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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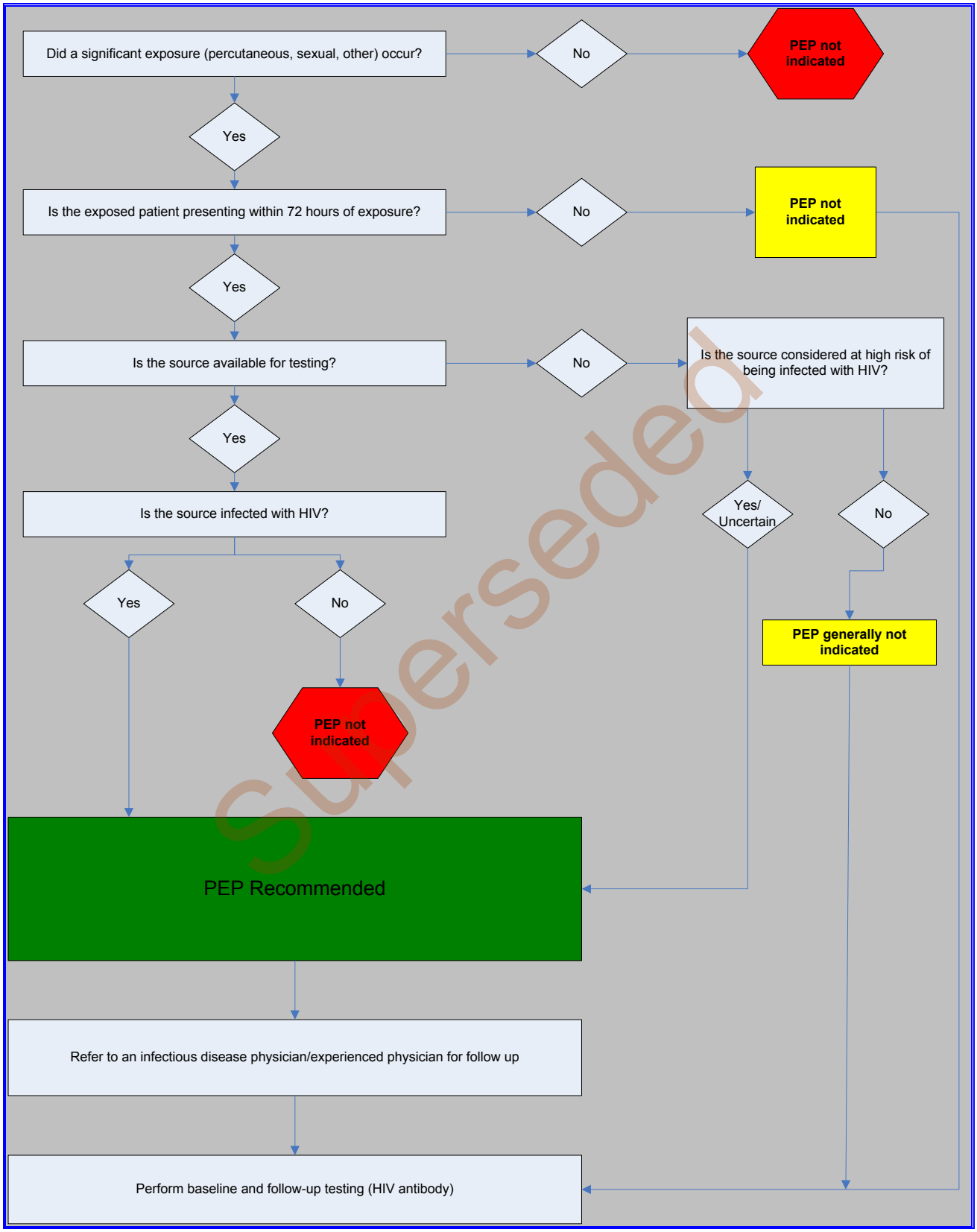
ACRONYM LIST

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
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

QUICK REFERENCE GUIDES

HIV POST-EXPOSURE PROPHLYLAXIS FOLLOWING BLOOD AND BODY FLUID EXPOSURE



Testing			
Source (if possible):	**Recipient:**		
	Source Status	**Specific tests**	**Intervals**
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 infectious disease specialist. For testing under the Mandatory Testing and Disclosure Act please visit www.health.alberta.ca/professionals/mandatory-testing.html	Source HIV negative	None	Not applicable
	Source unknown, or known HIV positive	HIV antibody	Baseline 4-6 weeks 12 weeks
Hepatitis B surface antigen (HBsAg) For testing under the Mandatory Testing and Disclosure Act please visit www.health.alberta.ca/professionals/mandatory-testing.html	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 is unnecessary*	Hepatitis B surface antibody (anti-HBs) Hepatitis B surface antigen (HBsAg)	Baseline
		As indicated in the HBV Post-Exposure Prophylaxis table (see page 39)	Follow-up
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* For testing under the Mandatory Testing and Disclosure Act please visit www.health.alberta.ca/professionals/mandatory-testing.html	Source HCV-antibody negative	None	Not applicable
	Source unknown or HCV-antibody positive and/or HCV-RNA positive	HCV antibody Alanine Aminotransferase (ALT)	Baseline
		HCV-RNA	6 weeks

