009) [1/1000 – 1/10]
Receptive vaginal exposure	0.1 to 10% (CDC, 2005; Powers, 2008; Boily, 2009) [1/1000 – 1/10]
Receptive oral exposure	0.04% (Vittinghoff, 1999; PHAC, 2004) [1/2500]
Mucous membrane exposure to blood or bodily fluids contaminated with blood	0.09% [95% CI, 0.006 to 0.5] (Ippolito, 1993; PHAC, 2004) 0.1% (ANCAHRD, 2001) [1/1000].
Human Milk Exposure (single)	0.001% - 0.004% (Havens, 2003) [1/100,000 – 1/25,000]

Appendix A Table 2: Approximate Alberta Transmission Risks

Three Drugs	
Two Drugs	
None	

Exposure	Risk Percentage*	Transmission risks: source with unknown risks factors (AB)¶	Transmission risks: source with known risk factors **t** (AB)	Transmission risks: known HIV positive (AB)†
Hollow Bore Needle stick	0.3%	1/196,700	1/3030	1/333
Needle Sharing - IDU	0.67%	1/87,800	1/1360	1/149
Penile –vaginal intercourse (risk to male)	0.05%	1/1,176,500	1/18,180	1/2000
Penile –vaginal intercourse (risk to female)	0.1%	1/588,250	1/9,090	1/1000
Anal intercourse (risk to insertive partner)	0.06%	1/980,400	1/15,150	1/1667
Anal intercourse (risk to receptive partner)	0.5 – 3%	1/117,650 - 1/19,600	1/1818 - 1/303	1/200 - 1/33
Oral intercourse (risk to insertive partner)	0.005%	1/11,765,000	1/181,800	1/20,000
Oral intercourse (risk to receptive partner)	0.01%	1/5,882,400	1/90,900	1/10,000
Human Milk Exposure	0.001 – 0.004%	1/58,823,500 - 1/14,705,900	1/,909,100 - 1/227,300	1/100,000 - 1/25,000

* Source: From Table 1 – Summarized in US Centers for Disease Control MMWR January 21, 2005/Vol54/No.RR-2.

¶ Source: Alberta Health- Based on high range modeling of provincial prevalence of 17 per 10,000.

t Based on 11% prevalence rate. Determining the current prevalence data for risk groups is difficult as the number of individuals in each group is difficult to discern. This rate was chosen based on Ontario Modeling from 2005 – estimate IDU prevalence at 0.369% (Source: Injection Drug Use, HIV and HCV Infection in Ontario: The Evidence 1992 to 2004) and extrapolated to Alberta. This prevalence is believed to overestimate the HIV prevalence in other risk groups and provides a basis for PEP decisions in Alberta.

† The transmission risk associated with a percutaneous or sexual exposure from a known HIV-positive source is reduced but not eliminated. The risk of transmission is reduced sufficiently to affect the decision

for PEP and the number of drugs associated with PEP. An exposure to a source individual with demonstrated virologic suppression, defined as undetectable serum viral load (<50 copies/ml) for 3 consecutive tests with the most recent being within 3-4 months (extended to 6 months for adherent patients whose viral load has been suppressed for more than 2 years and whose clinical immunological status is stable) and has no changes in adherence to current regimen (e.g., interrupted dosing), should be assessed based on the risk profile outlined in the "Transmission risks with known risk factors" column.

Appendix A Table 3: Probability of HBV Transmission

Exposure (positive source)	Per episode probability of transmission
Sexual exposure	– not quantified; however, receptive anal intercourse > insertive anal intercourse > vaginal intercourse > oral-anal contact – oral-genital and oral-oral contact do not appear to be significant modes of transmission – estimated to be transmitted 8.6 fold more efficiently than HIV – increased risk of transmission if source more infectious (i.e., higher HBV DNA and/or HBeAg positive)
Needlestick Source: HBsAg positive & HBeAg positive	37-62% (Mast, 1993)
Needlestick Source: HBsAg positive & HBeAg negative	23-27%

Appendix A Table 4: Probability of HCV Transmission

Exposure	Per episode probability of transmission
Sexual exposure	Not quantified; however: – long-term discordant monogamous partnerships are at lower risk of acquisition (0 to 0.6% per year) as compared to persons with multiple partners or those at risk for sexually transmitted diseases (0.4 to 1.8% per year) – risk of transmission increased if source HIV co-infected
Needlestick	1.8% (range 0 to 7%) (Alter, 1997; Lanphear, 1994; Puro, 1995; Mitsui, 1992)

