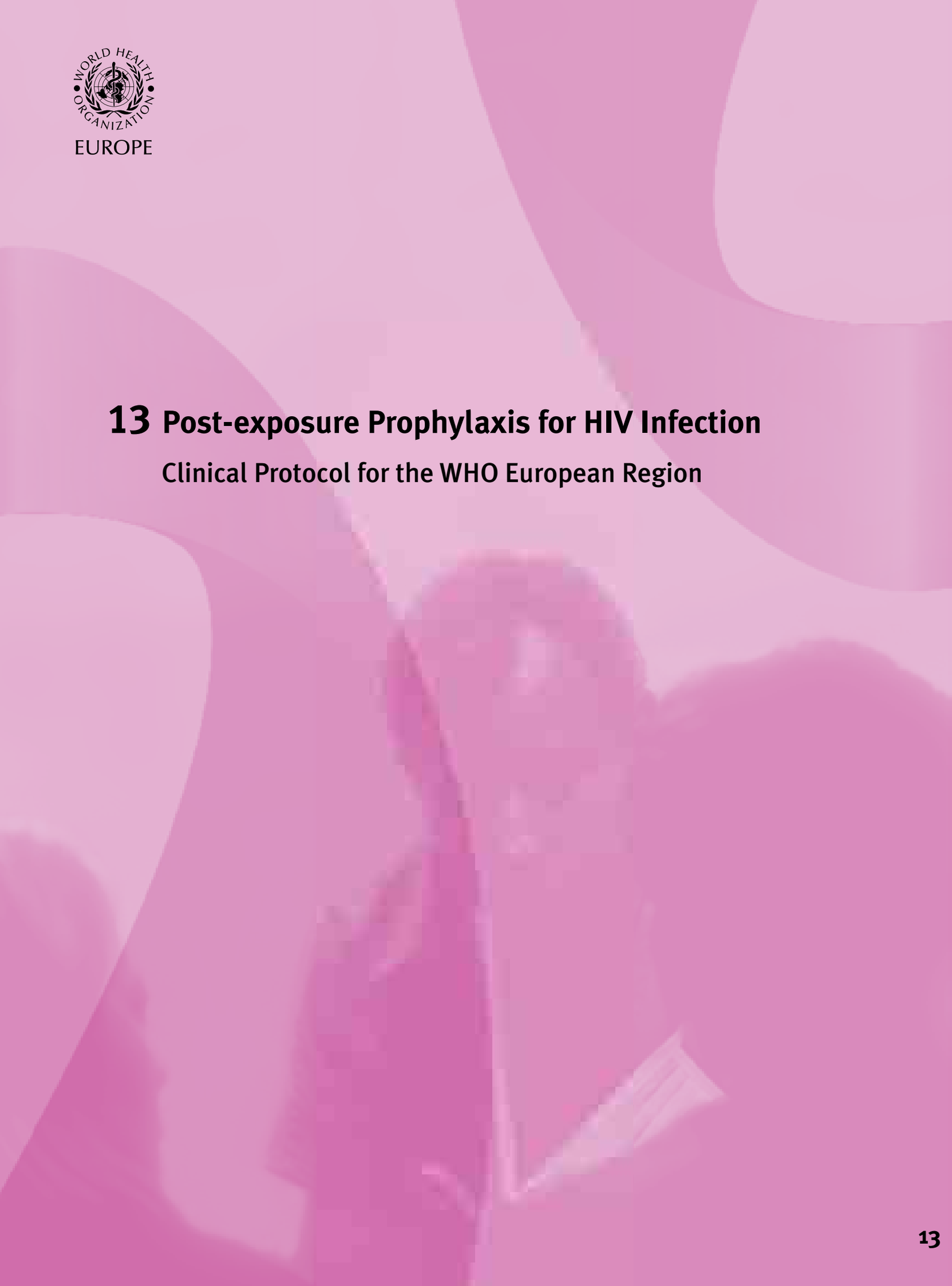
EUROPE

13 Post-exposure Prophylaxis for HIV Infection

Clinical Protocol for the WHO European Region



Contents

I. Policy issues

Following exposure to HIV, there are currently only two known means to reduce the risk of developing HIV infection: post-exposure prophylaxis (PEP) and interventions to prevent mother-to-child transmission (see Protocol 10, *Prevention of HIV transmission from HIV-infected mothers to their infants*).

- PEP policy should be part of a comprehensive national HIV/AIDS policy and also included any occupational health and post sexual assault services policies.
- PEP services should be integrated into existing health services and provided as part of a comprehensive standard precautions package that reduces workplace exposure to infectious hazards.
- Eligibility for and access to PEP should be equitable, without discrimination on grounds of age, gender, sexual orientation, citizenship, occupation or incarceration.
- Decisions about whether to provide PEP should be based on clinical consideration of risk factors.
- PEP services should be provided after:
  - occupational exposure to HIV infection or potential HIV infection;
  - accidental non-occupational exposure to HIV infection or potential HIV infection, including nosocomial exposure.
- The human rights and confidentiality of people accessing PEP should be respected.
- In the context of exposure and/or the provision of PEP, informed consent needs to be obtained for HIV testing and counselling in accordance with both client and provider initiated counselling and testing guidelines. (See Annexes 1 and 2 for examples of informed consent forms.)
- In special situations where the individual has limited or no capacity to consent to an HIV test (such as a child or an unconscious or mentally ill adult), a legal guardian, custodian or other person designated in advance by the patient may be able to provide consent, depending on national or regional legislation.

II. Background and general considerations

PEP is a medical response given to prevent the transmission of pathogens after potential exposure. PEP for HIV refers to a set of comprehensive services to prevent HIV infection in exposed individuals. These services include, first aid care, counselling and risk assessment, HIV testing based on informed consent, and depending on risk assessment, the provision of short term (28 days) antiretroviral (ARV) drugs, with follow up and support.

1. Occupational exposure to HIV

1.1. Definition

According to the ILO/WHO guidelines for occupational PEP, "an occupational exposure is defined as a percutaneous, mucous membrane or non-intact skin exposure to blood or body fluids that occurs during the course of an individual's employment. This applies to health care workers (HCW) and to non-health workers." *(1)* An occupational exposure may place a worker[1] at risk of HIV infection through injuries such as those involving a potentially contaminated needle or sharp instrument or chapped, abraded skin or contact with mucous membranes.

1.2. Risk for transmission

The risks for occupational transmission of HIV vary with the type and severity of exposure *(2, 3)*.

- The average risk for HIV transmission after a percutaneous exposure to HIV-infected blood has been estimated to be approximately 0.23% (95% confidence interval (CI) = 0.00–0.46%) *(3)*.
- The average risk after a mucous membrane exposure is estimated to be approximately 0.09% (CI = 0.006–0.5%) *(4)*.
- Factors associated with an increased likelihood of transmission include:
  - deep (intramuscular) injury
  - injury caused by a device that enters a blood vessel
  - injury with a hollow-bore needle
  - a source patient with a high viral load (VL).
- Episodes of HIV transmission have also been documented after non-intact skin exposure. Although the average risk for transmission by this route has not been precisely quantified, it is estimated to be much less than the risk for mucous membrane exposures.
- The risk for transmission after exposure to HIV-infected fluids or tissues other than blood has not been quantified either, but it is considered probably lower than for blood exposure.

1.3. Potentially infectious body fluids *(5)*

- Blood and visibly bloody body fluids are considered as potentially infectious.
- The risks of HIV transmission from cerebrospinal, synovial, pleural, peritoneal, pericardial and amniotic fluids are unknown.
- Semen and vaginal secretions have not been implicated in occupational transmission from patients to health care providers.
- Faeces, nasal secretions, saliva, sputum, sweat, tears, urine and vomitus are not considered potentially infectious unless they contain visible blood.