HIV Post-exposure Prophylaxis			
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 – large bore needle – deep puncture – visible blood (fresh) on device/syringe	PEP Recommended (see page 35)	PEP Recommended (see page 36)	PEP Not generally recommended but may be considered in exceptional circumstances (see page 37)
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 35)	PEP Not generally recommended but may be considered in exceptional circumstances (see page 36)	PEP Not recommended (see page 37)
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 35)	PEP Not recommended (see page 36)	PEP Not recommended (see page 37)
Anal, vaginal or oral penetration* without condom, condom broke or condom status unknown **Partial or complete insertion of penis (with or without ejaculation) into mouth, vagina or anus* OR Sexual assault/sexual abuse	PEP Recommended (see page 44)	PEP Recommended (see page 45)	PEP Not generally recommended but may be considered in exceptional circumstances (see page 46)

HIV Post-exposure Prophylaxis

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
No anal, vaginal or oral penetration OR Anal, vaginal or oral penetration with intact condom	PEP Not recommended (see page 44)	PEP Not recommended (see page 45)	PEP Not recommended (see page 46)

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 vaccination 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 39, 48)	PEP Recommended* (see page 39, 48)	PEP Recommended* (see page 39, 48)
	*Prophylaxis is recommended in all individuals non-HBV immune. 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 41, 50)	PEP Not available (see page 41, 50)	PEP Not available (see page 41, 50)

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 has 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 inform 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 Committee 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, January 1, 2013*" 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 by 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, January 1, 2013*. 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 the source 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

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).

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):

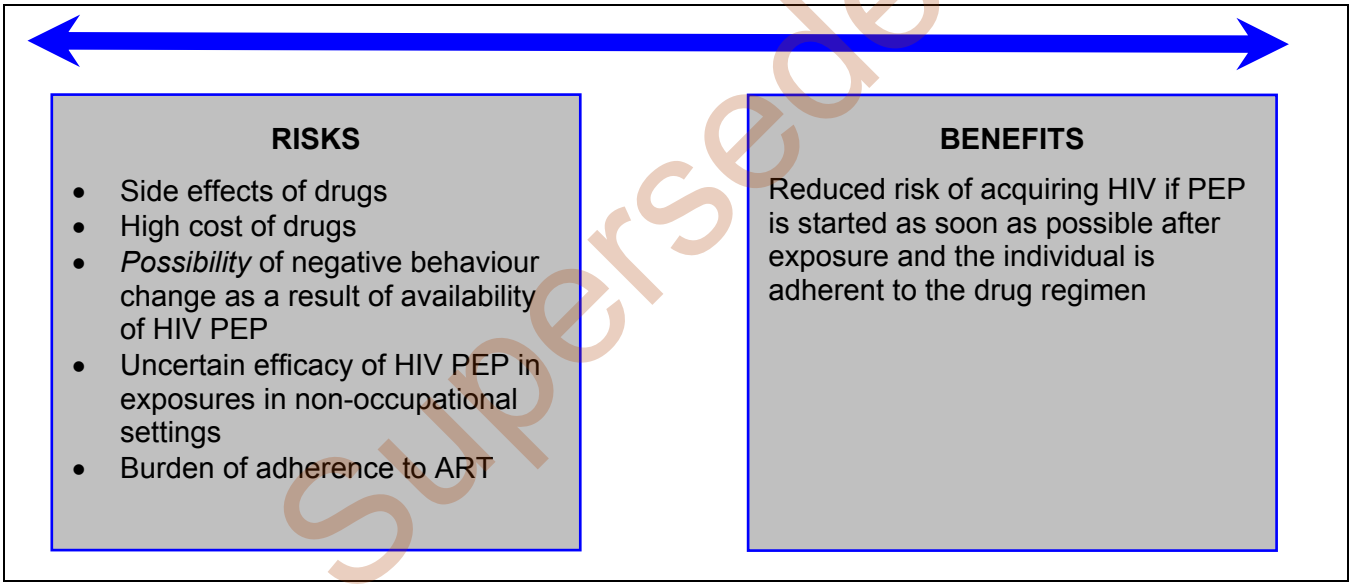
- PEP can preserve life and health;
- timely PEP is currently the only way of reducing the risk of acquiring HIV infection in an individual who has been exposed to the virus;
- Alberta's guidelines are founded on the principle of equity;
- Alberta's guidelines are based on clinical considerations of 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 Diagram 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 clinical evidence uncertainty. 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 a reasonable risk of transmission/acquisition and where PEP has the potential of limiting this risk.

Diagram 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

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.

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 decreases, but does not completely eliminate, transmission risk;
- 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.

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). 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 from PEP. 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). With the exception of nevirapine, which is immediately active intracellularly, the currently recommended PEP drugs 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.

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 AH'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.

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; Poyten, 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).