APPENDIX B - PREVALENCE OF HIV/AIDS

Appendix B Table 1: Estimated proportion of HIV in Alberta by exposure category, 2011
(Source: Alberta Health)

Exposure category	Estimated numbers		% of total
	Number of cases	Range	
MSM (men who have sex with men)	1500	1120 - 1880	30%
MSM-IDU	90	70 - 110	1.8%
IDU	1220	930 - 1510	24.4%
Heterosexual/non-endemic	1250	930 - 1570	25%
Heterosexual/endemic	900	680 - 1120	18%
Other	40	20 - 60	0.8%
TOTAL	5000	3800 - 6200	100%

Appendix B Table 2: Number of positive HIV test reports by province and sex for all ages
[Source: PHAC. HIV and AIDS in Canada: Surveillance Report to December 31, 2010. 2012]

Region	Male	Female
	HIV number	HIV number
British Columbia	11,577	2,030
Alberta	4,300	1,128
Saskatchewan	821	532
Manitoba	1,294	478
Ontario	25,859	4,830
Quebec	11,933	3,102
New Brunswick	337	56
Nova Scotia & PEI	667	111
Newfoundland	207	55
Yukon	39	16
NWT	37	11
Nunavut	3	0
Total – Canada	57,074	12,349

Appendix B Table 3: Estimated prevalence of HIV positive adults aged 15 to 49, by country (end 2009)
[Source: UNAIDS Report on the global AIDS epidemic 2010 (2010)
Available at: http://www.unaids.org/globalreport/Global_report.htm (Accessed September 1, 2011)]

Country	HIV prevalence
Australia	0.1%
Central and South America	0.5%
Canada	0.2%
Congo	3.4%
Dominican Republic	0.9%
Ethiopia	4.4% (2003)
Eritrea	0.8%
Germany	0.1%
India	0.9%
Kenya	6.3%
Mexico	0.3%
Russian Federation	1.0%
Rwanda	2.9%
South Africa	17.8%
Spain	0.4%
Thailand	1.3%
United Kingdom	0.2%
United States	0.6%

APPENDIX C - ANTIRETROVIRAL DRUGS USED FOR ADULT AND ADOLESCENT HIV POST-EXPOSURE PROPHYLAXIS

Adapted from ***Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in HIV-1-infected adults and adolescents, Department of Health and Human Services.*** **Available at www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf**

Appendix C, Table 1: Characteristics of Nucleoside Reverse Transcriptase Inhibitors (NRTIs) (Updated July, 2014)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Emtricitabine (FTC)/ Emtriva®	- 200 mg hard gelatin capsule* - 10 mg/mL oral solution* *only available in US	Adult/Adolescent (≥ 18 years) *Capsule:* 200 mg once daily *Oral solution:* 240 mg (24 mL) once daily Take without regard to meals	Renal excretion 86% Dosage adjustment in renal insufficiency recommended	10 hrs/ >20 hrs	• Minimal toxicity • Hyperpigmentation/skin discoloration • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue FTC
Tenofovir Disoproxil Fumarate (TDF)/ Viread®	300 mg tablet	Adolescent (≥ 12 years and weight ≥ 35 kg) / Adult: 300mg once daily Take without regard to meals	Renal excretion – primary route of elimination Dosage adjustment in renal insufficiency recommended	17 hrs/ >60 hrs	• Asthenia, headache, diarrhea, nausea, vomiting, and flatulence • Renal insufficiency, Fanconi syndrome, proximal tubulopathy • Osteomalacia, decrease in bone mineral density • Potential decrease in bone mineral density • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDF

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Also available as:					
Truvada® Combination tablet of FTC with TDF	FTC 200 mg + TDF 300 mg	1 tablet once daily	Dosage adjustment in renal insufficiency recommended		
Lamivudine (3TC)/ 3TC®	• 150, 300 mg tablets • 10 mg/mL oral solution	• Adult/Adolescent (age ≥16 years): Weight < 50 kg: 4 mg/kg/dose po BID (maximum 150 mg po BID) • ≥ 50 kg: 150 mg po BID or 300 mg po once daily Take without regard to meals	Renal excretion 70% Dosage adjustment in renal insufficiency recommended	5–7 hrs/ 18–22 hrs	• Minimal toxicity • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue 3TC
Zidovudine (ZDV)/ Retrovir® (generic available as well)	• 100 mg capsules • 10 mg/mL oral solution	Adult/Adolescent (18 years or older): 300 mg po BID Take without regard to meals	Metabolized to GAZT Renal excretion of GAZT Dosage adjustment in renal insufficiency recommended	1.1 hrs/ 7 hrs	• Bone marrow suppression: macrocytic anemia or neutropenia • Nausea, vomiting, headache, insomnia, asthenia • Nail pigmentation • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Also available as:					mellitus • Lipoatrophy • Myopathy
Combivir® Combination tablet of 3TC with ZDV	3TC 150 mg + ZDV 300 mg	1 tablet BID			

Appendix C, Table 2: Characteristics of Protease Inhibitors (PIs) (Updated July, 2014)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
Darunavir (DRV)/ Prezista®	75, 150, 400, 600, 800 mg tablets	ADULT/ADOLESCENT (≥ 12 YEARS): No DRV resistance associated mutation: • 30 kg to < 40 kg: 675 DRV/100 mg RTV po once daily • ≥ 40 kg: 800 mg DRV/100mg RTV po once daily <u>Adult (≥ 18 years)</u> At least one DRV resistance associated mutation: 600 mg darunavir/100 mg RTV po BID Unboosted DRV is **<u>not</u>** recommended Take with food	CYP3A4 inhibitor and substrate	15 hrs (when combined with RTV)	Room temperature (up to 25ºC or 77ºF)	• Skin rash (10%): DRV has a sulfonamide moiety; Stevens-Johnson syndrome, toxic epidermal necrolyisis, acute generalized exanthematous pustulosis, and erythrema multiforme have been reported • Hepatotoxicity • Diarrhea, nausea • Headache • Hyperlipidemia • Serum transaminase elevation

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
						• Hyperglycemia • Fat maldistribution
Lopinavir + Ritonavir (LPV/r)/ Kaletra®	Tablets: (Adult tablet: LPV 200 mg + RTV 50 mg) or (Pediatric tablet: LPV 100 mg + RTV 25 mg) Oral solution: Each mL contains (LPV 80 mg + RTV 20 mg) Oral solution contains 42% alcohol	Adult(≥ 18 years): – < 3 LPV associated mutations: 800 mg LPV/200 mg RTV po once daily or 400 mg LPV/100 mg RTV po BID – ≥ 3 LPV associated mutations: 400 mg LPV /100 mg RTV po BID – LPV associated mutations: L10F/I/R/V, K20M/N/R, L24I, L33F, M36I, I47V, G48V, I54L/T/V, V82A/C/F/S/T,and I84V – LPV/RTV once daily is not recommended with NVP or EFV *Tablet:* Take without regard to meals *Oral solution:* Take with food	CYP3A4 inhibitor and substrate	5–6 hrs	Oral tablet is stable at room temperature Oral solution is stable at 2°–8°C (36°–46°F) until date on label and is stable when stored at room temperature (up to 25ºC or 77ºF) for 2 months	• GI intolerance, nausea, vomiting, diarrhea • Pancreatitis • Asthenia • Hyperlipidemia (especially hypertriglyceridemia) • Serum transaminase elevation • Hyperglycemia • Insulin resistance/diabetes mellitus • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval prolongation • QT interval prolongation and torsades de pointes have been reported; however, causality could not be established

Appendix C, Table 3: Characteristics of Integrase Inhibitors (Updated January 10, 2011)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Adverse Events
Dolutegravir (DTG) Tivicay®	50 mg tablet	50 mg QD	UGT1A1-mediated glucuronidation Minor contribution from CYP3A4	~14 hours	• Hypersensitivity Reactions (HSRs) including rash, constitutional symptoms, and organ dysfunction (including liver injury) have been reported • Insomnia • Headache
Raltegravir (RAL) Isentress®	400 mg tablet Double Check PM CANADA before finalizing	400mg BID	UGT1A1-mediated glucuronidation	~9 hours	• Rash, including Stevens-Johnson syndrome, HSR, and toxic epidermal necrolysis • Nausea • Headache • Diarrhea • Pyrexia • CPK elevation, muscle weakness, and rhabdomyolysis