[1] Besides health care providers (physicians, dental personnel, nurses, laboratory and autopsy personnel, nursing assistants, medical technicians, pharmacists, medical students et al.), others at risk of workplace exposure include police, fire and ambulance personnel.

1.4. Factors affecting the risk for HIV transmission after an occupational exposure

Epidemiological and laboratory studies suggest that multiple factors might affect the risk for HIV transmission after an occupational exposure *(2, 3)*.

- For percutaneous exposure to HIV, increased risk for HIV infection is associated with exposure to blood from the source person, as indicated by:
  - a device (e.g. a needle) visibly contaminated with blood; or
  - a procedure that involved a needle being placed directly in a vein or artery or in a deep injury.
- High viral load in the source person is also a condition that may increase the risk of HIV transmission.

2. Non-occupational exposure

Due to ethical considerations, it is not possible to make prospective randomized controlled studies to evaluate the efficacy of PEP in preventing HIV after non occupational exposure. Neither are there data from studies or case reports providing definitive evidence of the efficacy of PEP after sexual, injecting drug or other non-occupational exposures to HIV. However, several related data sets from occupational exposure, mother-to-child transmission and animal studies support the biological plausibility of its effectiveness *(6–10)*.

2.1. Definition

Non-occupational exposure is any direct mucosal, percutaneous[2] or intravenous contact with potentially infectious body fluids that occurs outside perinatal or occupational situations *(11)*:

> [N]on-occupational exposure [is considered to be] all accidental and sporadic incidents in which contact with blood or other body fluids (semen, vaginal secretions, etc.) that pose a potential risk for HIV infection occurred … Non-occupational exposure includes unprotected sexual exposure, sexual exposure involving a broken or slipped condom, injecting drug users (IDUs) sharing equipment, accidental needlestick injuries, bite wounds, mucosal exposure, etc.

Non-occupational exposure also includes nosocomial exposure. Accidental exposure to HIV originating in a health care facility includes cases where a patient is exposed by a health care worker (HCW) or another patient *(12)*. Three scenarios can result in a patient being exposed to HIV nosocomially *(13)*:

- an HIV-infected HCW who does not know his/her HIV status performing an exposure-prone procedure;[3]
- an HIV-infected HCW performing a non-exposure-prone procedure (and when there is e.g. a spontaneous nosebleed or a physical assault on the HCW); or
- the event that an invasive device or product contaminated with HIV by use on one patient is accidentally reused on another patient.

[2] Percutaneous non-occupational exposure includes but is not limited to accidental or criminal sticks with needles contaminated with blood or other bodily fluids.

[3] Exposure-prone procedures are those in which there is a risk that injury to the HCW could result in exposure of the patient to the blood of the HCW, including some common procedures found in surgery, obstetrics, gynaecology, midwifery and dentistry *(13)*. HCWs who know that they are HIV infected, should not be involved in such procedures.

2.2. Risk for transmission

The estimated per-act transmission risk from unprotected exposure to a person known to be HIV-infected is low. It varies depending on the type of exposure.

Table 1. Estimated per-act risk for acquisition of HIV, by exposure route[a]

Exposure route	Risk per 10 000 exposures to an infected source	%
Blood transfusion *(3)*	9 250	92.5
Mother-to-child transmission *(15)*	1 500–3 000	15–30
Needle-sharing injecting drug use *(3)*	80	0.80
Receptive anal intercourse *(16, 17)*	50	0.50
Percutaneous needle-stick *(18)*	30	0.30
Mucosal membrane exposure *(19)*	10	0.10
Receptive penile-vaginal intercourse *(16, 17, 20–24)*	1–15	1.01–0.15
Insertive anal intercourse *(16, 17)*	6.5	0.065
Insertive penile–vaginal intercourse *(16, 17)*	1–15	0.01–0.15
Receptive oral intercourse *(17)*	1	0.01
Insertive oral intercourse *(17)*	0.5	0.005

[a] Estimates of risk for transmission from sexual exposure assume no condom use.
Source: adapted from Roland et al. (*14*).

III. Evaluation of the exposure, exposure source and exposed person

1. Evaluation of exposure

An exposure incident should be evaluated for the potential of HIV transmission based on the type of body substance involved, the transmission route and the severity of the exposure. The following factors should be considered in evaluating the risk of transmission:

- the type of exposure:
  - percutaneous injury
  - mucous membrane exposure
  - open wound exposure;
- the type and quantity of fluid/tissue:
  - blood;
  - a fluid that contains blood;
  - a potentially infectious fluid (e.g. seminal, vaginal, cerebrospinal, synovial, pleural, peritoneal, pericardial or amniotic fluid) or tissue;
  - concentrated virus (direct contact); and
- the recency of exposure.

2. Evaluation of the exposure source

When feasible, the person whose blood or body fluid is the source of potential exposure should be evaluated for HIV.

- If an exposure source is known and available, testing the source person for HIV is recommended as soon as possible, or testing the suspected exposure material (blood, tissue, etc) if the person is unavailable.
- Procedures that should be strictly followed for testing the source person include:
  - obtaining informed consent (see suggested form in Annex 1)
  - pre- and post-test counselling
  - referral if positive for appropriate post-test counselling, care and treatment.
- A rapid HIV-antibody test is preferred in situations where enzyme-linked immunosorbent assay (ELISA) tests cannot be completed within 24–48 hours.
- Two positive ELISA or rapid HIV-antibody tests are considered to be highly suggestive of infection, whereas a negative result is an excellent indicator of the absence of HIV antibody.
- In no way should administration of PEP for the exposed person, be delayed while waiting for test results.
- The routine use of direct virus assays (e.g. an HIV p24 antigen enzyme immunoassay (EIA) or HIV RNA tests) to detect infection among exposure sources is usually not recommended *(25)* because:
  - the infrequency of occupational seroconversion and the increased costs of these tests do not warrant routine use in this context; and
  - the relatively high rate of false-positive results for these tests in this context can lead to unnecessary anxiety or treatment *(14, 26)*.
- The exposure source should also be tested for hepatitis C and B viruses (HCV and HBV).
- Information to consider when evaluating an exposure source includes:
  - previous HIV test results; and
  - clinical symptoms (e.g. acute syndrome suggestive of primary HIV infection and history of possible HIV exposure within the last three months) or personal history suggesting possible exposure to HIV; and
  - history of tratment, duration, its success or failure, type of regime and adherence.

- *If the exposure source is unknown, cannot be tested or refuses to be tested*, the risk of HIV transmission should be assessed epidemiologically, if possible. Relevant information includes:
  - type of exposure
  - prevalence of HIV in the population where the source material originates.
- *If the source person is known to have HIV infection*, the following information is also useful to know in determining an appropriate PEP regimen:
  - clinical stage of the HIV infection;
  - CD4 cell count;
  - viral load, as a high plasma viral load increases the risk of transmission in all cases *(27)*;
  - antiretroviral treatment history;
  - genotypic or phenotypic viral resistance results (if available);
  - in a case of sexual exposure, the existence of genito-oral ulcers or other sexually transmitted infections (STIs), and whether menstruation or other bleeding occurred at the time *(24)*; and
  - in the case of an accidental needle-stick exposure, whether fresh blood was present and whether it was a deep injury or intravenous injection (all increase the risk of HIV transmission) *(6)*.
- If this information is not immediately available, initiation of PEP, if indicated, should not be delayed. Appropriate changes in the PEP regimen can be made if new information emerges after PEP has been started.
- If the source person's results are HIV seronegative at post-exposure evaluation and presents no clinical evidence of AIDS or HIV infection, no further testing of the source is indicated. The likelihood of the source person being in the "window period" of HIV infection with no symptoms of acute retroviral syndrome is extremely small.