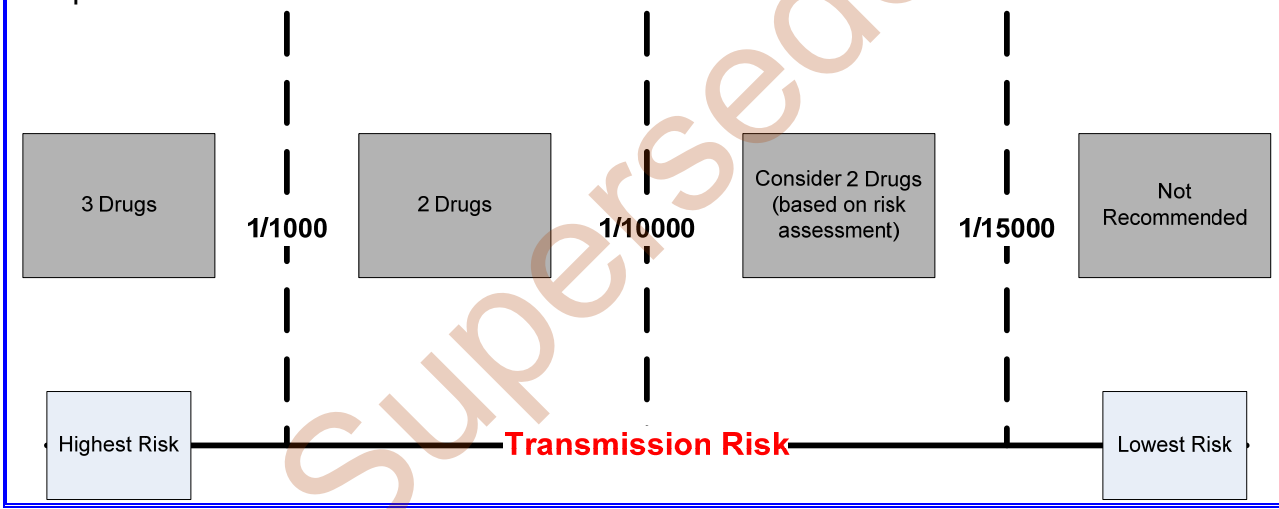
Drug selection for PEP must consider a number of factors including availability, evidence of effectiveness, cost of the regime, tolerability and side effects, pill burden, adherence and operational ease of use. Selection of the preferred or alternative PEP regime should try to minimize the risks of adverse 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 regime (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 regime 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 (Australian Government, 2007). 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. New classes of ARVs that are much better tolerated (e.g., integrase inhibitors) have become available and the safety and tolerability of three-drug regimes is increasing.

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 regime is preferred over a three-drug regime (Roland, 2007). These guidelines recommend a three-drug regime only in the highest risk exposures or if there is significant prevalence of viral resistance in the community. It may also be considered if the exposed individual may already be HIV positive as combination therapy reduces the risk of developing acquired drug resistance. 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 (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 regimes, 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 regime for PEP. A 28-day course of tenofovir-emtricitabine is now the preferred regime (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.

If a third drug is added, a protease inhibitor (PI), often boosted with low-dose ritonavir, is commonly used (Landovitz, 2009). Ritonavir improves the pharmacokinetics of three-drug regimes. Traditionally lopinavir-ritonavir has been the preferred protease inhibitor for a three-drug regimen due to effectiveness, availability and cost. Alternative regimes 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). Darunavir-ritonavir is now the recommended PI when no clear superior benefit for use of the other drugs exists. Atazanavir-ritonavir is considered an alternate as it must be used with caution and with appropriate dosing separation when combined with antacids and H2 blockers (US Department of Health and Human Services, 2011;,Bristol-Meyer Squibb Canada, Reyata PM, 2011).

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, efavirenz has been either noninferior or superior to every comparator with which it has been studied (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 regimes due to the high rate of serious adverse events associated with its use for PEP (CDC, 2001; MMWR, 2001; Patel, 2004).

A study of the combination use of raltegravir (an integrase inhibitor) and tenofovir-emtricitabine demonstrated that individuals reported fewer side effects and better completion rates compared to historical controls using a protease inhibitor in combination with two NRTIs for PEP (Mayer, 2009). Raltegravir is not metabolized through the cytochrome p450 enzyme system and therefore has 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). Recent data also 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). 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 integrase inhibitors or CCR5 antagonists as preferred agents for HIV PEP. Insentress may be considered as alternate if serious drug-drug interactions are possible or

serious side effects and adherence are a concern. The recommendations for regimens using integrase inhibitors, CCR5 antagonists or new drug classes such as the fusion inhibitors will be reviewed on an ongoing basis.

Alberta's recommended regimens for post-exposure prophylaxis in **ADULTS** are outlined in Table 2.

Table 2: ADULT Regimens for 28-day Post-exposure Prophylaxis for HIV infection.
Adapted from Landovitz RJ, Currier JS. Postexposure prophylaxis for HIV infection. N Engl J Med 2009;361:1768-75.

	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‡	Tenofovir – Emtricitabine‡ **Plus** Darunavir – Ritonavir
Alternate	Zidovudine – Lamivudine§	Tenofovir – Emtricitabine‡ **or** Zidovudine – Lamivudine§ **Plus** Atazanavir – Ritonavir **or** Lopinavir – Ritonavir **OR** Tenofovir – Emtricitabine‡ **or** Zidovudine – Lamivudine§ **Plus** Raltegravir†

¶ 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 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.
§ Zidovudine–lamivudine is not recommended in patients with a creatinine clearance of less than 50 ml per minute.
† Raltegravir should be considered as the third drug when significant drug interactions with other regimens are possible, or serious side effects and adherence may be an issue.

Increasingly, triple NRTI drug regimes are being recommended as regimes (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 to maintain consistency and simplicity.

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). Therefore, both two- and three-drug regimes are outlined 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 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 remain the same for children and adolescents.

Table 3: Recommended Regimens for Pediatric Post-Exposure Prophylaxis.
Adapted from New York State Department of Health. HIV post-exposure prophylaxis for children beyond the perinatal period. New York State Department of Health 2010.

AGE		Two-drug regimen (See Appendix C for drug dosages and side effects)	Three-drug regimen (See Appendix C for drug dosages and side effects)
Children >14 days - <6 years of age ***or*** **For those who cannot swallow pills**	Preferred	Zidovudine syrup - Lamivudine oral solution	Zidovudine syrup – Lamivudine oral solution **Plus** Lopinavir - Ritonavir¶ oral solution §
Children 6 years - <12 years of age	Preferred	Zidovudine – Lamivudine	Zidovudine - Lamivudine **Plus** Darunavir – Ritonavir¶
Adolescents ≥ 12 years of age	Preferred	Tenofovir – Emtricitabine‡	Tenofovir‡ – Emtricitabine ‡ **Plus** Darunavir – Ritonavir¶
	Alternate	Zidovudine – Lamivudine	Tenofovir – Emtricitabine ‡ **or** Zidovudine – Lamivudine **Plus** Lopinavir – Ritonavir

¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ Truvuda 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 Truvuda in pediatric patients less than 12 years of age have not been established. Tenofovir has been shown to decrease bone mineral density in children.