APPENDIX D - ANTIRETROVIRAL DRUGS USED FOR PEDIATRIC HIV POST-EXPOSURE PROPHYLAXIS

Adapted from Guidelines for the Use of Antiretroviral Agents in Pediatric HIV Infection*, Department of Health and Human Services. August 11, 2011; 1–116.* UPDATED April 1, 2014. Available at http://aidsinfo.nih.gov/contentfiles/lvguidelines/pediatricguidelines.pdf

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-Lives	Adverse Events
Lamivudine (3TC)/3TC®	Oral solution: 10 mg/mL Tablets150 mg and 300 mg; 100 mg (Heptovir®)	**Neonate/infant dose (age <4 weeks)** **2 mg/kg/dose** twice daily **Pediatric dose (age ≥ 4 weeks)** **4 mg/kg/dose** (up to 150 mg) twice daily	• Renal excretion-dosage adjustment required in renal insufficiency. • Combivir® (fixed-dose combination products) should not be used in patients with creatinine clearance (CrCl) <50 mL/min, patients on dialysis, or patients with impaired hepatic function	5–7 hrs/ 18–22 hrs	• Minimal toxicity • Exacerbation of hepatitis has been reported after discontinuation of 3TC in the setting of chronic hepatitis B infection
Zidovudine (ZDV)/ Retrovir® (generic available)	Capsules: 100mg Syrup: 10 mg/mL	**Pediatric dose (6 weeks to <18 years of age):** • PO: 240 mg/m^2/dose po q12h or: • mg/kg dosing: (6 weeks of age and older) – 4 kg to < 9 kg: 12 mg/kg/dose po BID – 9 kg to < 30 kg: 9 mg/kg/dose po BID – ≥ 30 kg: 300 mg po BID	Metabolized to GAZT Renal excretion of GAZT Dosage adjustment in patients with renal insufficiency is recommended	1.1 hours/ 7 hours	• Bone marrow suppression: macrocytic anemia or neutropenia • Nausea, vomiting, headache, insomnia, asthenia • Lactic acidosis/severe hepatomegaly with hepatic steatosis • Nail pigmentation • Hyperlipidemia • Insulin resistance/diabetes

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-Lives	Adverse Events
					mellitus • Lipoatrophy • Myopathy
Lopinavir + Ritonavir (LPV/r)/ Kaletra®	**Pediatric oral solution:** 80 mg LPV/20 mg RTV per mL (contains 42.4% alcohol by volume) **Film-coated tablets:** 100 mg/25 mg LPV/r, 200 mg/50 mg LPV/r	**Dosing for individuals not receiving concomitant nevirapine (NVP) or efavirenz (EFV):** **Infant dose (14 days–12 months) Oral Solution:** • Once-daily dosing is **not** recommended. • 300 mg/m^2/dose LPV (75 mg/m^2/dose RTV) twice daily NOTE: Use of 300 mg/75 mg LPV/r per m^2 of body surface area in infants aged 12 months or younger is associated with lower LPV trough levels than those found in adults; in infants, LPV dosing should be adjusted for growth at frequent intervals (see text below) **Pediatric dose (>12 months–18 years) Oral Solution:**	Cytochrome P (CYP) 3A4 inhibitor and substrate • Dosing of LPV/r in patients with hepatic impairment: LPV/r is primarily metabolized by the liver. Caution should be used when administering LPV to patients with hepatic impairment. No dosing information is currently available for children or adults with hepatic insufficiency • In the coformulation of LPV/r, the RTV acts as a pharmacokinetic enhancer, not as an ARV agent. It does this by inhibiting the metabolism of LPV and increasing LPV plasma concentrations	5–6 hrs	• Gastrointestinal (GI) intolerance, nausea, vomiting, diarrhea, taste alteration • Asthenia • Hyperlipidemia, especially hypertriglyceridemia • Elevated transaminases • Hyperglycemia • Fat maldistribution • Possible increased bleeding in patients with hemophilia • PR interval prolongation • QT interval prolongation and torsade de pointes • Risk of toxicity- including life-threatening Cardiotoxicity- is increased in premature infants