3. Evaluation of the exposed person

Evaluation of exposed persons (regardless if it is occupational or non-occupational) has to be done as soon as possible and within hours after an exposure. The following evaluations are recommended:
- an HIV serological baseline test to establish infection status at the time of exposure, with pre- and post-test counselling and based on informed consent (see Annex 2);
- direct virus assays for any exposed person who has an illness compatible with an acute retroviral syndrome, regardless of the time elapsed since exposure;
- evaluation of circumstances, medical conditions and medications that might influence drug selection for PEP (e.g. pregnancy or breastfeeding);

It is useful to perform the following baseline tests if resources are available:
- baseline laboratory testing to monitor for adverse reactions:
  - complete blood count (CBC) with differential and platelets
  - liver function tests (LFTs) (asparate aminotransferase (AST), alanine aminotransferase (ALT), bilirubin)
  - urea or serum creatinine; and
- baseline serological tests for hepatitis C and B (HCV antibodies and hepatitis B surface antigen (HBsAg)).

3.1. Additional considerations for non-occupationally exposed people

In addition, those seeking care after potential non-occupational exposure to HIV should also be evaluated for the following information:
- frequency of exposures to HIV;
- history of specific sexual, drug-injecting or other behaviours that might have heightened the risk for acquiring HIV infection;
- if an accidental needle-stick exposure, whether there was fresh blood and whether it was a deep injury or intravenous injection *(6)*; and
- if a sexual exposure:

- condom use
- presence of STIs (as determined by testing)
- need for emergency contraception or pregnancy testing (for females)
- presence of sexual assault, by one or more persons
- whether menstruation or other bleeding was present at time of exposure.

IV. Clinical management of people incidentally exposed to HIV

1. First aid

For a potential exposure to HIV, "first aid" refers to the actions that should be taken immediately afterwards. The aim of first aid is to reduce contact time with the source person's body fluids (including blood) and tissues, and to clean and decontaminate the exposure site to reduce the risk of infection *(28)*.

If the skin is broken following an injury with a used needle or other sharp instrument, take the following steps.

- Wash the injury immediately, using soap.
- Encourage the puncture wound to bleed freely under running water for several minutes or until bleeding ceases.
- If running water is not available, clean site with a gel or hand cleaning solution.
- **Do not** use any strong solutions, such as alcohol, bleach or iodine, as they may irritate the wound and make the injury worse.
- **Do not** squeeze or rub the injury site.
- **Do not** suck a puncture wound.

After a splash of blood or body fluids, do the following:

- *for a splash on unbroken skin:*
  - wash the area immediately;
  - if running water is not available, clean the area with a gel or hand rub solution;
  - **do not** use any strong solutions, such as alcohol, bleach or iodine, as they may irritate the affected area;
  - use mild disinfectants, such as Chlorhexidine gluconate 2–4%;
  - **do not** rub or scrub area;
  - **do not** use a dressing.
- *for a splash in the eye:*
  - irrigate the exposed eye immediately with water or normal saline. Sit in a chair, tilt the head back and have a colleague gently pour water or normal saline over the eye, gently pulling the eyelids up and down to make sure the eye is cleaned thoroughly;
  - if wearing contact lenses, leave them in place while irrigating, as they form a barrier over the eye and will help protect it; once the eye has been cleaned, remove the contact lenses and clean them in the normal manner, which will make them safe to wear again;
  - **do not** use soap or disinfectant on the eye.
- *for a splash in the mouth:*
  - spit the fluid out immediately;
  - rinse the mouth thoroughly, using water or saline, and spit out again. Repeat this process several times.
- **do not** use soap or disinfectant in the mouth.

2. Counselling an exposed person

After the evaluation, health care workers should provide counselling on risk-reduction behaviour to the exposed person regardless of how the individual was exposed, and of whether or not antiretroviral (ARV) drugs will be recommended for PEP, as such, counselling can reduce the risk of future exposures *(29, 30)*.

It should be made clear during the counselling session that PEP is not mandatory. An informed consent form (see Annex 2) should be signed if the exposed person opts for PEP. In addition to the information outlined on the informed consent form, the exposed people should be counselled on:

- avoiding pregnancy and seeking safe alternatives to breastfeeding;
- avoiding blood, tissue or sperm donation;
- using condoms for sexual intercourse up to the sixth month test confirming that the exposed person remains seronegative;
- standard precaution measures for those at risk of workplace exposure; and
- the need for clinical and serological follow-up.

As stated on the consent form, there is a strong need for adherence to PEP regimens, for further information on adherence refer to Protocol 1, *Patient evaluation and antiretroviral treatment for adults and adolescents*, for information on adherence issues.

Psychological support should be an integral part of counselling and include appropriate referrals as needed.

Counselling on risk-reduction behaviour after non-occupational exposure should also focus, where indicated, on:

- safer injecting practices, with referral to harm-reduction programmes and drug-dependence treatment services;
- STI treatment, with referral to appropriate services; and
- contraception and condom use.

Furthermore, counselling on sexual abuse should be provided, where needed, with appropriate referrals, such as legal services.

3. No indication for ARV use for PEP purposes

Some situations do not require initiation of ARVs for prophylaxis purposes. They include *(26)*:

- if the exposed person has previously tested positive for HIV (this needs to be documented);
- if exposure is chronic (occurring regularly versus occurring occasionally[4]), e.g. between serodiscordant sex partners who rarely use condoms or IDUs who share injecting equipment;
- if the exposure does not pose a risk of transmission, e.g.:
  - exposure of *intact skin* to potentially infectious body fluids;
  - sexual intercourse with proper *condom* use during which the condom remained intact;
  - exposure to *non-infectious body fluids* (such as faeces, saliva, urine, sweat) with no blood contamination;
  - exposure to body fluids from a person *known* to be HIV-seronegative, unless identified as at high risk for recent infection within the "window period"; and
- if the exposure was more than 72 hours previous (however, consider referring for counselling, testing and clinical follow-up).

Note that the final decision for prescribing or not prescribing PEP should be made on the basis of risk evaluation, the patient–physician relationship, bearing in mind that PEP should never be considered a primary prevention strategy *(11)*.

[4] People who are occasionally or episodically exposed to HIV, such as sexually assaulted sex workers who otherwise use condoms, episodically abused children, medical waste workers with repeated sharps injuries, et al should be considered for PEP based on previously described evaluation (see section III of this document).

4. Time of initiation and duration of PEP

PEP should be initiated within hours of exposure – ideally within 2 hours and not later than 72 hours after exposure and should not be delayed while waiting for tests results.

The optimal duration of PEP is unknown. Data show that four weeks of ZDV has appeared protective in occupational and animal studies. PEP should be administered for four weeks if tolerated *(9, 31–33)*.

5. Considerations in choosing an ARV regimen for PEP

The only PEP efficacy data are from a retrospective case control study *(6)* on a zidovudine monotherapy, taken as prophylaxis measure. The model in the study indicates reducing risk of HIV acquisition by approximately 81% in health care workers after percutaneous exposure.

No evidence indicates that a three-ARV combination is more effective than a two-ARV combination, or two-ARV combination is more effective than three-ARV combination. Some data suggest that there is significant toxicity associated with three-ARV regimens, while two-ARV combinations are generally well tolerated *(29, 34)*. Offering a two-drug regimen is a viable option, primarily because the benefit of completing a full course of this regimen exceeds the potential benefit of adding a third agent and risking non-completion *(35)*.

For the vast majority of exposure cases, whether occupational or non-occupational, and whether due to percutaneous injuries or to contact with mucous membrane or non-intact skin, the regimen with two ARVs considered to be sufficient. However, suspected or proven drug resistance in a source person might guide a decision to prescribe a three ARV drug regimen.

If a question exists concerning whether to use a two-drug or three-drug regimen, start the two-drug regimen immediately rather than delay administering PEP.