Pregnancy and Breastfeeding

Pregnancy

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).

A relationship between preterm birth and ARV therapy has recently 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.

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). Darunavir, tipranavir and fosamprenavir are not recommended during pregnancy based on limited efficacy and safety data (Sturt, 2011). 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 regime for pregnant HIV-1 infected women who meet treatment criteria. This differs from the US treatment guideline that prefers zidovudine-lamivudine (Panel on Treatment of HIV-Infected Pregnant Women and Prevention of Perinatal Transmission, 2010). Due to evidence of bone-related toxicity and growth restrictions in infants of macaques, tenofivir is only recommended in situations of resistance or contraindications (including hepatitis B infection). In Canada, tenofivir-emtricitabine is recommended for use in pregnant women

only when the potential benefits outweigh the potential risk to the fetus (Gilead Sciences Canada, Inc. Pr-Truvada PM, 2009).

Dual nucleoside regimes are not recommended for perinatal transmission (Sturt, 2011) because these more complex regimes do not provide clear benefits in terms of transmission prevention (perinatal) as compared with zidovudine and nevirapine. However, nevirapine is not recommended for PEP so dual nucleoside regimens remain favored for PEP. US guidelines recommend lopinavir-ritonavir as a preferred protease inhibitor 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). Other more complex regimes 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 preferred ART regimes for pregnancy.

Consideration should be given to continuing ART through to delivery (longer than 28 days) if PEP is started after 30 weeks gestation to protect the fetus from perinatal transmission in case of PEP failure. Decisions on the continuation of ART during labour and delivery should be done in consultation with a physician knowledgeable about HIV.

Table 4: Recommended antiretroviral therapy regimen for post-exposure prophylaxis during pregnancy or breastfeeding

PEP ART During Pregnancy or Breastfeeding		
Preferred	**Alternate**	**Contraindicated or Not Recommended**
2 Drug : NRTI Regimen		
Zidovudine – Lamivudine		Efavirenz Didanosine and stavudine (combined) Darunavir Tipranavir Fosamprenavir Indinavir (unboosted) in the 2nd or 3rd trimester Raltegravir
3 Drug : NRTI plus PI Regimen	**3 Drug : NRTI plus PI Regimen**	
Zidovudine – Lamivudine **Plus** Lopinavir – Ritonavir¶	Tenofovir – Emtricitabine‡ **Plus** Lopinavir – Ritonavir¶	

¶ The boosting agent ritonavir is not considered to be an active drug in tabulating the number of agents in the three-drug regimen.
‡ Recommended for use in pregnant women only when the potential benefits outweigh the potential risk to the fetus. Due to evidence of bone-related toxicity and growth restrictions in infants of macaques, only recommend tenofovir in situations of resistance or contraindications including HBV infection. It is the preferred NRTI in HBV co-infection.

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 decrease 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 protease inhibitor should ideally be followed by, or in conjunction with, a medical specialist expert in HIV ART.

Initial PEP will most often be started in ER departments with dispensing of starter kits to cover the patient until a physician who will provide ongoing care can assess the patient. 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 reported to be transmitted 8.6 times more efficiently than HIV (Kingsley, 1990). Similar to STI, several factors increase the risk of transmission of HBV including:

- increasing number of sexual partners;
- 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.

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). 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).

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 behaviour 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 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 Incivek® (telaprevir) taken in combination with pegylated interferon and ribavirin showed to be effective in the treatment of genotype 1 chronic HCV infection in adult patients (Vertex Pharmaceuticals Incorporated, 2012) but were not evaluated for post-exposure management and prophylaxis.

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 probably 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 virulence 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, it is recommended by many national guidelines including Canada and the United States (CDC, 2010; PHAC 2010).

RECOMMENDATIONS FOR TESTING AND PEP (EXCLUDING PERINATAL EXPOSURES, SEXUAL EXPOSURES, AND SEXUAL ASSAULT/ABUSE)

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)

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 of 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 antibody 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) patient is HCV infected/co-infected, or 3) there is a strong indication of potential exposure to HIV-2.

<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 regimes</td><td>Pediatrics: Three-drug regimen
See Table 3 for preferred pediatric regimes</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>

†An infectious disease/HIV specialist/medical specialist expert in HIV PEP should 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.

HIV Post-exposure Prophylaxis (See Appendix C for drug dosages and side effects)		
Source: HIV status unknown, however, high risk* for HIV		
Type of exposure	**HIV PEP**	
Percutaneous injury – large bore needle – deep puncture – visible blood (fresh) on device/syringe	**Recommended†**	
	Adults: two- or three-drug regimen (see Table 1) See Table 2 or 4 for recommended drug regimes	**Pediatrics: two- or three-drug regimen (see Table 1)** See Table 3 for preferred pediatric regimes
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	**Not generally recommended; but may be considered in exceptional circumstances** (e.g., deep injury, extensive mucosal/non-intact skin exposure to blood)	
Mucous membrane exposure to non-blood containing bodily fluids OR Intact skin exposure to blood or visible blood-stained bodily fluid	**Not recommended**	

* 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.

†An infectious disease/HIV specialist/medical specialist expert in HIV PEP should 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.