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-Lives	Adverse Events
		• Once-daily dosing is **not** recommended • 230 mg/m^2/dose LPV/ 57.5 mg/m^2/dose RTV po BID • < 15 kg: approximately 12 mg/kg/dose LPV/3 mg/kg/dose RTV po BID • 15 kg to 40 kg: approximately 10 mg/kg/dose LPV/2.5 mg/kg/dose RTV po BID **Pediatric dose (>12 months–18 years) Tablets:** Dose based on weight for 100 mg LPV/ 25 mg RTV tablets: • <15kg: Not recommended. Use oral solution • 15 kg to 25 kg: 2 tablets (200/50 mg) po BID • > 25 to 35 kg: 3 tablets (300/75 mg) po BID • > 35 kg: 4 tablets (400/100 mg) po BID			
Raltegravir (RAL) Isentress®	400 mg tablet 25 and 100mg chewable tablets	**Children Aged 2 to <12 Years***:* • <25 kg: Chewable tablet twice daily (maximum of 300 mg twice daily). See	UGT1A1-mediated glucuronidation	~9 hrs	• Rash including Stevens Johnsons syndrome, HSR, and toxic epidermal necrolysis

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<td></td>
<td>table below for chewable tablet dose
• ≥25 kg: 400-mg film-coated tablet twice daily or chewable tablets twice daily. See table for chewable tablet dose

Dose for chewable tablet and film-coated tablet not interchangeable

Chewable Tablet Dosing Table
<table>
<tr><td>Dosing[a] of chewable tablets in children aged 2 to <12 years:</td></tr>
</table>
<table>
<tr><th>Body Weight (kg)</th><th>Dose</th><th>Number of Chewable Tablets</th></tr>
<tr><td>11 to <14</td><td>75 mg twice daily</td><td>3 x 25 mg twice daily</td></tr>
<tr><td>14 to <20</td><td>100 mg twice daily</td><td>1 x 100 mg twice daily</td></tr>
<tr><td>20 to <28</td><td>150 mg twice daily</td><td>1.5 x 100 mg[b] twice daily</td></tr>
<tr><td>28 to <40</td><td>200 mg twice daily</td><td>2 x 100 mg twice daily</td></tr>
<tr><td>≥40</td><td>300 mg twice daily</td><td>3 x 100 mg twice daily</td></tr>
</table>
a The weight-based dosing recommendation for the chewable tablet is based on approximately 6 mg/kg/dose twice daily
b The 100-mg chewable tablet</td>
<td></td>
<td></td>
<td>• Nausea
• Headache
• Diarrhea
• Pyrexia
• CPK elevation, muscle weakness and rhabdomyolysis</td>
</tr>
</table>

<table>
<tr><th>Generic Name (abbreviation)/ Trade Name</th><th>Formulations</th><th>Dosing Recommendations</th><th>Elimination</th><th>Serum/ Intracellular Half-Lives</th><th>Adverse Events</th></tr>
<tr><td></td><td></td><td>can be divided into equal halves

Note: Maximum dose of chewable tablets is 300 mg twice daily

Adolescent (Aged ≥12 Years)
• 400-mg film-coated tablet twice daily</td><td></td><td></td><td></td></tr>
<tr><td>Darunavir (DRV)/ Prezista®</td><td>75, 150, 600, 800 mg tablets</td><td>Unboosted DRV is <u>not</u> recommended

Adolescent (Aged ≥12 Years)/Adult Dose<table><tr><th>Body Weight (kg)</th><th>Dose</th></tr><tr><td>30 to <40</td><td>DRV 675 mg plus RTV 100 mg (tablet or 1.25 mLb)

once daily</td></tr><tr><td>≥40 kg:</td><td>DRV 800 mg plus RTV 100 mg (tablet or

1.25 mLb) once daily</td></tr></table>a The 675 mg DRV dose is rounded for convenience
b RTV 80 mg/mL oral solution

Take with food</td><td>CYP3A4 inhibitor and substrate</td><td>15 hrs (when combined with RTV)</td><td>• Skin rash (10%)
• DRV has a sulfonamide moiety
• Stevens-Johnson syndrome, toxic epidermal necrolyisis, acute generalized exanthematous pustulosis, and erythrema multiforme have been reported
• Hepatotoxicity
• Diarrhea, nausea
• Headache
• Hyperlipidemia
• Serum transaminase elevation
• Hyperglycemia
• Fat maldistribution</td></tr>
</table>

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-Lives	Adverse Events
Dolutegravir (DTG) Tivicay®	50 mg tablet	50 mg QD	UGT1A1-mediated glucuronidation Minor contribution from CYP3A4	~14 hours	• Hypersensitivity Reactions (HSRs) including rash, constitutional symptoms, and organ dysfunction (including liver injury) have been reported • Insomnia • Headache

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