6. Antiretroviral regimens and drugs for PEP

6.1. Two ARV drug regimens

The two-drug ARV regimen (see Table 2) consists of two nucleoside or nucleotide reverse transcriptase inhibitors (NRTIs).

Table 2. Two-drug ARV regimens

Preferred	ZDV + 3TC[a] (or FTC)
Alternatives	TDF + FTC[b] (or 3TC) or d4T + 3TC

[a] The combination ZDV + 3TC is available as a fixed-dose combination (FDC) (Combivir), one tablet twice daily (BID).
[b] The combination TDF + FTC is available as an FDC (Truvada), one tablet once daily (OD).

6.2. Three ARV drug regimens

Expanded ARV regimens (see Table 3) are combinations of three ARVs (two NRTIs + one protease inhibitor (PI)). They are recommended for exposures that pose an increased risk of transmission or that involve a source in whom antiretroviral drug resistance is likely (see section 5).

Table 3.	Thre- drug ARV regimens
Preferred	ZDV + 3TC[a] + LPV/r
Alternatives	ZDV + 3TC[a] + SQV/r or ATV/r or FPV/r or TDF + FTC[b] + SQV/r or ATV/r or FPV/r or d4t + 3TC +SQV/r or ATV/r or FPV/r

[a] The combination of ZDV + 3TC is available as an FDC (Combivir), one tablet BID.
[b] The combination of TDF + FTC is available as an FDC (Truvada), one tablet OD.

6.3. ARV dosages

- ZDV: 300 mg per os (PO), BID with food
- 3TC: 150 mg PO, BID or 300 mg PO, OD
- FTC: 200 mg, PO, OD
- TDF: 300 mg, PO, OD
- d4T: 30 mg PO, BID
- LPV/r: 400 mg/100 mg PO, BID with food
- SQV/r: 1000 mg/100 mg PO, BID
- ATV/r: 300 mg/100 mg PO, OD
- FPV/r: 700 mg/100 mg PO, BID

In cases involving children who need PEP, dosages should be adjusted accordingly (please refer to Protocol 11, *Paediatric HIV/AIDS treatment and care*). For further details regarding essential information about ARVs please refer to Protocol 1, *Patient evaluation and antiretroviral treatment for adults and adolescents*, Annex 4.

6.4. ARVs not recommended for PEP

Some ARVs are not recommended for use in PEP, primarily because of a higher risk for potentially serious life-threatening events: abacavir (ABC), the combination of didanosine (ddI) and d4T, and NVP *(36, 37)*. Amprenavir (APV) should not be given to pregnant or lactating women *(38–40)*. In addition, EFV is not recommended because of low genetic barrier.

An exceptional use of efavirenz (EFV) may be considered when:
- the exposed person *cannot* tolerate available boosted PIs;
- the source is known to be infected with drug-resistant HIV that is sensitive to EFV.

7. Follow-up of exposed persons

People who have been potentially exposed to HIV, whether occupationally or non-occupationally, should receive follow-up treatment.
- Counselling, post-exposure testing and medical evaluation should be provided to all exposed people, regardless of whether they receive PEP or not.
- If taking ARVs patients should be followed up for adherence and possible side-effects of ARVs (e.g. nausea or diarrhoea) should be managed symptomatically without changing the regimen. For more information, please refer to Protocol 1, *Patient evaluation and antiretroviral treatment for adults and adolescents*.

- After baseline testing at the time of exposure, follow-up testing using enzyme immunoassay should be performed at 6 weeks, 12 weeks, and 6 months after exposure, *even* if PEP is declined.
- Direct virus assays may be performed on any exposed person who has an illness compatible with an acute retroviral syndrome, regardless of the interval since exposure.
- For those who become infected with HCV after exposure to a source coinfected with HIV and HCV, extended HIV follow-up (for 12 months) is recommended *(41)*.
- If an exposed person seroconverts after PEP, he or she should be referred for HIV treatment and care services.
- Psychological support should be provided and referrals suggested as appropriate, including needle and syringe exchange for IDUs.
- If the exposure is due to rape, it is important to arrange for counselling and support. The victim also needs to be provided with information regarding STIs, pregnancy and legal matters.
- If the exposed person is a child or adolescent, or if the exposure is due to rape, it may be worthwhile to cooperate with other specialists, e.g. a paediatrician or a rape counsellor.
- Health care providers caring for people exposed to HIV should report these cases to their health departments regardless of whether or not PEP has been prescribed, and a national PEP registry should be maintained. (See the proposed occupational exposure report in Annex 3 and the proposed non-occupational exposure report in Annex 4).

V. Prevention of occupational and nosocomial exposure

After occupational exposure, it is recommended to evaluate work place safety measures and strengthen standard precautions measures.

The importance of primary prevention in any setting where HIV can be transmitted should be reinforced in every programme that provides PEP. Health care workers (HCW) and other exposed workers should receive appropriate information on PEP availability and the reference centres. It is important to underline that PEP is not ever likely to be 100% effective, and thus it should always be integrated into a larger HIV exposure prevention strategy based on standard precaution principles. Quality control and evaluation of safety conditions at work should be re-evaluated after exposure.

Provided that the procedures for preventing occupational transmission of bloodborne viruses are adhered to at all times, most clinical procedures pose no risk of transmission of HIV from an infected HCW to a patient *(42)*.[5]

1. Standard precautions

Standard precautions are infection control measures that reduce the risk of transmission of bloodborne pathogens through exposure to the blood or other body fluids of patients and health care providers. As it is not possible to identify everyone who may be infected with a bloodborne pathogen, protecting HCWs and patients against HIV and hepatitis viruses should be based on the concept that all patients and HCWs are assumed to be infected with bloodborne diseases.

The application of standard precautions requires that all blood and other body fluids should be regarded as potentially infectious and appropriate protective action taken. To help protect HCWs and patients from bloodborne infections, including HIV, WHO advises that standard infection control precautions be used, as follows.

- Wash hands with soap and water before and after procedures.
- Use protective barriers such as gloves, gowns, aprons, masks and goggles for direct contact with blood and other body fluids.
- Disinfect instruments and other potentially contaminated equipment.
- Handle soiled linen properly (see next section).
- Using new, single-use injecting equipment for all injections is highly recommended.
- Sterilizable injections should only be considered if single-use equipment is not available and if their sterility can be documented with time, steam and temperature indicators.
- Discard contaminated sharps immediately without recapping in puncture- and liquid-proof containers that are closed, sealed and destroyed before completely full.
- Document the quality of sterilization for all medical equipment used in percutaneous procedures *(45)*.

Please see Annex 5 for a checklist of standard precautions for HCWs.

2. Reducing occupational exposure in health care settings

2.1. Basic preventive measures and workplace practices

In addition to standard precautions, workplace practices should be instituted and followed to reduce exposure to bloodborne pathogens and other infectious materials. Avoid accidental injuries

[5] The overall risk of an infected HCW transmitting HIV to a patient is low. Worldwide, only two possible reports of such transmission have been reported, both during exposure-prone procedures *(43, 44)*.

and exposure routes that can transmit bloodborne infections. The following guidelines should be adhered to:

- Institute procedures to ensure and monitor compliance with safety measures.
- Only allow health care professionals to perform a duty involving exposure to body fluids if they have undergone training and education in infection control and preventive measures, including the correct methods for cleaning up accidental spills of blood and other body fluids.
- Avoid splashing, spraying, splattering and generating droplets of blood or other potentially infectious materials.
- Clean all equipment and environment surfaces immediately after contact with blood or other potentially infectious materials.
- Place potentially infectious specimens in properly labelled containers that will prevent leakage during collection, handling, processing, storage, transport and shipping. Use a secondary container if the primary container becomes contaminated or punctured.
- *Hand-washing is essentisal.*
  - Wash hands and any other exposed skin with soap and water before and after procedures, including after removal of gloves and other personal protective equipment or attire.
  - Following the contact of body areas with blood, other potentially infectious materials or contaminated surfaces, wash hands and flush mucous membranes with water immediately or as soon as feasible.
  - Use soap and *running* water. If running water is not available, use an appropriate antiseptic hand cleanser and clean towels or antiseptic towelettes, followed by regular hand-washing as soon as feasible.
  - If minimal skin lesions are already present on hands (e.g. cuts), they need to be properly addressed before using gloves. Bear in mind that glove use requires consideration of additional safety precautions (see Annex 5).
- *Proper handling of soiled linen is essential.*
  - Soiled linen should be handled as little as possible.
  - Gloves and leak-proof bags should be used if necessary.
  - Bags and containers of soiled linen should be labelled.
  - Soiled linen should be cleaned and laundered outside patient areas, using detergent and hot water.
- Place all regulated waste in closable, leak-proof containers.