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**

†An infectious disease/HIV specialist/medical specialist expert in HIV PEP should 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.

Hepatitis B Virus (HBV)

HBV Post-exposure Testing		
Source *(if possible):	**Recipient*:**	
	Interval	**Specific tests**
Hepatitis B surface antigen (HBsAg)	Baseline	Hepatitis B surface antibody (anti-HBs) Hepatitis B surface antigen (HBsAg)
	Follow-up	As indicated in the HBV Post-exposure Prophylaxis table

*If recipient is known to be immune to HBV (anti-HBs ≥ 10 IU/L) or HBsAg positive, source and recipient testing is unnecessary.

HBV Post-exposure Prophylaxis

(Adapted from: *Canadian Immunization Guide*, 7th edition, 2006; Alberta Immunization Policy)

RECIPIENT± Immunization & baseline antibody response (antiHBs) 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	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	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	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 (Alberta Immunization Policy, 2007 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 Testing			
Source (if possible):	**Recipient:**		
	Source	**Intervals**	**Specific tests***
Hepatitis C antibody If source tests positive, a follow-up HCV-RNA should be performed If source tests negative, no further testing routinely required in recipient †	Source HCV-antibody negative	None	None
	Source unknown **or** Source HCV-antibody positive and/or HCV-RNA positive	Baseline	HCV antibodyΨ Alanine Aminotransferase (ALT)‡
		6 weeks	HCV-RNA†

* 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.
† Regular follow-up with 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 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).
‡ If at any time the serum ALT level is elevated in the exposed person, an HCV-RNA test should be completed to assess for acute HCV infection.

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.

RECOMMENDATIONS FOR TESTING AND PEP IN 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 percutaneous or mucosal exposure 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)

HIV Post-exposure Testing		
Source (if possible):	**Recipient:**	
	Intervals	**Specific tests**
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.	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 of 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 antibody 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; 1) where PEP has been extended significantly past 28 days, 2) patients with HCV infection, or 3) where there is an indication of potential exposure to HIV-2.

<table>
<tr><th colspan="3">HIV Post-exposure Prophylaxis
(See Appendix C for drug dosages and side effects)</th></tr>
<tr><td colspan="3">Source: Known HIV-positive assailant*</td></tr>
<tr><td colspan="3">Recipient:</td></tr>
<tr><td>Type of exposure</td><td colspan="2">HIV PEP</td></tr>
<tr><td rowspan="2">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)</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: Three-drug regimen
See Tables 2 or 4 for recommended regimes</td><td>Pediatrics: Three-drug regimen
See Table 3 for preferred pediatric regimes</td></tr>
<tr><td>No anal, vaginal or oral penetration
OR
Anal, vaginal or oral penetration with intact condom</td><td colspan="2">Not recommended</td></tr>
</table>

† An infectious disease/HIV specialist/medical specialist expert in HIV PEP should 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.

<table>
<tr><th colspan="3">HIV Post-exposure Prophylaxis
(See Appendix C for drug dosages and side effects)</th></tr>
<tr><td colspan="3">Source: Assailant with high risk* factors for HIV</td></tr>
<tr><td colspan="3">Recipient:</td></tr>
<tr><td>Type of exposure</td><td colspan="2">HIV PEP</td></tr>
<tr><td rowspan="2">Anal, vaginal or oral penetrationΨ without condom or condom broke or condom status unknown

ΨPartial 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)</td><td colspan="2">Recommended†</td></tr>
<tr><td>Adults: two- or three- drug regimen (see Table 1)

See Table 2 or 4 for recommended drug regimes</td><td>Pediatrics: two- or three-drug regimen (see Table 1)

See Table 3 for preferred pediatric regimes</td></tr>
<tr><td>No anal, vaginal or oral penetration

OR

Anal or vaginal or oral penetration with intact condom</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.

† An infectious disease/HIV specialist/medical specialist expert in HIV PEP should 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.

HIV Post-exposure Prophylaxis (See Appendix C for drug dosages and side effects)	
Source: Unknown assailant or assailant with low risk factors for HIV	
Recipient:	
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**

† An infectious disease/HIV specialist/medical specialist expert in HIV PEP should 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.

Hepatitis B Virus (HBV)

HBV Post-exposure Testing		
Source *(if possible):	**Recipient*:**	
	Interval	**Specific tests**
Hepatitis B surface antigen (HBsAg)	Baseline	Hepatitis B surface antibody (anti-HBs) Hepatitis B surface antigen (HBsAg)
	Follow-up	As indicated in the HBV Post-exposure Prophylaxis table

***** If recipient is known to be immune to HBV (anti-HBs ≥ 10 IU/L) or HBsAg positive, source and recipient testing is unnecessary.

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.

HBV Post-exposure Prophylaxis

(Adapted from: *Canadian Immunization Guide*, 7th edition, 2006; Alberta Immunization Policy)

RECIPIENT± Immunization & baseline antibody response (antiHBs) 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	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	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	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.
** 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 within 14 days of exposure.
‡ Hepatitis B vaccine *(Alberta Immunization Policy 2007 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 Testing			
Source (if possible):	**Recipient:**		
	Source	**Intervals**	**Specific tests***
Hepatitis C antibody If source tests positive, a follow-up HCV-RNA should be performed If source tests negative, no further testing routinely required in recipient †	Source HCV-antibody negative	None	None
	Source unknown **or** Source HCV-antibody positive and/or HCV-RNA positive	Baseline	HCV antibodyΨ Alanine Aminotransferase (ALT)‡
		6 weeks	HCV-RNA†

* 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.
† Regular follow-up with 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 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). Refer to GUIDE TO SERVICES Alberta Health Services – The Provincial Laboratory for Public Health (Microbiology) and The Division of Medical Microbiology; University of Alberta Site, Edmonton, Alberta available at www.provlab.ab.ca/guide-to-services.pdf.
‡ If at any time the serum ALT level is elevated in the exposed person, an HCV-RNA test should be completed to assess for acute HCV infection.