In addition, health care workers must observe the following restrictions:

- Do not eat, drink, smoke, apply cosmetics, apply lip balm or handle contact lenses in work areas where occupational exposure to bloodborne pathogens is likely.
- Do not keep food and drink in refrigerators or other locations where blood or other potentially infectious materials are present.
- Never use the mouth to pipette or suction blood or other potentially infectious materials.
- Never use hands to pick up broken glassware that may be contaminated.
- Do not bend, recap, break or remove contaminated needles or other contaminated sharps.
- Never use hands to reach into, open, empty or clean reusable sharps containers *(46)*.

2.2. Protective material and equipment

Protective equipment and controls should be instituted in all health care settings. To prevent transmission of bloodborne pathogens, the following precautions should be taken:

- *Protective equipment and clothes* should be made available to and worn by all workers who come into contact with blood or body fluids, including:
  - gloves
  - liquid-resistant gowns
  - face and eye protection.

- *Safety measures for needles and syringes include the following.*
  - Use new, single-use, self-sheathing needles or other new disposable injecting equipment for all injections.
  - Only consider sterilizable injections if single-use equipment is not available and if the sterility can be documented with time, steam and temperature indicators.
  - Use needleless intravenous (IV) access systems.
  - Use a mechanical device that protects the hand or a safe one-handed technique if needle recapping or removal is absolutely necessary.
  - In general, containers for sharps should be wall-mounted when not in use to avoid accidents that may occur from patients (especially children) playing with or trying to open them.
- *Safety measures for other sharps include the following.*
  - Discard contaminated sharps immediately and without recapping in puncture- and liquid-proof containers that are closed, sealed and destroyed before completely full.
  - Position sharps disposal containers so that they are easily accessible and maintained upright throughout use.
  - Replace sharps disposal containers regularly and do not allow them to overfill.
  - Before moving a container of contaminated sharps, close it completely. Place it in a secondary container if leakage is possible.
- *Safety measures for dental instruments, devices and equipment include the following (47).*
  - Follow normal heat-sterilization procedures for surgical instruments, periodontal scalers, scalpel blades, surgical dental burs, dental mouth mirrors, amalgam condensers, reusable dental impression trays and dental handpieces.
  - If disinfecting instruments or other equipment that is heat-sensitive, use high-potency disinfectant.
  - Devices connected to the dental water system that enter a patient's mouth (e.g. handpieces, ultrasonic scalers, air abrasion devices and air/water syringe tips) should operate for a minimum of 20–30 seconds after each patient to discharge water and air and flush out any patient material.
  - Where possible, use dental units that prevent retraction of oral fluids.
  - Components that are permanently attached to dental unit waterlines (e.g. the handles and dental unit attachments of saliva ejectors, high-speed air evacuators and air/water syringe tips) should be covered with impervious barriers that are changed after each use.
- Appropriate first-aid equipment should always be readily available for dealing with spilled body fluids, and staff should be trained to institute safety precautions following any accident.
- Containers appropriate for waste disposal should always be available – as should guidelines for such disposal.

2.3. Technological controls

Technological controls can help isolate and remove bloodborne pathogens from the workplace.

- Document the quality of the sterilization for all medical equipment used for percutaneous procedures.
- Disinfect instruments and other contaminated equipment.
- Before servicing or shipping, decontaminate any equipment that is contaminated with blood or other potentially infectious materials. If decontamination is impossible, attach a label that states which portions of the equipment remain contaminated.
- Set up quality control charts to monitor standard precautions in technical procedures and instrument use.

2.4. Personal protective equipment and its use

If the potential for occupational exposure still remains after an HCW uses up to date technological controls and standard work practice precautions, the employer must also provide personal protective equipment (PPE). This equipment must be provided in a readily accessible location and at no cost to the HCW.

- *Gloves* include special gloves if an HCW is allergic to conventional medical gloves.
  - Single-use gloves should not be reused, nor should reusable gloves that show signs of deterioration.
  - Petroleum-based lubricants should not be used, as they can eat through latex rubber.
- *Gowns/laboratory coats should be used.*
  - Outer garments should be worn in occupational exposure situations.
  - Surgical caps/hoods and shoe covers/boots should be worn only if potential gross contamination of the head or feet is anticipated.
- *Face shields/masks/eye protection should be used.*
  - Chin-length face shields or masks should be worn in combination with eye protection devices and side shields whenever splashes, spray, spatter or droplets of blood or other potentially infectious materials may be generated.
  - Regular eye-glasses do not provide sufficient protection against bloodborne contaminants.

Personal protective equipment must not permit blood or other potentially infectious materials to pass through to or reach work clothes, street clothes, undergarments, skin, eyes, mouth or other mucous membranes under normal conditions of use during the time in which the protective equipment will be used. Heavy gloves and protective clothing and appropriate training should be provided for all cleaners and waste disposal handlers.

If a protective garment is penetrated by blood or another potentially infectious material, it should be removed as soon as possible. Wash the affected area with soap and water. Remove all PPE prior to leaving the work area and place it in a designated receptacle. Employers are responsible for cleaning, laundering, repairing, replacing and disposal of used PPE.

VI. Suggested minimum data to be collected at the clinical level

Based on the proposed occupational and non-occupational reporting forms (Annexes 3 and 4), the clinical level should aggregate the detailed information about patients requiring PEP, receiving PEP and outcomes (patients who become infected or not).

Annex 1. Informed consent form for source person

(Informed consent to perform an HIV test and authorization for release of HIV-related information for purposes of providing post-exposure care to a person accidentally exposed occupationally or non-occupationally[*]*)*

A person has been exposed to your blood or a body fluid in a manner that may pose a risk for the transmission of a bloodborne infection. Many individuals may not know whether they have a bloodborne infection because people can carry these viruses without having any symptoms. We are therefore asking for your consent to test for the presence of human immunodeficiency virus (HIV). You will also be tested for hepatitis B virus (HBV) and hepatitis C virus (HCV). HIV testing is voluntary and requires your consent in writing; consent can be withdrawn for the test at any time. Your blood will be tested by a rapid or enzyme immunoassay serological test. The test result will be used to help determine whether the exposed person is actually at risk for HIV and requires treatment for that exposure.

We will inform you of the test results, helping you understand their implications as well as assisting you in accessing any services you may need.

Meaning of HIV test results

You also are being asked to authorize the release of confidential HIV-related information related to this request to the health professional, named below, who is treating the exposed person. This release is necessary to provide appropriate care and to counsel the exposed person about his or her risk of becoming infected and possibly infecting others. Confidential HIV-related information can only be given to persons you allow to have it by signing a release. These individuals are prohibited by law from subsequently disclosing these test results or your identity.

_____

Name of exposed person's health care provider to whom HIV test result will be disclosed:

Prior to executing this consent, you will be counselled about the implications of HIV testing and your confidentiality protections under the law.

I understand the purpose for which I am being asked to submit a specimen for HIV testing. My questions about the HIV test were answered. I agree to be tested for HIV, and I authorize the release of this information to the health care provider for the exposed person. This release is effective for one year after the date listed below.

_____ _____

Name of person to be tested Date

_____

Signature of the person to be tested, or of the person consenting if different from the person to be tested

I provided pretest counselling. I answered the above individual's questions about the test and offered him/her an unsigned copy of this form.

Signature _____ Title _____

Facility/provider _____

[*] This form is recommended only for cases of accidental non-intentional exposure. In cases of intentional exposure (e.g. a needle-stick or non-consensual sex), the issue of consent to be tested for HIV and the release of information about an individual's HIV status is regulated by national laws.

Annex 2. Informed consent form for exposed person

Name _____ **Record number** _____

I understand that I have had an exposure which may be a risk for HIV transmission.

I have been given the following information about post-exposure prophylaxis (PEP):
- the risk of HIV transmission with and without PEP for the specific exposure;
- the benefits of HIV testing (now, at 6 weeks, at 12 weeks and at 6 months);
- the benefits and risks of taking PEP;
- the use of PEP during pregnancy;
- that PEP is not guaranteed to prevent HIV transmission;
- the importance of receiving post test counselling;
- other recommended blood tests;
- the importance of using methods that will prevent HIV transmission (e.g. using condoms, not sharing needles and not breastfeeding) for the next six months;
- the prohibition against donating blood, semen or tissues for the next six months;
- the usual duration of PEP (four weeks) and my ability to stop at any time (though this will reduce its effectiveness);
- the importance of treatment adherence (taking the correct dose of medications at the right time);
- possible side-effects of and drug interactions with the PEP medications; and
- (for HCWs): the safe work practices that are necessary to observe for the next six months.

I have understood this information and have been given the opportunity to ask questions and have received satisfactory answers.

☐ I voluntarily consent to post-exposure prophylaxis (PEP).

☐ I decline post-exposure prophylaxis (PEP).

Name _____

Date _____ **Signature** _____

I confirm that I have explained information about PEP as above.

Name _____ **Signature** _____

Position _____ **Date** _____

Annex 3. Proposed occupational exposure report (confidential)

<table>
<tr><td colspan="2">Name (last, first, middle)</td><td colspan="2">Address (work)</td><td>Address (home)</td></tr>
<tr><td>Birth date</td><td>Sex</td><td>Position</td><td>Years in practice</td><td>Telephone no</td></tr>
<tr><td>Date/time of exposure

Date/time of consultation</td><td colspan="2">Location exposure occurred</td><td colspan="2">Activity at time of exposure</td></tr>
<tr><td colspan="5">Nature of injury (e.g. cut, splash or needle-stick, including bore of needle)</td></tr>
<tr><td colspan="5">Details of the procedure being performed, including where and how the exposure occurred</td></tr>
<tr><td colspan="5">Details of the exposure, including the type and amount of fluid or material and the severity of the exposure

Reporting officer/procedure</td></tr>
<tr><td colspan="3">Details about exposure source
The source material contained:
HBV:
HCV:
HIV:
Whether the source is HIV-infected:
Clinical disease stage:
Viral load:</td><td colspan="2">Details about exposed person
Infected with:
HBV:
HCV:
HIV:
Concomitant diseases:</td></tr>
</table>

<table>
<tr><td>History of antiretroviral treatment:

Antiretroviral resistance:
Pretest counselling provided:</td><td>Hepatitis B vaccination:
Vaccine-response status:
Pretest counselling provided:</td></tr>
<tr><td rowspan="2">Test results
HBV:
HCV:
HIV:
Post-test counselling provided:
Referral:</td><td>Test results:
HBV:
HCV:
HIV:
Post-test counselling provided:
Referral:</td></tr>
<tr><td>PEP commenced:

Informed consent obtained:

PEP regimen administered:</td></tr>
</table>

Post-exposure management:	CBC with differential	Serum liver enzymes	Signs and symptoms
Week 1 consultation			
Week 2 consultation			
Week 3 consultation			
Week 4 consultation			
HIV antibody test results 1 month: 3 months: 6 months:			
Signature/stamp			Date

Annex 4. Proposed non-occupational exposure report (confidential)

<table>
<tr><td colspan="2">Name (last, first, middle)</td><td rowspan="2">Address (work)</td><td>Address (home)</td></tr>
<tr><td>Birth date</td><td>Sex</td><td>Telephone no.</td></tr>
<tr><td colspan="4">Date/time of exposure

Date/time of consultation

Other possible exposures
• Last month:

• Last six months:</td></tr>
<tr><td colspan="4">Nature of exposure (for example injection, sexual contact)

Risks of exposure</td></tr>
<tr><td colspan="4">Details of exposure, including the type and amount of fluid or material and the severity of exposure
• Related to sexual exposure

• Related to injection exposure</td></tr>
</table>

Details about exposure source	*Details about exposed person*
Source material contained:	Infected with:
HBV:	HBV:
HCV:	HCV:
HIV:	HIV:
Whether source is HIV-infected:	Concomitant diseases:
Clinical disease stage:	
Viral load:	
History of antiretroviral treatment:	
Antiretroviral resistance (if known):	Hepatitis B vaccination:
Pretest counselling provided:	Vaccine-response status:
	Pretest counselling provided:

Test results: HBV: HCV: HIV: Post-test counselling provided: Referral:	Test results: HBV: HCV: HIV: Post-test counselling provided: Referral:
	PEP commenced (date): Informed consent obtained: yes _____ no _____ ARV regimen administered for PEP:

Post-exposure management:	CBC with differential	Serum liver enzymes	Signs and symptoms
Week 1 consultation			
Week 2 consultation			
Week 3 consultation			
Week 4 consultation			
HIV antibody test results 1 month: 3 months: 6 months:			
Pregnancy test result (for female patients)			
Signature/stamp			Date

Annex 5. Standard precautions – an aide memoire[5]

Infection control standard precautions in health care

Background

Standard precautions are meant to reduce the risk of transmission of bloodborne and other pathogens from both recognized and unrecognized sources.

They are the basic level of infection control precautions which are to be used, as a minimum, in the care of all patients.

Hand hygiene is a major component of standard precautions and one of the most effective methods to prevent transmission of pathogens associated with health care. In addition to hand hygiene, the use of **personal protective equipment** should be guided by risk assessment and the extent of contact anticipated with blood and body fluids, or pathogens.

In addition to practices carried out by health workers when providing care, all individuals (including patients and visitors) should comply with infection control practices in health-care settings. The control of spread of pathogens from the source is key to avoid transmission. Among source control measures, **respiratory hygiene/ cough etiquette**, developed during the severe acute respiratory syndrome (SARS) outbreak, is now considered as part of standard precautions.

Worldwide escalation of the use of standard precautions would reduce unnecessary risks associated with health care. Promotion of an **institutional safety climate** helps to improve conformity with recommended measures and thus subsequent risk reduction. Provision of adequate staff and supplies, together with leadership and education of health workers, patients, and visitors, is critical for an enhanced safety climate in health-care settings.

Important advice

- Promotion of a safety climate is a cornerstone of prevention of transmission of pathogens in health care.
- Standard precautions should be the minimum level of precautions used when providing care for all patients.
- Risk assessment is critical. Assess all health-care activities to determine the personal protection that is indicated.
- Implement source control measures for all persons with respiratory symptoms through promotion of respiratory hygiene and cough etiquette.

✓ Checklist

Health policy

- ☐ Promote a safety climate.
- ☐ Develop policies which facilitate the implementation of infection control measures.