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 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))
	4 weeks 12 weeks	Syphilis serology should be repeated at 4 and 12 weeks after exposure

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.* 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)

(Public Health Agency of Canada, 2010)

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. – If available, both tests (culture and NAAT) should be performed. – 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.
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)	
Recipient: pre-pubertal† or peri-pubertal† children	
Specimen* type by gender	**Condition or organism to be detected**
Urine: 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. – 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.
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)	
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.

Considerations for Other STI Post-exposure Prophylaxis

Other STI should be considered during the assessment and follow-up for sexual assault/abuse. 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 an STI,
- requested by the patient/parent/guardian,
- the patient has signs or symptoms of an STI, 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.

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

STI Post-exposure Prophylaxis	
STI	**PEP**
Gonorrhea	**Adults (Heterosexual/Pregnant Women)** Preferred: cefixime 800mg po as a single dose PLUS co-treatment for chlamydia with 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 co-treatment for chlamydia with 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	**Non-pregnant adults** azithromycin 1 gm po single dose *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 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 6 month 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.

FOLLOW-UP

Clinicians should closely monitor individuals receiving HIV PEP to detect ARV-induced toxicities.

Ideally a physician experienced in prescribing ARVs should follow patients continuing on HIV PEP. All patients prescribed a PI (e.g., darunavir-ritonavir) should ideally be followed by, or in conjunction with, an infectious disease/HIV specialist/medical specialist expert in HIV ART.

Appropriate referral should be made as necessary and available (e.g., to sexual assault teams, local police/RCMP, psychologist support, local victim support organizations, etc).

Suggested frequency of clinic visits/laboratory tests and reasons for follow-up for individual receiving HIV PEP is outlined:

Follow-up Testing Recommendations		
	Timeline	**Testing**
Nucleoside Reverse Transcriptase Inhibitor only (two-drug regimen)	Baseline visit	– Complete blood count with differential (CBCD) – Creatinine (Cr) – Review possible side effects of medications – Review need for 100% adherence with medications and need to complete full course
	Two week follow-up	– CBCD, Cr – Assess adherence with medications – Review for side effects
	One month follow-up (New York State Dept of Health AIDS Institute, 2010)	– CBCD, Cr – Assess adherence with medications – Review for side effects
Nucleoside Reverse Transcriptase Inhibitor plus Protease Inhibitor (three-drug regimen)	Baseline visit	– CBCD, Cr, ALT – review past medical history and concurrent medications for potential drug interactions e.g., with darunavir plus ritonavir (See Appendix C) – review possible side effects of medications – review need for 100% adherence with medications and need to complete full course
	Two week follow-up	– CBCD, Cr, ALT – Assess adherence with medications – Review for side effects
	One month follow up (New York State Dept of Health AIDS Institute, 2010)	– CBCD, Cr, ALT – Assess adherence with medications – Review for side effects

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

Table 1: Probability of Transmission HIV	
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]

Table 2: 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%

Table 3: 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

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%

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

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 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. January 10, 2011; 1–166.*** **Available at www.aidsinfo.nih.gov/ContentFiles/AdultandAdolescentGL.pdf**

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

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Abacavir (ABC)/ Ziagen **Also available as:**	Ziagen - 300-mg tablets - 20-mg/mL oral solution	Ziagen 300 mg BID or 600 mg once daily Take without regard to meals	Metabolized by alcohol dehydrogenase and glucuronyl transferase Renal excretion of metabolites 82% Dosage adjustment for ABC recommended in patients with hepatic insufficiency	1.5 hrs/ 12–26 hrs	• *Hypersensitivity reactions (HSR):* Patients positive for HLA-B*5701 are at highest risk. HLA screening should be done prior to initiation of ABC. Rechallenge is not recommended. • Symptoms of HSR may include fever, rash, nausea, vomiting, diarrhea, abdominal pain, malaise, or fatigue or respiratory symptoms such as sore throat, cough, or shortness of breath. • Some cohort studies suggest increased risk of myocardial infarction (MI) with recent or current use of ABC, but this risk is not substantiated in other studies.
Trizivir ABC with ZDV+3TC	Trizivir ABC 300 mg + ZDV 300 mg + 3TC 150 mg	Trizivir 1 tablet BID			
Epzicom ABC with 3TC	Epzicom ABC 600 mg + 3TC 300 mg	Epzicom 1 tablet once daily			

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Emtricitabine (FTC)/ Emtriva **Also available as:**	Emtriva - 200-mg hard gelatin capsule - 10-mg/mL oral solution	Emtriva *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.
Atripla FTC with EFV+TDF	Atripla FTC 200 mg + EFV 600 mg + TDF 300 mg	Atripla 1 tablet at or before bedtime Take on an empty stomach to reduce side effects			
Truvada FTC with TDF	Truvada FTC 200 mg + TDF 300 mg	Truvada 1 tablet once daily			
Lamivudine (3TC)/ Epivir **Also available as:**	Epivir • 150-, 300-mg tablets • 10-mg/mL oral solution	Epivir 150 mg BID or 300 mg 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.
Combivir 3TC with ZDV	Combivir 3TC 150 mg + ZDV 300 mg	Combivir 1 tablet BID			
Epzicom 3TC with ABC	Epzicom 3TC 300 mg + ABC 600 mg	Epzicom 1 tablet once daily			
Trizivir 3TC with ZDV+ABC	Trizivir 3TC 150 mg + ZDV 300 mg + ABC 300 mg	Trizivir 1 tablet BID			