Hand hygiene

- ☐ Perform hand hygiene by means of hand rubbing or hand washing (see overleaf for detailed indications).
- ☐ Hands should always be washed with soap and water if hands are visibly soiled, or exposure to spore-forming organisms is proven or strongly suspected, or after using the restroom. For other indications, if resources permit, perform hand rubbing with an alcohol-based preparation.
- ☐ Ensure availability of hand-washing facilities with clean running water.
- ☐ Ensure availability of hand hygiene products (clean water, soap, single use clean towels, alcohol-based hand rub). Alcohol-based hand rubs should ideally be available at the point of care.

Personal protective equipment (PPE)

- ☐ ASSESS THE RISK of exposure to body substances or contaminated surfaces BEFORE any health-care activity. Make this a routine!
- ☐ Select PPE based on the assessment of risk:
  - ☐ clean non-sterile gloves.
  - ☐ clean, non-sterile fluid-resistant gown.
  - ☐ mask and eye protection or a face shield.

Respiratory hygiene and cough etiquette

- ☐ Education of health workers, patients and visitors.
- ☐ Use of source control measures.
- ☐ Hand hygiene after contact with respiratory secretions.
- ☐ Spatial separation of persons with acute febrile respiratory symptoms.

[5] The overall risk of an infected HCW transmitting HIV to a patient is low. Worldwide, only two possible reports of such transmission have been reported, both during exposure-prone procedures *(43, 44)*.
Source: WHO (*48*).

Infection control standard precautions in health care

KEY ELEMENTS AT A GLANCE

1. Hand hygiene[1]

Summary technique:

- Hand washing (40–60 sec): wet hands and apply soap; rub all surfaces; rinse hands and dry thoroughly with a single use towel; use towel to turn off faucet.
- Hand rubbing (20–30 sec): apply enough product to cover all areas of the hands; rub hands until dry.

Summary indications:

- Before and after any direct patient contact and between patients, whether or not gloves are worn.
- Immediately after gloves are removed.
- Before handling an invasive device.
- After touching blood, body fluids, secretions, excretions, non-intact skin, and contaminated items, even if gloves are worn.
- During patient care, when moving from a contaminated to a clean body site of the patient.
- After contact with inanimate objects in the immediate vicinity of the patient.

2. Gloves

- Wear when touching blood, body fluids, secretions, excretions, mucous membranes, nonintact skin.
- Change between tasks and procedures on the same patient after contact with potentially infectious material.
- Remove after use, before touching non-contaminated items and surfaces, and before going to another patient. Perform hand hygiene immediately after removal.

3. Facial protection (eyes, nose, and mouth)

- Wear a surgical or procedure mask and eye protection (face shield, goggles) to protect mucous membranes of the eyes, nose, and mouth during activities that are likely to generate splashes or sprays of blood, body fluids, secretions, and excretions.

4. Gown

- Wear to protect skin and prevent soiling of clothing during activities that are likely to generate splashes or sprays of blood, body fluids, secretions, or excretions.
- Remove soiled gown as soon as possible, and perform hand hygiene.

5. Prevention of needle stick injuries[2]

Use care when:

- handling needles, scalpels, and other sharp instruments or devices
- cleaning used instruments
- disposing of used needles.

6. Respiratory hygiene and cough etiquette

Persons with respiratory symptoms should apply source control measures:

- cover their nose and mouth when coughing/sneezing with tissue or mask, dispose of used tissues and masks, and perform hand hygiene after contact with respiratory secretions.

Health care facilities should:

- place acute febrile respiratory symptomatic patients at least 1 metre (3 feet) away from others in common waiting areas, if possible.
- post visual alerts at the entrance to health-care facilities instructing persons with respiratory symptoms to practise respiratory hygiene/cough etiquette.
- consider making hand hygiene resources, tissues and masks available in common areas and areas used for the evaluation of patients with respiratory illnesses.

7. Environmental cleaning

- Use adequate procedures for the routine cleaning and disinfection of environmental and other frequently touched surfaces.

8. Linens

Handle, transport, and process used linen in a manner which:

- prevents skin and mucous membrane exposures and contamination of clothing.
- avoids transfer of pathogens to other patients and or the environment.

9. Waste disposal

- Ensure safe waste management.
- Treat waste contaminated with blood, body fluids, secretions and excretions as clinical waste, in accordance with local regulations.
- Human tissues and laboratory waste that is directly associated with specimen processing should also be treated as clinical waste.
- Discard single use items properly.

10. Patient care equipment

- Handle equipment soiled with blood, body fluids, secretions, and excretions in a manner that prevents skin and mucous membrane exposures, contamination of clothing, and transfer of pathogens to other patients orthe environment.
- Clean, disinfect, and reprocess reusable equipment appropriately before use with another patient.

[1] For more details, see: WHO guidelines on hand hygiene in health care: (http://www.who.int/patientsafety/information_centre/ghhad_download/en/index.html).
[2] The SIGN Alliance: (http://www.who.int/injection_safety/sign/en/).
Source: WHO (*48*).

References

1. *Occupational and non-occupational post-exposure prophylaxis for HIV infection (HIV-PEP): Joint ILO/WHO Technical Meeting for the Development of Policy and Guidelines: summary report.* Geneva, World Health Organization, 2005 (http://www.who.int/entity/hiv/topics/arv/HIV-PEPflyer081606.pdf, accessed 28 November 2006).
2. Centers for Disease Control (CDC). Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for post exposure prophylaxis. *MMWR*, 2001, 50(RR-11):1–52.
3. Baggaley RF et al. Risk of HIV-1 transmission for parenteral exposure and blood transfusion: a systematic review and meta-analysis. *AIDS*, 2006, 20:805–812.
4. Ducel G, Fabry J, Nicolle L, eds. *Prevention of hospital-acquired infections: a practical guide*, 2nd ed. Geneva, World Health Organization, 2002 (http://www.who.int/csr/resources/publications/whocdscsreph200212.pdf, accessed 27 October 2006).
5. Centers for Disease Control and Prevention (CDC). Updated U.S. public health service guidelines for the management of occupational exposures to HIV and recommendations for postexposure prophylaxis. *MMWR*, 2005, 54(RR-9): 1–17 (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5409a1.htm, accessed 6 December 2006).
6. Cardo DM et al. A case-control study of HIV seroconversion in health care workers after percutaneous exposure. *The New England Journal of Medicine*, 1997, 337:1485–1490.
7. Wade NA et al. Abbreviated regimens of zidovudine prophylaxis and perinatal transmission of the human immunodeficiency virus. *The New England Journal of Medicine*, 1998, 339(20):1409–1414.
8. Taha TE et al. Short postexposure prophylaxis in newborn babies to reduce mother-to-child transmission of HIV-1: NVAZ randomised clinical trial. *The Lancet*, 2003, 362(9391):1171–1177.
9. Otten RA et al. Efficacy of postexposure prophylaxis after intravaginal exposure of pig-tailed macaques to a human-derived retrovirus (human immunodeficiency virus type 2). *Journal of Virology*, 2000, 74(20):9771–9775.
10. Van Rompay KK et al. Prophylactic and therapeutic benefits of short-term 9-[2-(R)-(phosphonomethoxy)propyl]adenine (PMPA) administration to newborn macaques following oral inoculation with simian immunodeficiency virus with reduced susceptibility to PMPA. *Journal of Virology*, 2000, 74(4):1767–1774.
11. Almeda J et al. Proposed recommendations for the management of HIV post-exposure prophylaxis after sexual, injecting drug or other exposures in Europe. *Euro Surveillance*, 2004, 9:35–40 (http://www.rki.de/cln_006/nn_334588/DE/Content/InfAZ/H/HIVAIDS/Prophylaxe/Leitlinien/non__occupational__exposure,templateId=raw,property=publicationFile.pdf/non_occupational_exposure, accessed 8 November 2006).
12. Preventing nosocomial infections. In: Tietjen L, Bossemeyer D, McIntosh N. *Infection prevention guidelines for healthcare facilities with limited resources.* JHPIEGO 2003 Baltimore, MD USA (http://www.reproline.jhu.edu/English/4morerh/4ip/IP_manual/20_Nosocomial.pdf, accessed 17 November 2006).
13. *HIV post-exposure prophylaxis: guidance from the UK Chief Medical Officers' Expert Advisory Group on AIDS*, February 2004 ed. London, United Kingdom Department of Health, 2004 (http://www.dh.gov.uk/assetRoot/04/08/36/40/04083640.pdf, accessed 29 November 2006).
14. Roland ME et al. HIV RNA testing in the context of nonoccupational postexposure prophylaxis. *The Journal of Infectious Diseases*, 2004, 190:598–604.
15. De Cock KM et al. Prevention of mother-to-child HIV transmission in resource-poor countries: translating research into policy and practice. *JAMA*, 2000, 283(9):1175–1182.
16. European Study Group on Heterosexual Transmission of HIV. Comparison of female to male and male to female transmission of HIV in 563 stable couples. *BMJ*, 1992, 304:809–813.
17. Varghese B et al. Reducing the risk of sexual HIV transmission: quantifying the per-act risk for HIV on the basis of choice of partner, sex act, and condom use. *Sexually Transmitted Diseases*, 2002, 29:38–43.
18. Bell DM. Occupational risk of human immunodeficiency virus infection in healthcare workers: an overview. *The American Journal of Medicine*, 1997, 102:9–15.
19. Ippolito G et al. Simultaneouas infection with HIV and hepatitis C virus following occupational conjunctival blood exposure. *JAMA*, 1998, 280(1):28.