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Stavudine (d4T)/ Zerit	Zerit • 15-, 20-, 30-, 40-mg capsules • 1-mg/mL oral solution	**Body weight ≥ 60 kg:** 40 mg BID **Body weight <60 kg:** 30 mg BID* Take without regard to meals *WHO recommends 30 mg BID dosing regardless of body weight.	Renal excretion 50% Dosage adjustment in renal insufficiency recommended	1 hr/ 7.5 hrs	Peripheral neuropathy • Lipoatrophy • Pancreatitis • Lactic acidosis/severe hepatomegaly with hepatic steatosis (rare but potentially life-threatening toxicity) • Hyperlipidemia • Insulin resistance/diabetes mellitus • Rapidly progressive ascending neuromuscular weakness (rare)
Tenofovir Disoproxil Fumarate (TDF)/ Viread **Also available as:**	Viread 300-mg tablet	Viread 1 tablet once daily Take without regard to meals	Renal excretion Dosage adjustment in renal insufficiency recommended	17 hrs/ >60 hrs	• Renal insufficiency, Fanconi syndrome • Osteomalacia • Potential decrease in bone mineral density • Severe acute exacerbation of hepatitis may occur in HBV-coinfected patients who discontinue TDF • Asthenia, headache, diarrhea, nausea, vomiting, and flatulence
Atripla TDF with EFV+FTC	Atripla TDF 300 mg + EFV 600 mg + FTC 200 mg	Atripla 1 tablet at or before bedtime Take on an empty stomach to reduce side effects			

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum/ Intracellular Half-lives	Adverse Events
Truvada TDF with FTC	Truvada TDF 300 mg + FTC 200 mg	Truvada 1 tablet once daily Take without regard to meals			
Zidovudine (ZDV)/ Retrovir (generic available; dose same as retrovir) **Also available as:**	Retrovir • 100-mg capsules • 300-mg tablets • 10-mg/mL intravenous solution • 10-mg/mL oral solution	Retrovir 300 mg BID or 200 mg TID 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 mellitus • Lipoatrophy • Myopathy
Combivir ZDV with 3TC	Combivir ZDV 300 mg + 3TC 150 mg	Combivir 1 tablet BID			
Trizivir ZDV with 3TC+ABC	Trizivir ZDV 300 mg + 3TC 150 mg + ABC 300 mg	Trizivir 1 tablet BID			

Appendix C, Table 2. Characteristics of Protease Inhibitors (PIs) (Updated January 10, 2011)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
Atazanavir (ATV)/ Reyataz	100-, 150-, 200-, 300-mg capsules	ARV-naive patients: 400 mg once daily or (ATV 300 mg + RTV 100 mg) once daily With TDF or for ARV-experienced patients: (ATV 300 mg + RTV 100 mg) once daily With EFV in ARV-naive patients: (ATV 400 mg + RTV 100 mg) once daily (For dosing recommendations with H_2 antagonists and proton pump inhibitor (PPIs), refer to Table 16a) Take with food	CYP3A4 inhibitor and substrate Dosage adjustment in hepatic insufficiency recommended	7 hrs	Room temperature (up to 25ºC or 77ºF)	• Indirect hyperbilirubinemia • PR interval prolongation: First degree symptomatic atrioventricular (AV) block reported. Use with caution in patients with underlying conduction defects or on concomitant medications that can cause PR prolongation. • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Nephrolithiasis • Skin rash (20%) • Serum transaminase elevations • Hyperlipidemia (especially with RTV boosting)
Darunavir (DRV)/ Prezista	75-, 150-, 300-, 400-, 600-mg tablets	ARV-naive patients or ARV-experienced patients with no	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

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
		DRV mutations: (DRV 800 mg + RTV 100 mg) once daily ARV-experienced patients with at least one DRV mutation: (DRV 600 mg + RTV 100 mg) BID Unboosted DRV is **not** recommended Take with food				syndrome and erythrema multiforme have been reported • Hepatotoxicity • Diarrhea, nausea • Headache • Hyperlipidemia • Serum transaminase elevation • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Lopinavir + **Ritonavir** (LPV/r)/ Kaletra	Tablets: (LPV 200 mg + RTV 50 mg) or (LPV 100 mg + RTV 25 mg) Oral solution: Each 5 mL contains (LPV 400 mg + RTV 100 mg) Oral solution contains 42% alcohol	LPV/r 400-mg/100-mg BID or LPV/r 800-mg/200-mg once daily Once-daily dosing is not recommended for patients with ≥3 LPV-associated mutations, pregnant women, or patients receiving EFV, NVP, FPV, NFV, carbamazepine, phenytoin, or phenobarbital.	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

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
		With EFV or NVP (PI-naive or PI-experienced patients): LPV/r 500-mg/125-mg tablets BID (Use a combination of two LPV/r 200-mg/50-mg tablets + one LPV/r 100-mg/25-mg tablet to make a total dose of LPV/r 500 mg/125 mg) or LPV/r 533-mg/133-mg oral solution BID *Tablet:* Take without regard to meals *Oral solution:* Take with food				hemophilia • PR interval prolongation • QT interval prolongation and torsades de pointes have been reported; however, causality could not be established
Nelfinavir (NFV)/ Viracept	• 250-, 625-mg tablets • 50-mg/g oral powder	1,250 mg BID or 750 mg TID May dissolve tablets in a small amount of water; once dissolved, patients should mix the cloudy liquid well and consume it immediately.	CYP2C19 and 3A4 substrate—metabolized to active M8 metabolite; CYP 3A4 inhibitor	3.5–5 hrs	Room temperature (15º–30ºC/ 59º–86ºF)	• Diarrhea • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • Serum transaminase elevation