20. Leynaert B, Downs AM, De Vincenzi I. Heterosexual transmission of HIV: variability of infectivity throughout the course of infection. *American Journal of Epidemiology,* 1998, 148:88–96..
21. Vittinghoff E et al. Per-contact risk of human immunodeficiency virus transmission between male sexual partners. *American Journal of Epidemiology*, 1999, 150(3):306–11.
22. Downs AM, De Vincenzi I. Probability of heterosexual transmission of HIV: relationship to the number of unprotected sexual contacts. European Study Group in Heterosexual Transmission of HIV. *Journal of Acquired Immune Deficiency Syndrome Human Retrovirology*, 1996, 11(4):388–95.
23. Louria DB et al. HIV heterosexual transmission: a hypothesis about an additional potential determinant. *International Journal of Infectious Diseases*, 2000:4(2):100–6.
24. Royce R et al. Sexual transmission of HIV. *New England Journal of Medicine*, 1997, 336(15):1072–8.
25. Busch MP, Satten GA. Time course of viremia and antibody seroconversion following human immunodeficiency virus exposure. T*he American Journal of Medicine,* 1997, 102(Suppl. 5B):117–124.
26. Rich JD et al. Misdiagnosis of HIV infection by HIV-1 plasma viral load testing: a case series. *Annals of Internal Medicine*, 1999, 130:37–39.
27. Quinn TC et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. *The New England Journal of Medicine, 2000*, 342:921–929
28. *Post exposure prophylaxis for HIV: guidelines and policies for the use of occupational and non-occupational post exposure prophylaxis (PEP) to human immunodeficiency Virus (HIV).* Geneva, World Health Organization, in press.
29. Kahn JO et al. Feasibility of postexposure prophylaxis (PEP) against human immunodeficiency virus infection after sexual or injection drug use exposure: the San Francisco PEP Study. *The Journal of Infectious Diseases*, 2001, 183(5):707–714.
30. Martin JN et al. Post-exposure prophylaxis (PEP) for sexual exposure to HIV does not lead to increases in high risk behavior: the San Francisco PEP Project. *8th Conference on Retroviruses and Opportunistic Infections, Chicago, 4–8 February 2001*.
31. Shih C-C et al. Postexposure prophylaxis with zidovudine suppresses human immunodeficiency virus type 1 infection in SCID-hu mice in a time-dependent manner. *The Journal of Infectious Diseases*, 1991, 163:625–627.
32. Tsai C-C et al. Prevention of SIV infection in macaques by (R)-9-(2-phosphonylmethoxypropyl) adenine. *Science*, 1995, 270:1197–1199.
33. Tsai C-C et al. Effectiveness of postinoculation (R)-9-(2-phosphonylmethoxypropyl) adenine treatment for prevention of persistent simian immunodeficiency virus SIV_{mne} infection depends critically on timing of initiation and duration of treatment. *The Journal of Virology*, 1998, 72:4265–4273.
34. Laporte A et al. Post-exposure prophylaxis after non-occupational HIV exposure: impact of recommendations on physicians' experiences and attitudes. *AIDS*, 2002, 16(3):397–405.
35. Bassett IV, Freedberg KA, Walensky RP. Two drugs or three? Balancing efficacy, toxicity, and resistance in postexposure prophylaxis for occupational exposure to HIV. *Clinical Infectious Diseases*, 2004, 39:395–401.
36. Johnson S et al. Adverse effects associated with use of nevirapine in HIV postexposure for 2 health care workers [letter]. *JAMA*, 2000, 284:2722–2723.
37. Centers for Disease Control (CDC). Serious adverse events attributed to nevirapine regimens for postexposure prophylaxis after HIV exposures: worldwide, 1997–2000. *MMWR*, 2001, 49:1153–1156.
38. Grabar S et al. Clinical outcome of patients with HIV-1 infection according to immunologic and virologic response after 6 months of highly active antiretroviral therapy. *Annals of Internal Medicine*, 2002, 133(6):401–10.
39. United States National Library of Medicine. MedlinePlus drug information: amprenavir [onlinde database]. Bethesda, MD, United States National Institutes of Health, 2005 (http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a699051.html, accessed 7 November 2006).
40. United States National Library of Medicine. MedlinePlus drug information: efavirenz [onlinde database]. Bethesda, MD, United States National Institutes of Health, 2006 (http://www.nlm.nih.gov/medlineplus/druginfo/medmaster/a699004.html, accessed 7 November 2006).
41. Ridzon R et al. Simultaneous transmission of human immunodeficiency virus and hepatitis C virus from a needle-stick injury. *The New England Journal of Medicine*, 1997, 336:919–922.
42. United Kingdom Department of Health. *HIV infected health care workers: guidance on management and patient notification*. London, Department of Health Publications, 2002 (http://www.dh.gov.uk/assetRoot/04/11/64/16/04116416.pdf, accessed 17 November 2006).

43. Lot F et al. Probable transmission of HIV from an orthopaedic surgeon to a patient in France. *Annals of Internal Medicine*, 1999, 130:1–6.
44. Ciesielski C et al. Transmission of human immunodeficiency virus in a dental practice. *Annals of Internal Medicine*, 1992, 116:798–805.
45. *Universal precautions, including injection safety.* Geneva, World Health Organization, (http://www.who.int/hiv/topics/precautions/universal/en, accessed 24 June 2006).
46. *Prevention of occupational exposure to HIV: Occupational Safety and Health Administration bloodborne pathogens standard.* Tallahassee, United States Occupational Safety and Health Administration (OSHA) (http://www.continuingeducation.com/nursing/hivexposure2/safety.html, accessed 29 November 2006).
47. Centers for Disease Control and Prevention (CDC). Guidelines for infection control in dental health-care settings: 2003. MMWR, 2003, 52(RR-17):1–61 (http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5217a1.htm, accessed 11 October 2006).
48. Epidemic and Pandemic Alert and Response. *Aide-memoire: infection control standard precautions in health care*. Geneva, World Health Organization, 2006 (http://www.who.int/csr/resources/publications/4EPR_AM2.pdf, accessed 27 October 2006).