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
		Take with food				
Ritonavir (RTV)/ Norvir	• 100-mg soft gel capsules • 100-mg tablets • 80-mg/mL oral solution Oral solution contains 43% alcohol	As pharmacokinetic booster for other PIs: 100–400 mg per day in 1–2 divided doses (refer to other PIs for specific dosing recommendations) *Tablet*: Take with food *Capsule and oral solution:* Take with food, if possible, to improve tolerability.	CYP3A4 >2D6 substrate; potent 3A4, 2D6 inhibitor	3–5 hrs	Refrigerate capsules Capsules can be left at room temperature (up to 25ºC or 77ºF) for up to 30 days Tablets do not require refrigeration Oral solution should **not** be refrigerated; store at room temperature 20º–25ºC (68º–77ºF)	• GI intolerance, nausea, vomiting, diarrhea • Paresthesias—circumoral and extremities • Hyperlipidemia (especially hypertriglyceridemia) • Hepatitis • Asthenia • Taste perversion • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia
Saquinavir tablets and hard gel capsules (SQV)/ Invirase	• 500-mg tablets • 200-mg hard gel capsules	(SQV 1,000 mg + RTV 100 mg) BID Unboosted SQV is not recommended Take with meals or within 2 hours after a meal	CYP3A4 inhibitor and substrate	1–2 hrs	Room temperature (15º–30ºC/ 59º–86ºF)	• GI intolerance, nausea, and diarrhea • Headache • Serum transaminase elevation • Hyperlipidemia • Hyperglycemia • Fat maldistribution • Possible increased bleeding episodes in patients with hemophilia • PR interval

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Storage	Adverse Events
						prolongation • QT interval prolongation, torsades de pointes have been reported Patients with pre-SQV QT interval >450 msec should not receive SQV (See Table 5b.)

Appendix C, Table 3. Characteristics of Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTIs) (Updated January 10, 2011)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Adverse Events
Nevirapine (NVP)/ Viramune	• 200-mg tablets • 50-mg/5-mL oral suspension	200 mg once daily for 14 days (lead-in period); thereafter, 200 mg BID Take without regard to meals Repeat lead-in period if therapy is discontinued for >7 days In patients who develop mild to moderate rash without constitutional	CYP450 substrate, inducer of 3A4 and 2B6; 80% excreted in urine (glucuronidated metabolites, <5% unchanged); 10% in feces	25–30 hrs	• Rash, including Stevens-Johnson syndrome* • Symptomatic hepatitis, including fatal hepatic necrosis, has been reported‡

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Adverse Events
		symptoms, continue lead-in period until rash resolves but no longer than 28 days total			

* During clinical trials, NNRTI was discontinued because of rash among 7% of NVP-treated, 4.3% of DLV-treated, 1.7% of EFV-treated, and 2% of ETR-treated patients. Rare cases of Stevens-Johnson syndrome have been reported with all NNRTIs; the highest incidence was seen with NVP.
† Adverse events can include dizziness, somnolence, insomnia, abnormal dreams, confusion, abnormal thinking, impaired concentration, amnesia, agitation, depersonalization, hallucinations, and euphoria. Approximately 50% of patients receiving EFV may experience any of these symptoms. Symptoms usually subside spontaneously after 2–4 weeks, but may necessitate discontinuation of EFV in a small percentage of patients.
‡ Symptomatic, sometimes serious, and even fatal hepatic events (accompanied by rash in approximately 50% of cases) occur at significantly higher frequency in ARV-naive female patients with pre-NVP CD4 counts >250 cells/mm^3 or in ARV-naive male patients with pre-NVP CD4 counts >400 cells/mm^3. NVP should not be initiated in these patients unless the benefit clearly outweighs the risk. This toxicity has not been observed when NVP is given as single doses to mothers or infants for prevention of mother-to-child transmission of HIV.

Appendix C, Table 4 Characteristics of Integrase Inhibitors (Updated January 10, 2011)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Adverse Events
Raltegravir (RAL)/ Isentress	400 mg tablets	400 mg BID <u>With rifampin:</u> 800 mg BID Take without regard to meals	~9 hrs	UGT1A1-mediated glucuronidation	• Nausea • Headache • Diarrhea • Pyrexia • CPK elevation, muscle weakness and rhabdomyolysis

Appendix C, Table 5 Characteristics of CCR5 Antagonist (Updated January 29, 2008)

Generic Name (abbreviation)/ Trade Name	Formulations	Dosing Recommendations	Elimination	Serum Half-life	Adverse Events
Maraviroc (MVC)/ Selzentry	150-, 300-mg tablets	• **150 mg BID** when given with strong CYP3A inhibitors (with or without CYP3A inducers) including PIs (except TPV/r) • **300 mg BID** when given with NRTIs, T-20, TPV/r, NVP, RAL, and other drugs that are not strong CYP3A inhibitors or inducers • **600 mg BID** when given with CYP3A inducers, including EFV, ETR, etc. (without a CYP3A inhibitor) Take without regard to meals	14–18 hrs	CYP3A4 substrate	• Abdominal pain • Cough • Dizziness • Musculoskeletal symptoms • Pyrexia • Rash • Upper respiratory tract infections • Hepatotoxicity • Orthostatic hypotension

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